

Spartan *'04 windows*

Tutorial and User's Guide



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Scope of this Guide

This guide provides a general reference for both Spartan'04 and the Essential Edition of Spartan'04 for Windows. Following a brief summary of “**What's New in Spartan'04**”, it is divided into 17 chapters grouped into three sections, along with several appendices.

Section I (Introduction, Chapter 1) introduces Spartan'04 as a tool for exploring organic, bioorganic, inorganic and organometallic chemistry by way of molecular mechanics and quantum chemical calculations, together with an array of graphical models for conveying the results of these calculations.

Section II (Getting Started, Chapters 2 to 7) describes the overall operating environment of Spartan'04 for Windows, and then provides an extensive set of “hands-on” tutorials. Most of the tutorials can be completed with the Essential Edition, and sections which can not be completed are marked as such. This section is the place to start for new users of the program, and should also be perused by users of previous versions of SPARTAN.

Section III (Features and Functions, Chapters 8 to 17) describes in detail the functions available from the menus and dialogs incorporated into the graphical user interface for Spartan'04. The focus is on graphical input and manipulation of structure, input of other required information, and text, spectral and graphical output resulting from molecular mechanics and quantum chemical calculations. This section is intended as a general reference to Spartan'04 for Windows.

What this guide *does not do* is document the “performance” and “cost” of the different molecular mechanics and quantum chemical models available in Spartan'04, or recommend specific models or combinations of models for use on “real” chemical problems. Neither does it show the utility of graphical models in presenting and interpreting the results of the calculations. These topics are covered in depth in “**A Guide to Molecular Mechanics and Quantum**

Chemical Calculations” available from Wavefunction, which also provides a collection of illustrative examples.

Appendices provide an overview of the program’s overall architecture as well as its present capabilities and limitations (**A**), a directory of functions under its menus (**B**), a listing of commonly-used options (**C**), a listing of units (**D**), NMR chemical shift standards (**E**), the proper citation for the program (**F**), instructions for installing the Cambridge Structural Database (**G**), directions for making databases from Spartan calculations (**H**) and directions for installing a network HASP (**I**). Several of these appendices are included as part of the program’s “On Line Help” facilities.

What's New in Spartan'04

Several significant capabilities have been introduced in Spartan'04, and promise to expand in the future.

- **NMR.** This is available for chemical shifts with Hartree-Fock models. Future development will implement coupling constants and to extend the overall capability to density functional models. Not available in Essential Edition.
- **Solvation via mixed quantum mechanics/molecular mechanics.** This allows not only calculation of the solvation energy but also the effect of the solvent on molecular properties. This is presently available for water as a solvent. Future development will extend this to other solvents. Not available in Essential Edition.
- **Spartan Molecular Database (SMD).** This is a database of calculated structures, energies and selected molecular properties. SMD presently comprises approximately 50,000 organic and main-group inorganic molecules, each of which is available at up to five different theoretical models: HF/3-21G, HF/6-31G*, EDF1/6-31G*, B3LYP/6-31G* and MP2/6-31G*. Additional models may also be added in the future. Database entries may either be used to directly replace structures built by or imported into Spartan, and may be accessed through substructure searches. SMD is expected to grow at 25%/year, and will soon include infrared, UV/vis and NMR spectra and to extend to transition-metal inorganic and organometallic compounds as well as transition states. EDF1/6-31G*, B3LYP/6-31G* and MP2/6-31G* entries not available in Essential Edition.
- **UV/vis Spectra.** This is presently limited to vertical excitation spectra based either on the difference in energy between Hartree-

Fock and CIS models or between density functional (local, BP, EDF1, BLYP and B3LYP functionals) and time-dependent density functional (TDDFT) models. Not available in Essential Edition.

- **Import of two-dimensional structures.** Input of SDF, TGF and SKC files and automatic conversion into 3D geometries.
- **Intrinsic Reaction Coordinate.** This constructs a series of steps which smoothly follow the reaction coordinate from the transition state to both reactants and products. Not available for semi-empirical models. Not available in Essential Edition.

A number of additional important improvements and enhancements are implemented in Spartan'04.

- Use of NOE data in conformational searching.
- Display of hydrogen bonds.
- Plotting of infrared spectra.
- Inversion of a chiral center.
- Control over animation speed.
- Tube and Ball-and-Spoke models (optionally) showing multiple bonds.
- Automatic centering of molecules on screen.
- Help functions in individual dialogs.

Spartan'04 is generally faster than Spartan'02 due to improved compilers. Some specific calculations, e.g., frequencies using density functional models, have been reworked and are significantly faster.

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Section I

Introduction

Molecular mechanics calculations and quantum chemical calculations play an ever-increasing role in modern chemistry. Traditionally, they have served to supply information about structures, relative stabilities and other properties of isolated molecules. Because of their inherent simplicity, molecular mechanics calculations on complex molecules have spread widely throughout the chemical community. Quantum chemical calculations, including Hartree-Fock molecular orbital calculations, but especially calculations which take account of electron correlation, are much more time demanding. Only recently, have fast enough computers become widely available to make their application routine among mainstream chemists.

Quantum chemical calculations may also be called on to furnish information about the mechanisms and product distributions of chemical reactions, either directly by calculations on transition states, or indirectly by modeling the steric and electronic demands of the reactants. Quantitative calculations, leading directly to information about the geometries of transition states, and about reaction mechanisms in general, are becoming more and more common, while qualitative models are still needed for systems which are too large to be subjected to the more rigorous treatments. Finally, quantum chemical calculations may be asked to supply information to complement existing experimental data or to replace it altogether, for example, atomic charges for QSAR analyses, and intermolecular potentials for molecular mechanics and molecular dynamics calculations.

Spartan'04 for Windows has been designed to address the ever increasing role which calculations play in chemistry and related fields. It represents a continued collaboration between Wavefunction, Inc., and Q-Chem, Inc. Q-Chem codes supplement and extend the traditional strengths of SPARTAN as an easy to learn and use tool for

molecular mechanics and semi-empirical and Hartree-Fock molecular orbital calculations, as well as for a wide range of graphical models, with a full range of density functional models as well as a selection of important post-Hartree-Fock models. All models have been implemented using what we believe are the most robust algorithms currently available, and have been especially tuned for high performance on Intel processors.

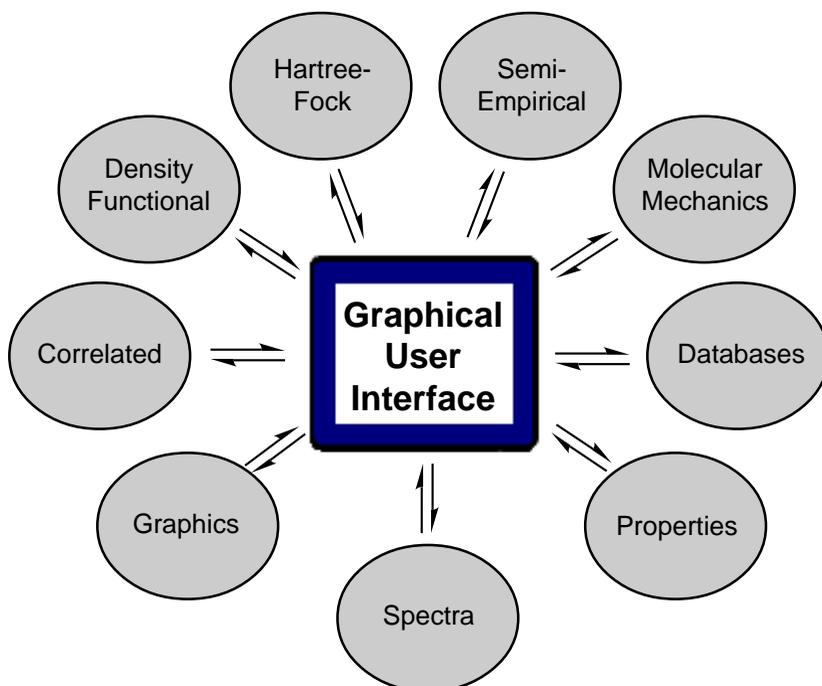
Spartan'04 *is intended to be utilized by chemists*, not only computational chemists who are already familiar with the capabilities of molecular mechanics and quantum chemical methods, but also experimental chemists who may have little or no prior experience, but who want to use calculations much in the same way as experimental techniques such as NMR spectroscopy. This ambitious goal is directly reflected in the program's overall design criteria: "convenient access to a full range of modern molecular mechanics and quantum chemical models", and clearly distinguishes Spartan'04 from other molecular modeling packages.

Chapter 1

Spartan'04 for Windows

This chapter provides a brief discussion of the architecture of Spartan'04 for Windows, focusing on the connectivity of graphics, database and computational components. Available molecular mechanics and quantum chemical methods are enumerated, and their overall role suggested.

Spartan'04 for Windows comprises a series of independent modules tightly connected via a graphical user interface, which is highly functional yet rather simple and uncluttered. It has been designed not only to greatly reduce the drudgery and possibility of human error associated with the preparation of input, but also to guide the interpretation of output. The interface is perhaps best viewed as an interactive and intuitive window into a full range of modern computational techniques.



Included in the interface are builders for organic, inorganic and organometallic molecules, polypeptides and polynucleotides, as well as a procedure for guessing transition states from a database of organic and organometallic reactions. Also included is the Spartan Molecular Database, a collection of over 50,000 calculated structures for organic and main-group inorganic molecules, each obtained from as many as five different theoretical models, as well as an interface to the Cambridge Structural Database, comprising over 300,000 experimental X-ray crystal structures for organic and organometallic molecules*. Finally, Spartan allows for import of a variety of “external” data files, most important among them being PDB (protein structures) and SDF (structure drawings). Thus, it is not only possible to construct molecules “from scratch”, but also to access a wide variety of existing structures.

Spartan’s interface also provides the gateway into a range of modern computational methods, including molecular mechanics models, semi-empirical and Hartree-Fock molecular orbital models, and a variety of so-called correlated models including density functional models. None of these models is “ideal” for every application**. While the most sophisticated quantum chemical models may yield excellent results, they will be likely be too expensive for routine application, and it will usually be necessary to contend with lesser treatments. Spartan’s interface facilitates “mixing and matching” different molecular mechanics and quantum-chemical models. Results from one model may easily be passed on for further analysis with another (better) model.

* The Cambridge Structural Database itself is not included with Spartan’04, but rather is available on a subscription basis from the Cambridge Crystallographic Data Centre or one of its distributors. Contact Wavefunction for information.

** Full discussion and assessment of the specific molecular mechanics and quantum chemical models available in Spartan’04 is provided in: W.J. Hehre, **A Guide to Molecular Mechanics and Quantum Chemical Calculations**, Wavefunction, Irvine, 2003. See also: W.J. Hehre, L. Radom, P.v.R. Schleyer and J.A. Pople, *Ab Initio Molecular Orbital Theory*, Wiley, New York, 1986; J. Kong, C.A. White, A.I. Krylov, C.D. Sherrill, R.D. Adamson, T.R. Furlani, M.S. Lee, A.M. Lee, S.R. Gwaltney, T.R. Adams, C. Ochsenfeld, A.T.B. Gilbert, G.S. Kedziora, V.A. Rassolov, D.R. Maurice, N. Nair, Y. Shao, N.A. Besley, P.E. Maslen, J.P. Dombroski, H. Daschel, W. Zhang, P.P. Korambath, J. Baker, E.F.C. Byrd, T. Van Voorhis, M. Oumi, S. Hirata, C.-P. Hsu, N. Ishikawa, J. Florian, A. Warshel, B.G. Johnson, P.M.W. Gill, M. Head-Gordon and J.A. Pople, *J. Computational Chem.*, **21**, 1532 (2000).

The simplest computational methods in Spartan'04 are molecular mechanics models using the SYBYL and MMFF94 force fields. These are applicable to the determination of equilibrium geometries and conformations of molecules comprising upwards of several thousand atoms. Molecular mechanics models are at present the only computational techniques which are applicable to biopolymers including proteins. Very large molecule calculations and conformational analysis on smaller molecules, including both assignment of lowest-energy conformer and identification of collections of “reasonable” low-energy conformers, are perhaps the most important role of molecular mechanics.

Quantum chemical models are required to account for the geometries of transition states as well as to obtain reaction energies (thermodynamics) and activation energies (kinetics). The simplest of these are semi-empirical molecular orbital models, which can be routinely applied to systems with one to two hundred atoms. Supported in Spartan'04 are the MNDO model (with “d” extensions for second-row and heavier main-group elements), the AM1 model, and the PM3 model with parameters for most transition metals.

Hartree-Fock molecular orbital models remain a mainstay of quantum chemical techniques, in particular, for equilibrium and transition-state structure determination, and for thermochemical comparisons. The models available in Spartan'04 may be routinely applied to molecules with fifty to one hundred atoms, that is, typical “real” organic molecules.

Hartree-Fock models are, however, not adequate for thermochemical comparisons where bonds are broken or formed, nor do they provide a proper account of the geometries of molecules incorporating transition metals. So-called correlated models are required. Several classes of correlated models are available in Spartan'04*: density functional models, Møller-Plesset models and coupled cluster models. Density functional models may be applied as widely as Hartree-Fock models. On the other hand, the simplest Møller-Plesset model (MP2) is limited to molecules comprising thirty or fewer atoms. An approximate “local

* Not available in the Essential Edition.

MP2” model, based on localized orbitals is available in Spartan’04. It is less “costly” than MP2 and applicable to larger systems, but is still significantly more expensive than either Hartree-Fock or density functional models. Higher-order (MP3 and MP4) Møller-Plesset models and coupled cluster models are even more expensive computationally and, therefore, much more limited in their application. Density functional models and MP2 models may be used for equilibrium and transition-state structure determination as well as energy calculations. The local MP2 model and higher-order correlated methods are available only for energy calculations.

Hartree-Fock and correlated models may be used with a variety of all-electron Gaussian basis sets. Hartree-Fock models are often quite successful with minimal and split-valence basis sets, while correlated models require at the very least polarization basis sets, and in some situations basis sets incorporating diffuse functions as well. Pseudopotentials are available for use with both Hartree-Fock and correlated models for calculations on molecules incorporating heavy elements.*

G3 and G3(MP2) energy calculations are also available in Spartan’04.* While applicable at present only to very small systems, these “procedures”, which are in fact made up of a combination of different models, have been shown to yield reaction energies in excellent accord with experiment and, therefore, provide “benchmarks” against which other calculations may be judged.

The majority of quantum chemical calculations have previously been performed on molecules in their electronic ground state. Only very recently have practical and reliable methods for excited-state species become available. Spartan’04 provides “singles” configuration interaction (CI) techniques* for energies, equilibrium and transition-state geometries and conformations. In addition, energy calculations (only) on excited states with the CIS (D) model as well as a range of density functional models*, may be performed.*

* Not available in the Essential Edition.

Spartan provides access to several common spectral quantities, in particular infrared spectra (molecular mechanics, semi-empirical, Hartree-Fock, density functional and MP2 models), NMR spectra* (Hartree-Fock models) and UV/vis spectra* (CIS, CIS(D) and density functional models). These are available both as numerical data (vibrational frequencies, chemical shifts, etc.) as well as spectral plots where appropriate.

Finally, Spartan'04 provides a variety of “visual tools” to assist chemists in interpreting the results of molecular mechanics and quantum chemical calculations. Not only do these include the usual variety of structure models, including structure models appropriate for biopolymers, but also molecular orbitals, electron and spin densities, local ionization potentials and electrostatic potentials which can be displayed as surfaces, slices and property maps and manipulated in real time. As many quantities as desired can be displayed simultaneously, and visual comparisons easily made among them both for single molecules and among different molecules. “Movies” may be made, based either on structural models alone or in combination with any graphical models, and these in turn are used to depict conformational change or chemical reaction.

* Not available in the Essential Edition.

Section II

Getting Started

The chapters in this section provide a brief introduction to the graphical user interface for Spartan'04 for Windows and, following this, a series of simple tutorials. The objective of the latter is both to provide “hands on” experience and, in doing so, illustrate the way in which molecular mechanics and quantum chemical calculations may be set up, performed and interpreted. This is the place to start for “new users”. Users of previous versions of SPARTAN are also advised to peruse this section.

No attempt has been made to illustrate all available program options. For this, the reader should consult **Section III** of this guide. Focus is on the use of Spartan'04 to calculate equilibrium and transition-state geometries, to search conformation space, to evaluate reaction thermochemistry and activation energetics and to obtain infrared and NMR spectra. Also no attempt has been made to assess the performance of the various molecular mechanics and quantum chemical models. In fact, the majority of tutorials make use only of molecular mechanics models and semi-empirical and Hartree-Fock molecular orbital models, which in some cases may not lead to “acceptable results”.^{*} Thorough assessment of all models available in Spartan'04 is provided in “**A Guide to Molecular Mechanics and Quantum Chemical Calculations**”.

Graphical models are illustrated in several of the tutorials which follow, and connections between specific models and chemical observables are pointed out, for example, between electrostatic potential maps and electrophilic character. A more complete account

* This is a deliberate decision, in that it “minimizes” the time required to complete the tutorials and allows nearly all tutorials to be completed using only the Essential Edition of Spartan'04 (which lacks density functional, MP2 and other correlated calculations). Tutorials or sections of tutorials which cannot be completed with the Essential Edition are indicated as such.

is provided in the aforementioned guide. Spartan'04 for Windows provides greatly enhanced capabilities over previous versions for display and manipulation of structure models for biopolymers, and these too are illustrated.

Operating Spartan'04 outlines the basic workings of Spartan'04's graphical user interface. It should be perused before starting the tutorials and referred back to as needed. The tutorials, which make up the bulk of this section, are divided across five chapters: *Organic Molecules*, *Groups of Organic Molecules*, *Organic Reactions*, *Biologically Interesting Molecules* and *Inorganic/Organometallic Molecules*. The first two of these cover a number of "basic" operations and should be completed first, and in that order. The remaining chapters cover more specialized topics.

Estimates for required computer time (in minutes, assuming a 2GHz P4) are indicated at the top of the first page of each tutorial.



5 mins

Where two times are provided, the second corresponds to the total time including the optional part. No times are provided where no actual calculations are to be performed.

Chapter 2

Operating Spartan'04

This chapter describes the general operating features of Spartan'04 for Windows. It should be read prior to starting the tutorial.

Starting and Quitting Spartan'04

To start, *click* on the **Start** button, then *click* on **Programs**, and finally *click* on **Spartan'04**. To quit, select **Exit** from the **File** menu.

Pull-Down Menus

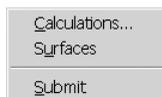
Program functions may be accessed using pull-down menus under the headings in the menu bar, e.g., the **Setup** menu.



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

Keystroke Equivalents

Keystroke equivalents for menus are designated by the underlined letter: **File**, **Edit**, **Model**, **Geometry**, **Build**, **Setup**, **Display**, **Search**, **Options** and **Help**. To access a menu, *press* the **Alt** key and the appropriate letter key (case insensitive), e.g., **Alt "S"** to access the **Setup** menu.



Each menu entry is designated by an underlined letter. To access the entry, *press* the appropriate letter key, e.g., *press* the **C** key to access the **Calculations** dialog.

Toolbars

Toolbars provide convenient access to selected functions under the **File, Build, Geometry and Search** menus.

 New	 Break Bond	 Constrain Angle
 Open	 Minimize	 Constrain Dihedral
 Close	 Measure Distance	 Define Point
 Save As	 Measure Angle	 Define Plane
 View	 Measure Dihedral	 Align Molecules
 Add Fragment	 Freeze Center	 Databases
 Delete	 Set Torsions	 Transition States
 Make Bond	 Constrain Distance	 Tautomers

If desired, one or more toolbars can be removed from view using functions under the **Options** menu (see **Chapter 16**).

Using the Mouse

The following functions are associated with the two-button mouse.

keyboard	button	
	left	right
–	picking, X/Y rotate, exchange ^a	X/Y translate
Shift	range picking, Z rotate	scaling ^b
Ctrl	global X/Y rotate ^c	global X/Y translate
Ctrl + Shift	multiple picking, global Z rotate ^c	scaling ^b
Ctrl (build mode)	fragment X/Y rotate, chirality invert ^a	fragment X/Y translate
Ctrl + Shift (build mode)	fragment Z rotate	scaling ^b
Alt	group picking, bond rotation	bond stretching

a) Requires *double clicking*.
b) Scaling is always applied to all open molecules and all fragments.
c) Global rotations can be either molecule or screen centered. This is controlled by **Global Rotate** in the **Miscellaneous Preferences** dialog (**Preferences...** under **Options** menu).

Mouse/keyboard operations may be broadly separated into two categories: selection (picking) and manipulation (translation/rotation).

Selection. The left button is used for picking of objects on screen and/or of menu items. Left and right buttons together are used to define a selection box for copying/cutting to the clipboard, as well as for multiple model selection. Together with the **Shift** key, the left button allows for picking over a range. Together with the **Ctrl (Control)** key, the left button allows for multiple picking. Both range and multiple picking applies not only to text items in lists, but to atoms and bonds in molecules as well. Together with the **Alt** key, the left button allows for selection of an entire group (detached molecular fragment). In build mode, *double clicking* the left button leads to atom or group exchange while *double clicking* on an atom with the **Ctrl** key depressed leads to inversion in chirality.

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, the left mouse button gives rise to rotation about the X and Y (screen) axes; the right mouse button gives rise to translation in the X and Y (screen) directions. Together with the **Shift** key, the left mouse button gives rise to rotation about the Z direction and the right mouse button gives rise to 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 “build 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 “build mode”, the default is focus on the full set of fragments which 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.

Use of the **Alt** key in addition to the left mouse button allows for rotation about a selected bond and, in addition to the right mouse button, for stretching of the selected bond.

Keyboard Functions

Additional keys control various Spartan'04 functions. These are enumerated below:

3	Shifts into 3D (stereo). Pressing 3 again returns to non-stereo display.
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	In build 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 <i>clicking</i> on screen. One-time fragment insertion can also be accomplished by <i>clicking</i> on the Insert button at the bottom of the model kit prior to <i>clicking</i> on screen. See “Entry Model kit” in Chapter 12 .
Delete	Allows deletion of a fragment, a free valence, reaction arrow, the contents of a selection box, a spectrum, a curve or a plot. Deletion is accomplished by holding down the Delete key and <i>clicking</i> on the fragment, etc. No warnings are provided. Deletion may also be invoked by selecting Delete from the Build menu or by <i>clicking</i> on the  icon, prior to <i>clicking</i> on the fragment, etc.

Selecting Molecules, etc.

Two or more molecules may be simultaneously displayed in Spartan'04's window. However, only one molecule may be selected. The selected molecule has access to all capabilities (molecule building, job setup and submission and text and graphical display and manipulation), while non-selected molecules may only be displayed as static images. The exceptions involve scaling and the use of the **Ctrl** key.

Selection of a molecule occurs by *clicking* on its structure model or on any of its associated graphical surfaces. This results in deselection of the previously selected molecule. Molecular properties for the selected molecule are available in the **Properties** dialog (**Display** menu). Atom, bond and surface display properties, as well as information about geometrical constraints may be accessed by subsequent *clicking* on an atom, bond, graphical display, or constraint marker respectively, associated with the selected molecule. Selected atoms, bonds and constraint markers are highlighted (colored gold). *Clicking* on the selected atom, bond or constraint marker resets the display to molecular properties. *Clicking* on another molecule results in display of molecular properties for that molecule. Information about plots (including spectra) and changes to plot style and range are also available from this dialog.

Where the molecule belongs to a list with more than a single member, selection from among the different members in the list may be made using either the  and  buttons or the scroll bar at the bottom left of the screen. Alternatively, if the spreadsheet for the list is open on screen (see **Chapter 14**), selection can be made by *clicking* on the name of the desired molecule at the left of the spreadsheet. *Clicking* on  at the bottom left of the screen “animates” the display of molecules in the list, that is, steps through them sequentially. This is useful for displaying a progression of graphical surfaces along a reaction coordinate. *Clicking* on  (which replaces ) stops the animation.

Two or more molecules from the same list may be displayed at once (although only one may be selected). Molecules are marked for display by *checking* the box immediately to the right of the molecule name in the spreadsheet (**Chapter 14**).

Dialogs

Dialogs are either “modal” (as indicated by “...” following their reference in a menu) or “non-modal”. Modal dialogs (**Open**, **Save As**, **Append Molecule(s)**, **Print** and **Print Setup** from the **File** menu, **Find** from the **Edit** menu, **Configure** from the **Model** menu, **Calculations** from the **Setup** menu, **Plots** from the **Display** menu

and **About**, **Preferences** and **Fonts** from the **Options** menu) need to be dismissed before program operation can continue, while non-modal dialogs may be kept open on screen. Non-modal dialogs fall into two categories: those which reference the selected molecule (or list of molecules) and those which reference a specific molecule (or list of molecules). Only one copy of each of the former may be open on screen, while several copies of the latter (each copy referring to a different molecule or list of molecules) may be open on screen. **Properties**, **Surfaces** and **Spectra** exemplify dialogs which refer to the selected molecule, while **Output** and **Spreadsheet** exemplify dialogs which refer to a specific molecule.

3-Dimensional Displays

Any object displayed on Spartan'04's screen may be rendered in 3D (stereo) using color filtration techniques. "Red/blue" glasses (supplied with Spartan'04) must be worn. 3D is turned "on" and "off" by toggling the "3" key, or by *checking Stereo* in the **Miscellaneous Preferences** dialog under the **Options** menu (**Chapter 16**).

Changing Colors and Setting Preferences

Colors and **Preferences...** under the **Options** menu (**Chapter 16**) allows for changing default background and graphical object colors, and for setting (and resetting) program defaults, respectively. Further control of color is discussed in **Chapter 14**.

Monitoring and Killing Jobs

Monitor under the **Options** menu (**Chapter 16**) allows for monitoring of executing jobs as well as for killing jobs.

Iconifying Spartan'04

Spartan'04 may be iconified by *clicking* on "☐" at the top right of the screen. A small icon appears at the bottom of the screen.



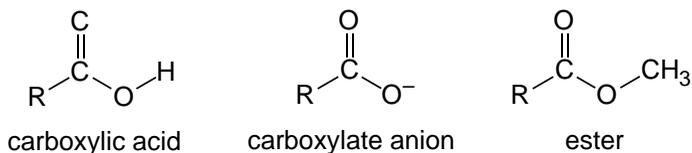
Clicking on this icon returns the user to Spartan'04.

Chapter 3

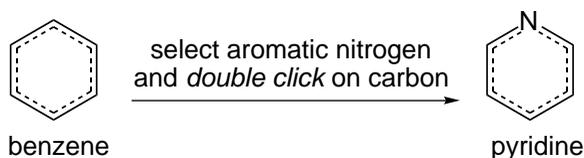
Organic Molecules

This chapter shows how to construct organic molecules from atomic fragments, functional groups and rings, how to carry out quantum chemical calculations, how to calculate and draw infrared and NMR spectra and how to interpret graphical models. It also illustrates use of the Spartan Molecular Database of calculated structures, energies and molecular properties as well as Spartan'04's interface to the Cambridge Structural Database.

The simplest building blocks incorporated into Spartan'04's entry model kit are "atomic fragments". These constitute specification of atom type, e.g., carbon, and local environment, e.g., tetrahedral. However, much of organic chemistry is organized around functional groups, collections of atoms the structure and properties of which are roughly the same in every molecule. The entry model kit also incorporates a small library of functional groups which can easily be extended or modified. For example, the carboxylic acid group may be modified to build a carboxylate anion (by deleting a free valence from oxygen), or an ester (by adding tetrahedral carbon to the free valence at oxygen).



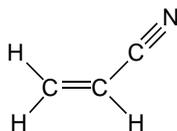
Polyatomic rings are also common components in organic molecules, and the entry model kit incorporates a library of commonly-encountered hydrocarbon rings, which can easily be modified by atom replacement. For example, pyridine can be built starting from benzene by selecting aromatic nitrogen from the list of atomic fragments, and then *double clicking* on one of the carbons.



Functional groups may also be modified in this manner.

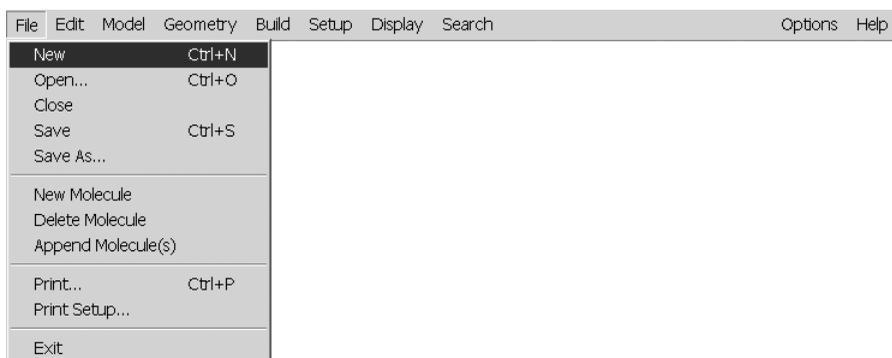
The tutorials in this chapter illustrate construction of organic molecules using atomic fragments, functional groups and rings. They also illustrate the way in which quantum chemical calculations are set up, their results examined and interpreted, and infrared and NMR spectra computed and displayed. A variety of graphical models are introduced and illustrated. Finally, examples of the use of the Spartan Molecular Database of calculated molecular structures, energies and properties and of the Cambridge Structural Database of experimental X-ray crystal structures are provided.

Acrylonitrile

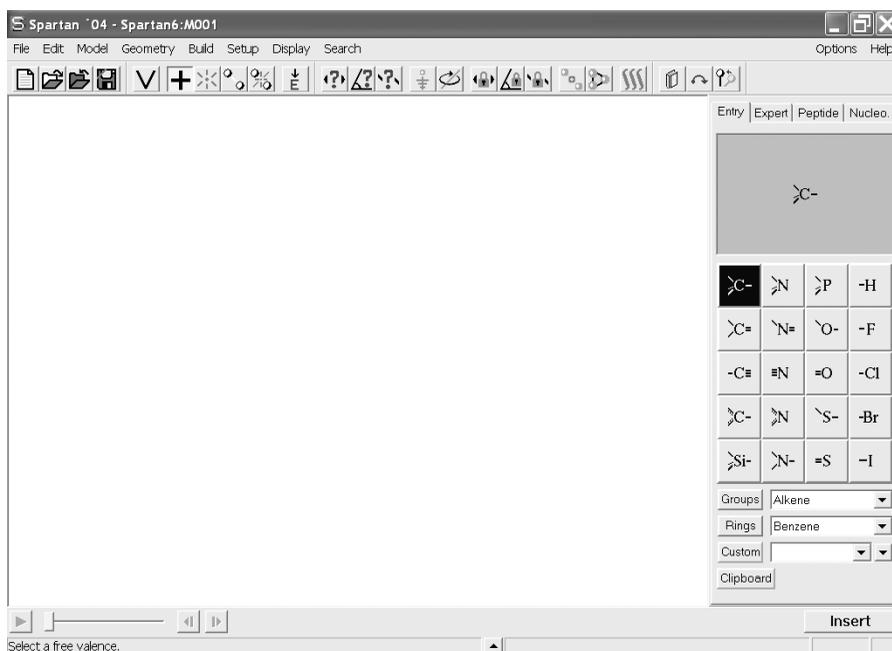


Acrylonitrile provides a good opportunity to illustrate the basics of molecule building in Spartan'04, as well as the steps involved in carrying out and analyzing a quantum chemical calculation.

1. *Click* with the left mouse button on **File** from the menu bar.



Then *click* on **New** from the menu which appears (or *click* on the  icon in the **File** toolbar). The “entry” model kit appears.



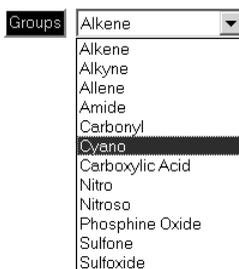
Among other things, it contains a library of atomic fragments. *Click* on trigonal planar sp^2 hybridized carbon  from the fragment library. The atom icon is shown in reverse video to indicate that it is “active”. In addition, a model of the fragment appears at the top of the model kit. Bring the cursor anywhere on screen and *click*. Rotate the carbon fragment (*drag* the mouse while holding down the left button) so that you can clearly see both the double free valence (“=”) and the two single free valences (“-”).

Spartan’04’s model kits connect atomic fragments (as well as groups, rings and ligands) through free valences. Any remaining free valences will automatically be converted to hydrogen atoms.

- 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. If you make a mistake and *click* instead on the single free valence, select **Undo** from the **Edit** menu. You can also start over by selecting **Clear** from the **Edit** menu.

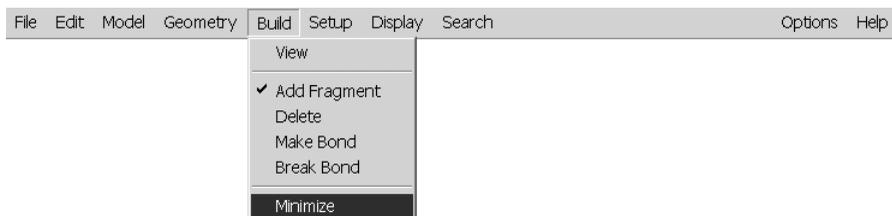
Spartan’04’s entry model kit allows only the same type of free valences to be connected, e.g., single to single, double to double, etc.

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



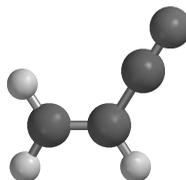
Click on any of the four single free valences on ethylene (they are all the same). This bonds the cyano group to ethylene, leaving you with acrylonitrile.*

4. Select **Minimize** from the **Build** menu (or *click* on the  icon in the **Build** toolbar).



The final molecular mechanics strain energy (8.65 kcal/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 in the **Build** toolbar). The model kit disappears, leaving only a ball-and-spoke model of acrylonitrile on screen.



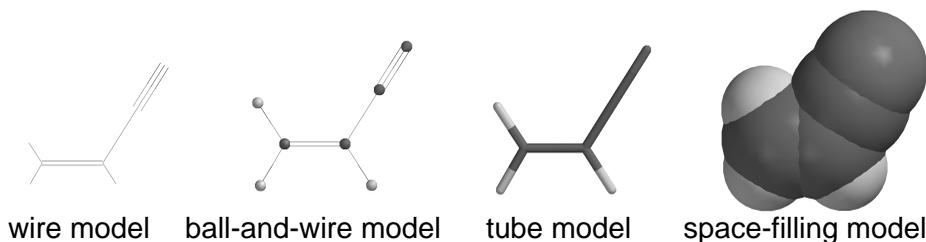
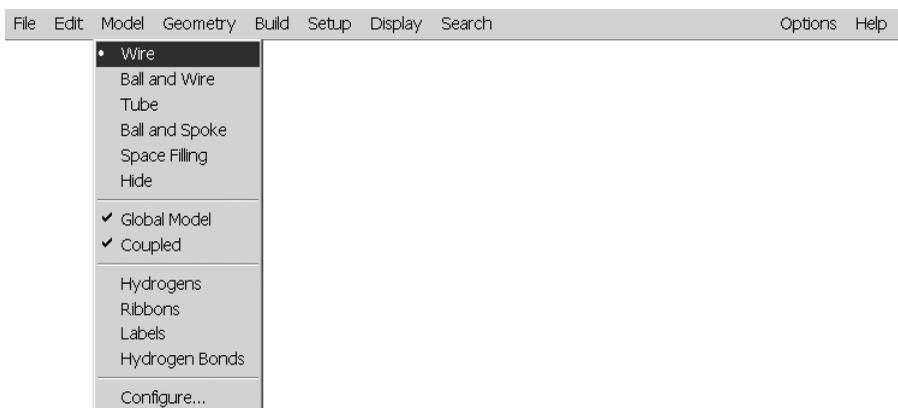
ball-and-spoke model

This model can be manipulated (rotated, translated and zoomed) by using the mouse (if necessary, 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

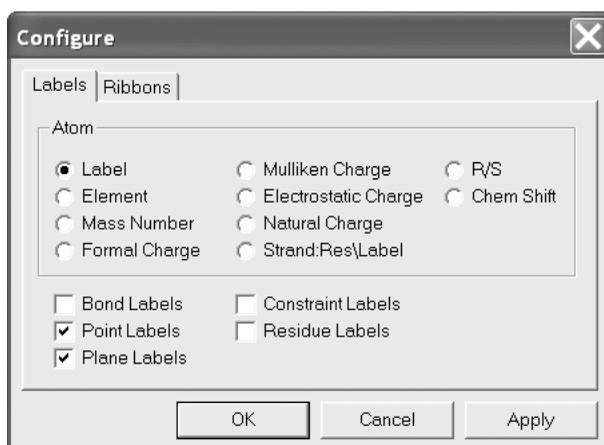
* You could also have built acrylonitrile without using the **Groups** menu. Starting from scratch (**Clear** from the **Edit** menu), first build ethylene as above, then select sp hybridized carbon  from the model kit and then *click* on one of the free valences on ethylene. Next, select sp hybridized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

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), hold down the **Shift** key in addition to the right button while *dragging* the mouse.

6. One after the other, select **Wire**, then **Ball and Wire**, then **Tube** and finally **Space Filling** from the **Model** menu.

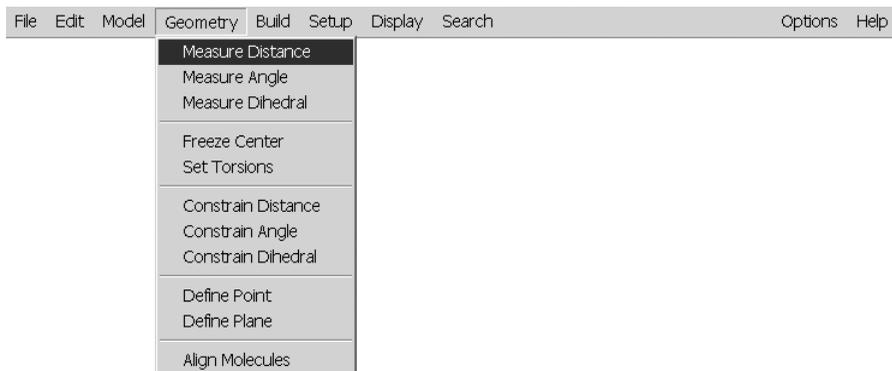


7. Return to a tube or ball-and-spoke model. Select **Configure...** from the **Model** menu, and *check Label* under “Atom” in the **Configure** dialog which appears.



Click on **OK** to remove the dialog. Numbers will appear next to the individual atoms together with atomic symbols. Remove the atom labels by selecting **Labels** from the **Model** menu.*

8. Select **Measure Distance** from the **Geometry** menu (or click on the  icon in the **Geometry** toolbar).



A message will appear at the bottom left of the screen.

Select two atoms, a bond,...

Click on two atoms, e.g., the two carbons involved in the double bond. Each atom will be colored gold, and the distance between the two will be displayed at the bottom right of the screen.

Distance(C1,C2) = 1.339 Å 

Where the two atoms are bonded, an alternative is to click on the bond. In this case, the bond will be colored gold. Another distance may be obtained by selecting another pair of atoms (or another bond), and so forth.

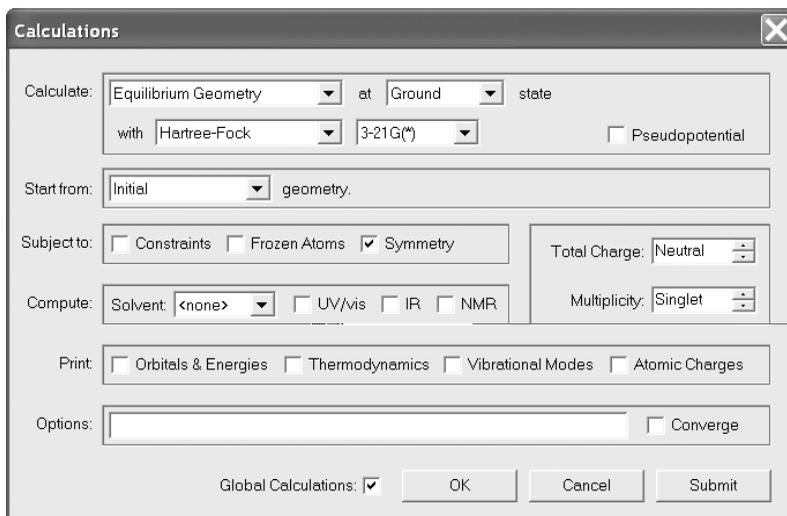
Measure Angle and **Measure Dihedral** from the **Geometry** menu ( and  icons from the **Geometry** toolbar) operate in a similar manner. In the former case, you will need to identify three atoms or two bonds, and in the latter case, you will need to identify four atoms or three bonds. When you are done, click on .

* **Labels** from the **Model** menu was automatically selected (turned “on”) following exit from the **Configure** dialog with **OK** or **Apply**.

9. Select **Calculations...** from the **Setup** menu.



Perform the following operations in the **Calculations** dialog which appears.



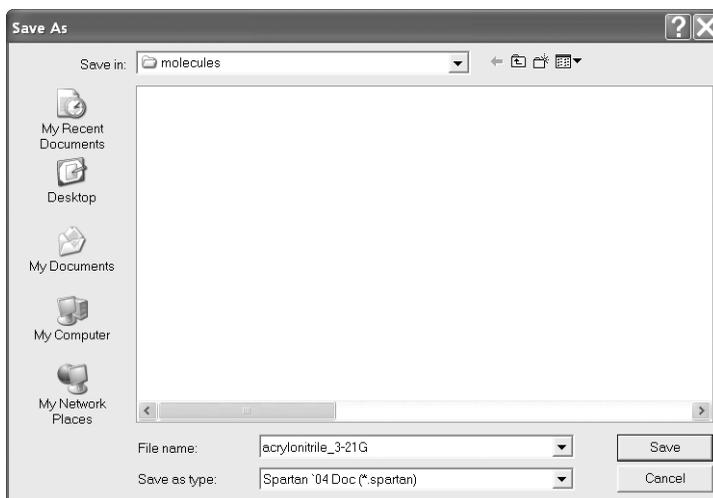
- Select **Equilibrium Geometry** from the top menu to the right of “Calculate”. This specifies optimization of equilibrium geometry.
- Select **Hartree-Fock** and then **3-21G(*)** from the two bottom menus to the right of “Calculate”. This specifies a Hartree-Fock calculation using the 3-21G split-valence basis set.*

When you finish, *click* on **OK** to remove the dialog.

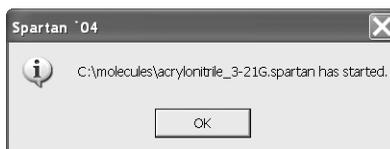
10. Select **Submit** from the **Setup** menu.** A file browser appears.

* 3-21G(*) indicates that the 3-21G basis set is to include polarization type functions on second-row and heavier, main-group elements. Polarization functions are not provided for hydrogen or first-row elements. For a discussion of basis sets supported by Spartan'04, see “**A Guide to Molecular Mechanics and Quantum Chemical Calculations**”.

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



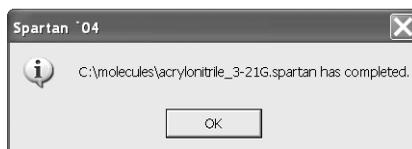
Type the name “acrylonitrile_3-21G” in the box to the right of “File name”, and then *click* on **Save**.* You will be notified that the calculation has been submitted.



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

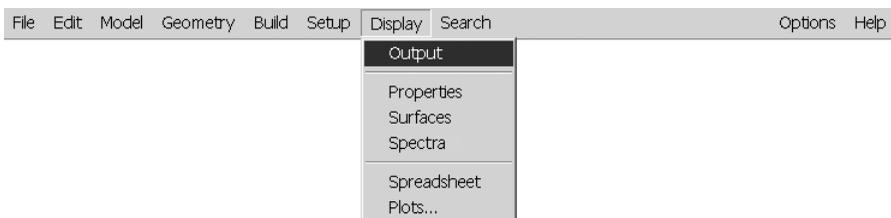
After a molecule has been submitted, and until the calculation has completed, you are not permitted to modify any dialogs or other information associated with it.

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

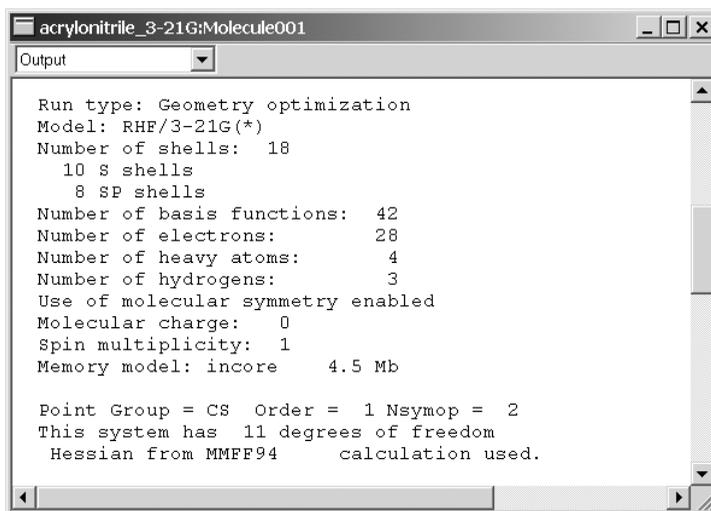


Click on **OK** to remove the message from the screen. Select **Output** from the **Display** menu.

* You can use default names (spartan1, spartan2, . . .) simply by *clicking* on **Save**.



A window containing “text output” for the job appears.



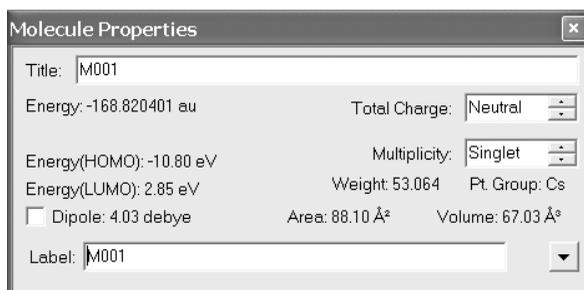
You can scan the output from the Hartree-Fock calculation by using the scroll bar at the right of the window. The information at the “top” of the dialog includes the task, basis set, number of electrons, charge and multiplicity, as well as further details of the calculation. Below this is the symmetry point group of the molecule that was maintained during the optimization.

Eventually, a series of lines appear, each beginning with “Cycle no:”. These tell the history of the optimization process. Each line provides results for a particular geometry; “Energy” gives the energy in atomic units (1 atomic unit = 627.5 kcal/mol = 2625 kJ/mol) for this geometry, “Max Grad.” gives the maximum Cartesian gradient, and “Max Dist.” gives the maximum displacement of atoms between cycles. “Neg. Eigen.” reports the number of negative eigenvalues uncovered in the optimization procedure. This column should be blank

(0) at the end of a geometry optimization. Ideally, the energy will monotonically approach a minimum value for an optimized geometry, and Max Grad. and Max Dist. will each approach zero. If the geometry was not optimized satisfactorily an error message, such as: “Optimization has exceeded N steps – Stop”, will be displayed following the last optimization cycle. You would then have been notified that the job had failed.

Near the end of the output are the final total energy (-168.82040 atomic units for acrylonitrile with the 3-21G basis set), and the computation time. *Click* on  in the top right-hand corner of the dialog to remove the dialog from the screen.

You may examine the final total energy and the dipole moment (among other properties) without having to go through the text output. Select **Properties** from the **Display** menu. The **Molecule Properties** dialog appears.

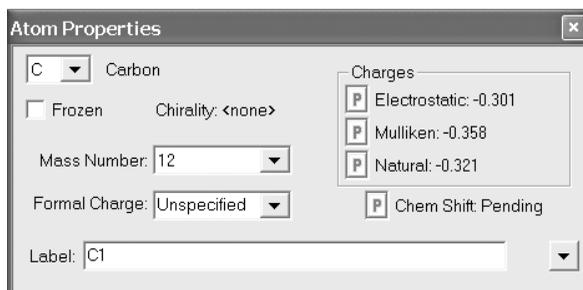


To see the dipole moment vector (indicating the sign and direction of the dipole moment), *check* the box to the left of **Dipole**. (A tube model is best for this display.)



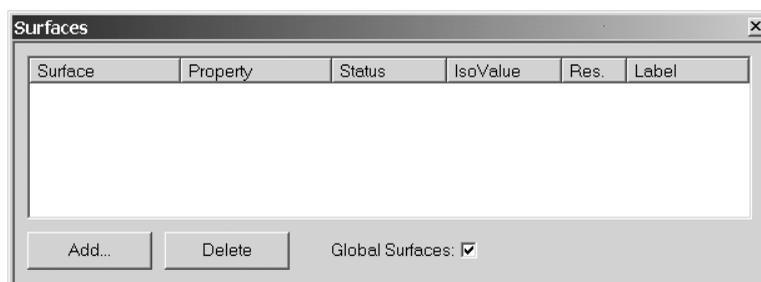
When you are done, turn “off” display of the dipole moment vector by *unchecking* the box.

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

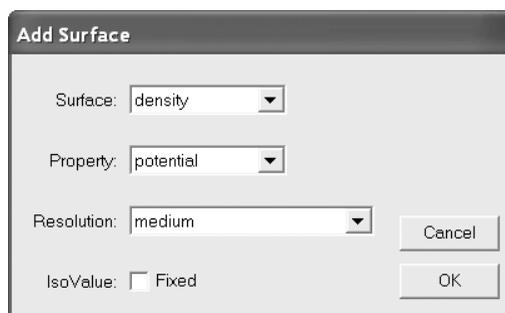


Among other things, this provides three different sets of atomic charges: “Electrostatic”, “Mulliken” and “Natural”. To obtain the charge on another atom, simply click on it. Inspect all the atomic charges on acrylonitrile (by *clicking* on the appropriate atoms). When you are done, *click* on **✕** at the top right of the **Atom Properties** dialog to remove it from the screen.

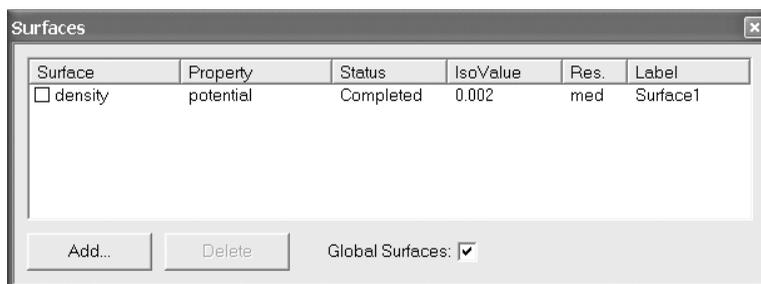
12. Select **Surfaces** from either the **Setup** or **Display** menu.



Click on **Add...** (at the bottom of the dialog) to bring up the **Add Surface** dialog.



Select **density** from the **Surface** menu and **potential** from the **Property** menu.* This requests an electrostatic potential map (an electron density surface onto which the value of the electrostatic potential has been mapped). *Click* on **OK**. A line “density potential . . .” appears at the top of the dialog. (If you make a mistake, *click* on this line and then *click* on **Delete** at the bottom of the dialog.)

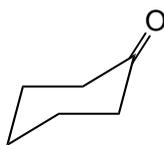


13. Submit the job (**Submit** from the **Setup** menu). When complete, *click* on the line “density potential . . .” inside the **Surfaces** dialog. The surface itself corresponds to the electron density and provides a measure of the overall size and shape of acrylonitrile. The colors indicate values of the electrostatic potential on this surface; 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.
14. Select **Close** from the **File** menu (or *click* on the  icon from the **File** toolbar) to remove acrylonitrile from the screen.** Also close any dialogs which may still be open.

* In this and other tutorials, **Resolution** will be set to **medium**. Both lower and higher resolution images can be obtained.

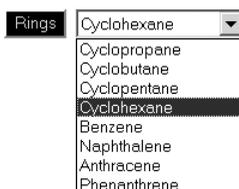
** While Spartan permits as many molecules as desired on screen at a given time, it will generally be less confusing for first-time users to handle but a single molecule.

Cyclohexanone



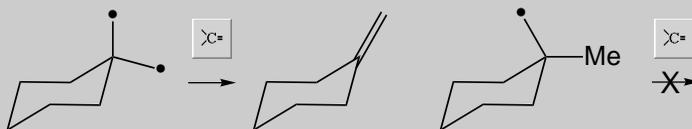
Cyclohexanone provides the opportunity to illustrate additional building features as well as graphical models for investigation of the stereoselectivity of an important class of organic reactions.

1. Click on . Click on **Rings** and select **Cyclohexane** from the menu of rings.



Click anywhere on screen and cyclohexane will appear. Select sp^2 carbon  from the model kit. *Double click* on any carbon (not free valence). The sp^3 hybridized center will be replaced by an sp^2 hybridized carbon.

Spartan'04's entry model kit allows replacement of fragments, 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 be available. This is possible for cyclohexane (above), but would not have been allowed for the substituted ring carbon in methylcyclohexane



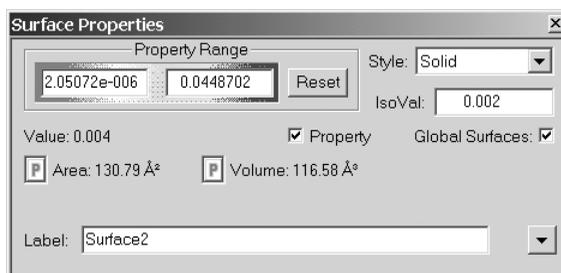
Select sp^2 oxygen  from the model kit. Click on the double free valence on the sp^2 carbon. You have made cyclohexanone. Click on  to produce a final structure with C_s symmetry, and then on  to remove the model kit.

2. Select **Calculations...** from the **Setup** menu. Specify **Equilibrium Geometry** from the top menu to the right of “Calculate”, and **Hartree Fock** and **3-21G(*)** from the two bottom menus to the right of “Calculate”. *Click* on **OK**.
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, enter the **Surfaces** dialog (**Setup** or **Display** menu). *Click* on **Add...**, and select **LUMO** from the **Surface** menu (**none** from the **Property** menu). *Click* on **OK**. 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...**, select **density** from the **Surface** menu and **|LUMO|** from the **Property** menu. *Click* on **OK**. Submit the job (**Submit** from the **Setup** menu) with the name “cyclohexanone_3-21G”.

Calculation of geometry and of graphical displays may either be completed in one submission (as in the present example), or in two or more submissions (as in the previous example). Spartan’04 keeps track of what has been done and will not perform unnecessary calculations.

4. After the calculations have completed, reenter the **Surfaces** dialog and *click* on the line “LUMO . . .”. The LUMO of cyclohexanone appears. As expected, this is a π^* orbital primarily localized on the carbonyl group.
5. Inside the **Surfaces** dialog, turn “off” the display of the LUMO by *clicking* on the line “LUMO . . .”. Next, *click* on the line “density |LUMO| . . .” to display the electron density surface onto which the (absolute) value of the LUMO has been mapped. Colors toward the red indicate small (absolute) values of the LUMO (near zero), while colors toward the blue indicate large (absolute) values of the LUMO. Note the “blue spot” directly over the carbonyl carbon. This corresponds to the maximum value of the LUMO and is where nucleophilic attack will occur.

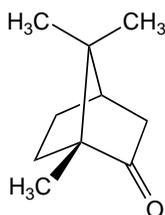
6. You will see that the “blue spot” over the *axial* face of the carbonyl carbon is “bigger” than that over the *equatorial* face. This indicates preferential attack by nucleophiles onto the *axial* face. Quantify the difference by measuring the (absolute) value of the LUMO on these two faces. Bring up the (**Molecule**) **Properties** dialog (**Display** menu) and *click* anywhere on the LUMO map. The **Surface Properties** dialog appears.



- Turn the map such that you can clearly see the *axial* face of the carbonyl carbon, and *click* two times* on the area of maximum blue. The (absolute) **Value** of the LUMO at the surface point you have selected is provided in the dialog. 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 point of maximum blue on this face. Do these values support your qualitative conclusions from viewing the image?
7. Remove cyclohexanone and any remaining dialogs from the screen.

* All controls in the **Properties** dialogs operate in a “toggle” manner. Thus, the first *click* on the surface “toggles” to the previous (molecule) mode and the second *click* back to the surface mode.

Camphor



Camphor illustrates how one molecule may be used as the starting point for another. It also illustrates a search on the Cambridge Structural Database (CSD).^{*} No calculations are involved in this example.

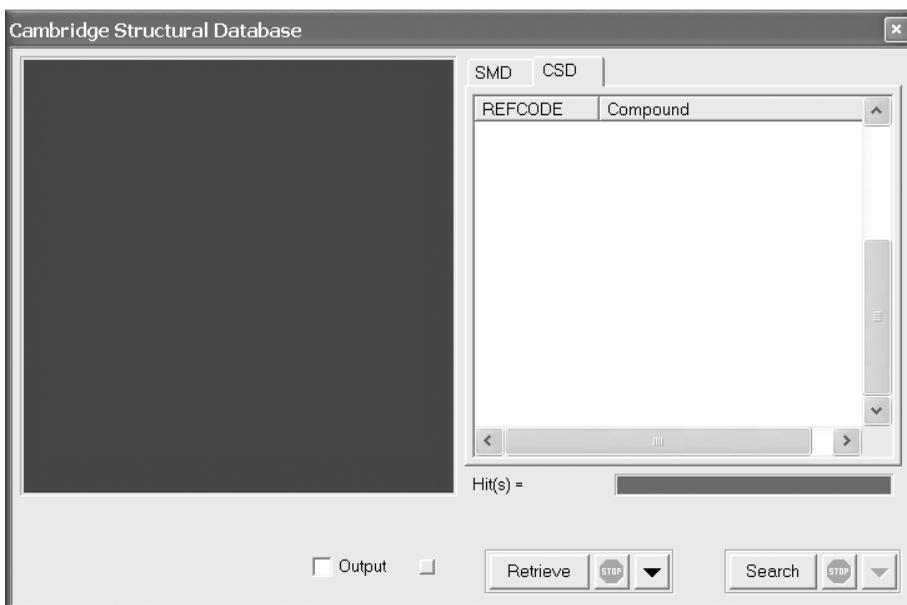
1. Bring “cyclohexanone_3-21G” (previous example) back onto the screen. Select **Open...** from the **File** menu (or *click* on the  icon from the **File** toolbar) and *double click* on “cyclohexanone_3-21G” in the dialog which results. Next select **Save As...** from the **File** menu (or *click* on the  icon from the **File** toolbar), supply the name “camphor” and *click* on **Save**.
2. Select **Add Fragment** from the **Build** menu (or *click* on the  icon from the **Build** toolbar) to bring up the entry model kit. *Click* on sp³ carbon  from the model kit and then *click* on the *axial* free valence two positions removed from the carbonyl carbon. You have made *axial* 3-methylcyclohexanone.
3. Select **Make Bond** from the **Build** menu (or *click* on the  icon from the **Build** toolbar). *Click* on one of the free valences of the sp³ carbon which you have just added and then on the *equatorial* free valence on the opposite side of the six-membered ring (adjacent to the carbonyl group). A bond will be drawn. *Click* on  to produce a refined (intermediate) structure. Finish the structure by adding three methyl groups (*click* on  from the model kit and, one after the other, *click* on the three appropriate free valences). Finally, *click* on  to give a minimized camphor geometry with C₁ symmetry. *Click* on  to remove the model kit.

^{*} In order to complete this tutorial, CSD will need to be licensed and installed. For information about a trial subscription, contact Wavefunction. For installation instructions, see **Appendix G**.

4. Select **Configure...** from the **Model** menu. *Check R/S* under “Atom” in the dialog which results, and *click* on **OK**. R/S labels now appear (only) on the two bridgehead carbons. Both should be R (or both S), depending on which enantiomer you have built. You can if you wish turn “off” the labels by selecting **Labels** from the **Model** menu.
5. Move the molecule to the far right of the screen. Then, select **Databases** from the **Search** menu (or *click* on the  icon from the **Search** toolbar).

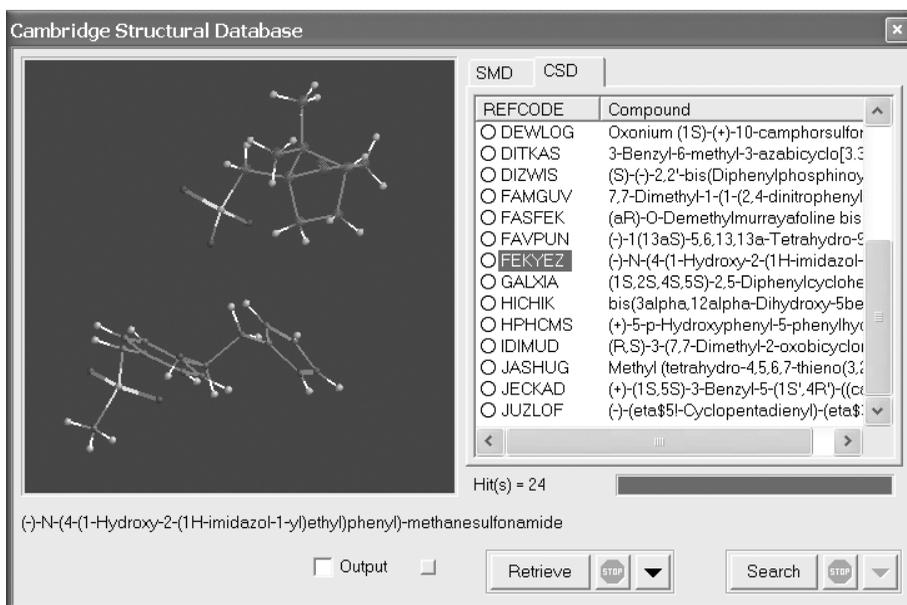


Click on the **CSD** tab at the top of the **Databases** dialog which results. This brings up the **CSD** dialog.



Click on one of the free valences on the “methyl group” which you added to the bridgehead carbon adjacent to the carbonyl group. The free valence is replaced by an orange cone. This signifies that the search is to be restricted to molecules which derive from substitution of camphor at this carbon.

6. Click on the **Search** button at the bottom of the dialog. “Hits” will appear in the text box at the right of the **CSD** dialog.

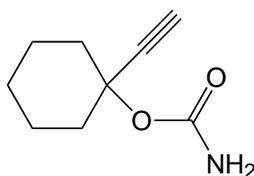


7. Wait for the search to complete, or terminate it at any time by clicking on  to the right of the **Search** button. Hits for which structural data are available are indicated by filled yellow circles. * Click on any one of these. Its name will be highlighted and a structure model will appear in the window at the top of the dialog. This model can be manipulated in the usual way.** (You need to position the cursor inside the window.)
8. When you are done, remove the **CSD** dialog (click on  at the top right) and close “camphor.”

* Unfilled circles correspond to “hits” for which structural data are unavailable.

** One (or more) structures may be transferred to Spartan’s file system using the **Retrieve** button. Full discussion is provided in **Chapter 15**.

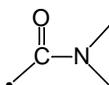
Ethinamate



Acrylonitrile, cyclohexanone and camphor are examples of molecules which can adopt only a single conformation. Much more common are molecules which can adopt more than one conformation, usually due to rotation about single bonds or puckering of rings. The sedative ethinamate is not atypical, and presents an interesting question of whether the alkyne or the carbamate occupies the “favored” *equatorial* position on the six-membered ring.

This tutorial, as well as the one immediately following, illustrate the simplest approach to dealing with conformationally-flexible molecules, that is, finding the lowest-energy conformer (the global minimum). Tutorials in later chapters address the more difficult problem of identifying “all reasonable” low-energy conformers. The present exercise is restricted to use of MMFF molecular mechanics.

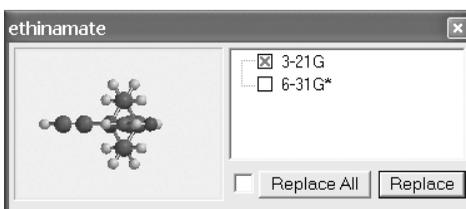
1. Bring up the entry model kit (). Click on **Rings**, select **Cyclohexane** from the menu and *click* anywhere on screen. Click on sp^3 oxygen () in the model kit and add to either an *equatorial* or *axial* free valence on cyclohexane. Click on **Groups** and select **Amide** from the menu. Make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



You can move the bonding position by repeatedly *clicking* on the icon. When you are satisfied, add the amide to oxygen to make the carbamate functionality. Finally, select **Alkyne** from the **Groups** menu and add to the same carbon on the cyclohexane ring as occupied by the carbamate group (using

the remaining *axial* or *equatorial* free valence). Click on  and then on  to remove the model kit.

2. Bring up the **Calculations** dialog (**Setup** menu). Select **Equilibrium Conformer** from the top menu to the right of “Calculate” and **Molecular Mechanics** and **MMFF** from the two bottom menus. You have requested that Spartan’04 examine “all possible” conformers*, but then select only the most stable conformer (according to the MMFF model). Click on **Submit** at the bottom of the dialog. Name the molecule “ethinamate_MMFF”.
3. When completed, the “preferred” conformer will replace the initial conformer (just like a calculated equilibrium geometry replaces a starting geometry). Which group, alkyne or carbonate, occupies the *equatorial* position?
4. Note that the name “ethanimat” appears at the bottom of the screen. This indicates that it is already available in the Spartan Molecular Database (SMD) of molecular structures and properties. Click on  immediately to the left of the name. This brings up the **SMD Preview** dialog.

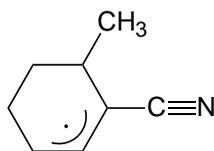


Listed at the right are theoretical models for which ethanimat is available, while a ball-and-spoke model of the selected SMD entry is displayed at the left. It can be manipulated using the mouse. Is the conformation of ethanimat in the database entries the same as you have found?

5. Close “ethinamate” as well as any open dialogs.

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

3-Cyano-4-methylcyclohexenyl Radical

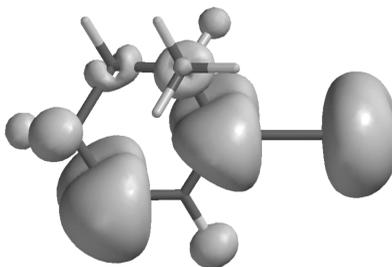


This tutorial illustrates how different models may be combined to achieve a desired result with minimum “cost”, both human and machine. MMFF molecular mechanics will be employed to establish equilibrium conformation, the semi-empirical AM1 model to establish equilibrium geometry and the Hartree-Fock 3-21G model to provide a basis for graphical calculations.

1. Build 3-cyano-4-methylcyclohexene. Start with **Cyclohexane** from the **Rings** menu, *click* on , and then *click* on *axial* free valences on any two adjacent carbons. Add **Cyano** from the **Groups** menu to one of the *equatorial* free valences on a carbon adjacent to the double bond. Finally, add a “methyl group” ( from the model kit) to the appropriate ring position using either the *equatorial* or *axial* free valence.
2. Select **Delete** from the **Build** menu (or *click* on the  icon from the **Build** toolbar), and *click* on the (*axial*) free valence on the carbon to which the cyano group is attached. *Click* on  to produce a refined geometry with C₁ symmetry. *Click* on  to remove the model kit.
3. Select **Calculations...** (**Setup** menu). Specify **Single Point Energy** from the top menu to the right of “Calculate” and **Hartree-Fock** and **3-21G(*)** from the two bottom menus. Next, specify **MMFF Conformer** from the menu to the right of “Start from”, and **AM1** from the menu which then appears to the right. You have requested that a Hartree-Fock energy is to be based on an AM1 geometry, which in turn is to be based on the best conformation according to MMFF.

This molecule has one unpaired electron. It is necessary to change **Multiplicity** from **Singlet** to **Doublet**. *Click* on **OK**.

4. Select **Surfaces** (**Setup** or **Display** menu). *Click* on **Add...**. Select **spin** from **Surface** menu and **none** from the **Property** menu, and *click* on **OK**. Again, *click* on **Add...**, and this time select **density** from the **Surface** menu and **spin** from the **Property** menu. *Click* on **OK**. You have requested two different representations of spin distribution. The first presents spin density as a surface of constant value, while the second color maps the value of the spin density onto an electron density surface. Also, request the singly-occupied molecular orbital (SOMO). *Click* on **Add...**. Select **SOMO** from the **Surface** menu (**none** from the **Property** menu) and *click* on **OK**.
5. Submit the job. Name it “3-cyano-4-methylcyclohexenyl radical_3-21G” When completed, examine the conformation. Is the methyl group *equatorial* or *axial*? Next, enter the **Surfaces** dialog. Display the spin density surface by *clicking* on the line “spin . . .”. Note that the spin density is delocalized over two of the ring carbons and onto the cyano group.



6. Again enter the **Surfaces** dialog. First, remove the spin density surface by *clicking* on the line “spin . . .”. Then, display the spin density map. *Click* on the line “density spin . . .”. Note that the areas of maximum spin (colored blue) exactly match those where the surface is large in the previous image.

Select **Properties** (**Display** menu) and *click* anywhere on the spin density map. This brings up the **Surface Properties** dialog. **Range** provides the range of spin density values. Note, in particular, that negative values of the spin density are possible.

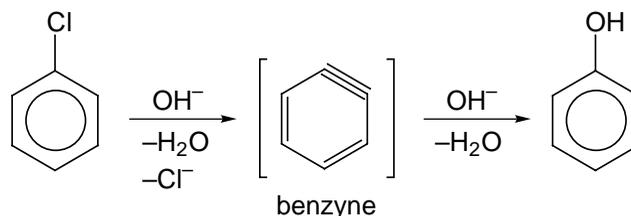
7. Enter the **Surfaces** dialog, and turn “off” display of the spin density map (*click* on the line “density spin . . .”). Then turn “on” display of the SOMO (*click* on the line “SOMO . . .”). Note that the singly-occupied molecular orbital is nearly identical to the previously-displayed image of the spin.
8. Turn “off” display of the SOMO by *clicking* on the line “SOMO . . .” in the **Surfaces** dialog. Next, *click* on **Add...** at the bottom of the (**Surfaces**) dialog, and select **Slice** from the **Surfaces** menu and **spin** from the **Properties** menu. *Click* on **OK**. A new line “Slice spin . . .” appears in the window at the top of the dialog.* *Click* on it.
9. A plane (a “slice” of spin density) surrounded by a frame appears in the middle of the model on screen. *Click* on the frame (or inside of it) to select. It will now be surrounded by a gold frame. Position the cursor outside the frame, then *press* both the **Shift** key and right button and move the mouse up and down. This will “zoom” the plane. You can also translate and rotate the plane independently of the molecule using the usual mouse operations. Alternatively, you can move the molecule and plane together by first *clicking* on the molecule (the frame will now turn white) and then using the mouse. For all operations, be certain to keep the cursor positioned outside of the frame. Size and orient the slice as you wish.**
10. Remove “3-cyano-4-methylcyclohexenyl radical” and any remaining dialogs from the screen.

* No further calculations are involved as this is just another way of representing the spin density.

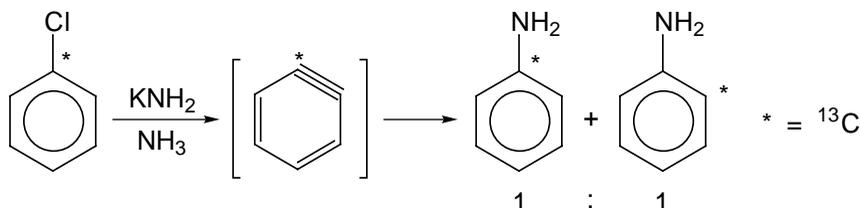
** You can change the display style from **Contours** to **Solid** or **Transparent** using the **Style** menu at the bottom right of the screen. This will appear only when the slice is selected.

Infrared Spectrum of Benzyne

Benzyne has long been implicated as an intermediate in nucleophilic aromatic substitution, e.g.



While the geometry of benzyne has yet to be conclusively established, the results of a ^{13}C labeling experiment leave little doubt that two (adjacent) positions on the ring are equivalent.



There is a report, albeit controversial, that benzyne has been trapped in a low-temperature matrix and its infrared spectrum recorded. Furthermore, a line in the spectrum at 2085 cm^{-1} has been assigned to the stretching mode of the incorporated "triple bond".

Here you will calculate the structure of benzyne using the Hartree-Fock 3-21G model and, following this, obtain an infrared spectrum for the molecule. Comparison with the experimental spectrum (specifically the line at 2085 cm^{-1} attributed to the $\text{C}\equiv\text{C}$ stretch) should allow you to comment one way or another about the controversial report.

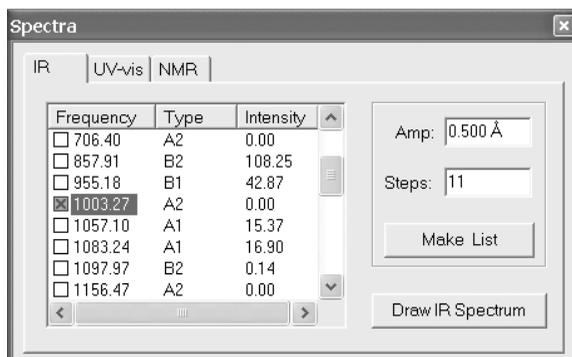
1. Bring up the entry model kit, select **Benzene** from the **Rings** menu and *click* anywhere on screen. *Click* on and *click* on two adjacent free valences on benzene. (Alternatively, hold down the **Delete** key while you *click* on the two free valences.) *Click* on and then on .
2. Enter the **Calculations** dialog (from the **Setup** menu). Select **Equilibrium Geometry** from the top menu to the right of

“Calculate” and **Hartree-Fock** and **3-21G(*)** from the two bottom menus. *Check IR* to the right of “Compute” in the center of the dialog. You have requested that an infrared spectrum be computed following optimization of geometry. *Click* on **Submit** and provide the name “benzyne_3-21G”.

3. While you are waiting for the calculation to complete, build 2-butyne, optimize its geometry with the same Hartree-Fock model and compute its infrared spectrum. Name the molecule “2-butyne_3-21G”. 2-butyne will serve as a “standard” with which to adjust the infrared spectrum of the benzyne.
4. When both calculations have completed, examine the geometry of benzyne. Does it incorporate a “real” triple bond? Compare the length with that in 2-butyne.

You should have two molecules on screen, benzyne and 2-butyne. Go between them by *clicking* on them in turn. All manipulations (except scaling) pertain only to the selected molecule as do all dialog operations.

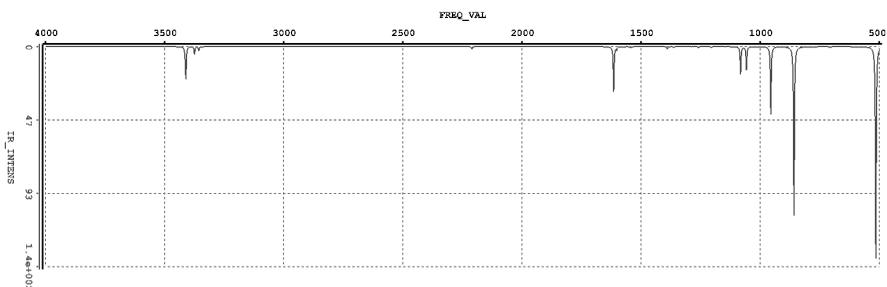
5. Select (*click* on) benzyne and then select **Spectra** from the **Display** menu. *Click* on the **IR** tab in the dialog which results to bring up the **IR Spectra** dialog.



One after the other, *check* the yellow boxes to the left of the frequencies in the dialog. In response, the vibrational motion associated with this frequency will be animated. Find the

frequency which best fits the description of a $\text{C}\equiv\text{C}$ stretch, and record its value. Do not close the **IR Spectra** dialog.

6. Select 2-butyne and find and record the frequency corresponding to the $\text{C}\equiv\text{C}$ stretch. It should be on the order of 12% larger than the experimental frequency (2240 cm^{-1}) at this level of calculation.* Compute a “scaling factor” based on the ratio of measured to calculated frequencies, and apply this to the calculated frequency in benzyne. Is your (scaled) frequency in reasonable accord with the reported experimental value of 2085 cm^{-1} ?
7. Again, select benzyne and *click* on **Draw IR Spectrum** inside the **IR Spectra** dialog.



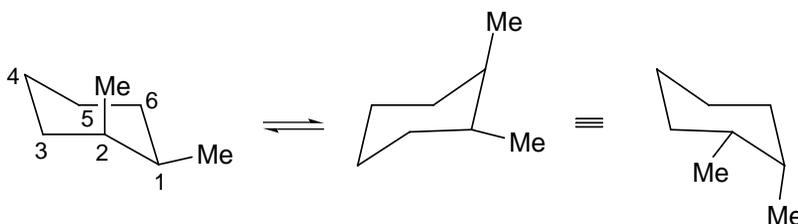
The resulting spectrum is like any other graphical object in that it can be translated and zoomed using the usual mouse commands. (It cannot be rotated.) You need to *click* on the spectrum to select it. Locate the line corresponding to the $\text{C}\equiv\text{C}$ stretch in the spectrum. Having done so, can you further comment one way or the other about the validity of the experimental result?

8. Close both molecules on screen together with any open dialogs.

* Rationalization of this behavior together with performance statistics for a number of theoretical models available in Spartan'04 is found in “**A Guide to Molecular Mechanics and Quantum Chemical Calculations**”.

^{13}C NMR of *cis*-1,2-Dimethylcyclohexane (cannot be completed with the Essential Edition)

At normal temperatures, the NMR spectrum of a conformationally-flexible molecule represents a (Boltzmann-weighted) average of the NMR spectra of all accessible conformers. Only when the temperature is lowered will the spectrum reveal its components, and its “complexity”. A particularly simple example is *cis*-1,2-dimethylcyclohexane, where there are only two “equivalent” conformers.



The room temperature ^{13}C spectrum contains only four lines at 34.9, 31.9, 24.2 and 16.4 ppm relative to TMS, corresponding to an equal weighting of C_1 and C_2 , C_3 and C_6 , and C_4 and C_5 and the two methyl carbons, respectively. Only when the sample is cooled sufficiently does the spectrum reveal eight distinct lines.

Here, you will calculate the (static) ^{13}C NMR spectrum of *cis*-1,2-dimethylcyclohexane, and then average chemical shifts for the three pairs of “equivalent” ring carbons to yield the observed (room temperature) spectrum. You will use the carbon shifts in cyclohexane as a “standard” (instead of TMS). Optionally, you will obtain a ^{13}C spectrum for *cis*-decalin to see to what extent it serves a model for “static” *cis*-1,2-dimethylcyclohexane. The Hartree-Fock 6-31G* model will be employed.

1. Build and minimize *cis*-1,2-dimethylcyclohexane. Inside the **Calculations** dialog, specify calculation of equilibrium geometry using the Hartree-Fock 6-31G* model. *Check NMR* to the right of “Compute”, and submit the job. Name it “cis-1,2-dimethylcyclohexane_6-31Gs”.
2. Perform the same calculation (6-31G* equilibrium geometry and NMR spectrum) on cyclohexane (name it “cyclohexane_

6-31Gs”. This will be used (in place of TMS) as the reference compound for the ring carbons in dimethylcyclohexane.

3. After the calculations have completed (several minutes), record chemical shifts for all ring carbons in *cis*-1,2-dimethylcyclohexane, either from the **Atom Properties** dialog (select **Properties** from the **Display** menu and *click* on a carbon) or by labeling the model (select **Configure...** from the **Model** menu and *check Chem Shift* under “Atom” in the dialog which results). In the latter case, you may want to remove the hydrogens (select **Hydrogens** from the **Model** menu) to simplify the display. Also, obtain the ^{13}C shift in cyclohexane and compute a “correction factor” based on its difference to the measured shift (27.6 ppm) to be added to the *cis*-1,2-dimethylcyclohexane shifts. Finally, average the calculated chemical shifts to obtain a room temperature ^{13}C spectrum. How do the averaged ^{13}C shifts compare with measured values?

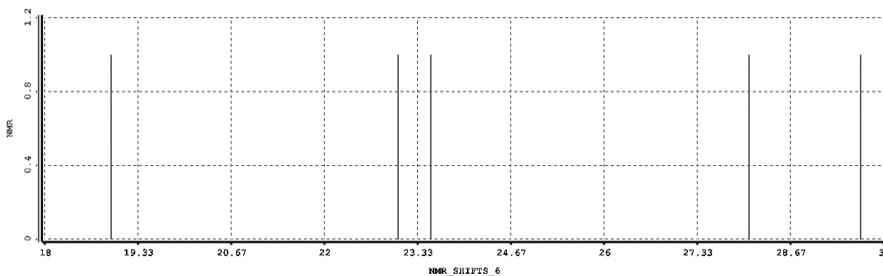
4 to 6 optional

4. *cis*-Decalin is a reasonable model for “static” *cis*-1,2-dimethylcyclohexane, in that it is unable to undergo (rapid) ring inversion.



Build *cis*-decalin. Instead of calculating its equilibrium geometry, get it from the Spartan Molecular Database (SMD). *Click* on  to the right of the name (*cis*-decalin) at the bottom of the screen to bring up the **SMD Preview** dialog. *Check 6-31G** and *click* on the **Replace** button at the bottom of the dialog. The SMD entry will replace the structure you built.

5. Enter the **Calculations** dialog. It should be set up for a single-point-energy calculation using the Hartree-Fock 6-31G* model. *Check NMR* to the right of “Compute” and *click* on **Submit**.
6. The calculation will require several minutes. When completed, select **Spectra** from the **Display** menu and *click* on the **NMR** tab. *Click* on **Draw ¹³C Spectrum**.



Because of the (C_2) symmetry of *cis*-decalin, your spectrum will contain only five lines, all of equal intensity. Relate these to the six lines corresponding to the ring carbons in “static” *cis*-1,2-dimethylcyclohexane. Pay particular attention to the differences in chemical shifts between carbons which average in the equilibrating molecule. Is *cis*-decalin a good model?

7. Close all molecules and any open dialogs.

Chapter 4

Groups of Organic Molecules

This chapter introduces and illustrates 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.

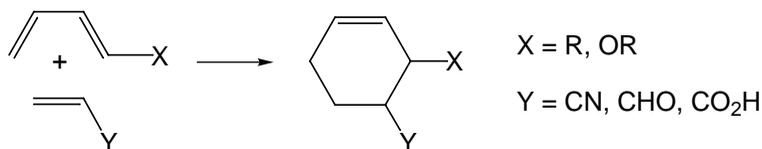
Computational investigations like experimental investigations are rarely restricted to single molecules, but rather may involve a series of related molecules. Here, it may be of interest to compare geometries, energies or other calculated properties, or to compare trends in calculated and measured properties. Spartan'04 provides facilities for these purposes. In particular, it allows molecules to be grouped, either “manually”, or automatically as a result of a conformational search, from following a particular vibrational motion, or from a “scan” of one or more geometrical variables. Once put into a group, molecules may be aligned based on their structures. Calculations may be performed either on individual molecules or, just as simply, on the complete group of molecules.

Associated with a group (including a group of one molecule) is a spreadsheet. This allows convenient access to virtually any calculated quantity. Additionally, data may be entered manually into the spreadsheet. Data in the spreadsheet may be manipulated, linear regression analyses performed and both 2D and 3D plots constructed.

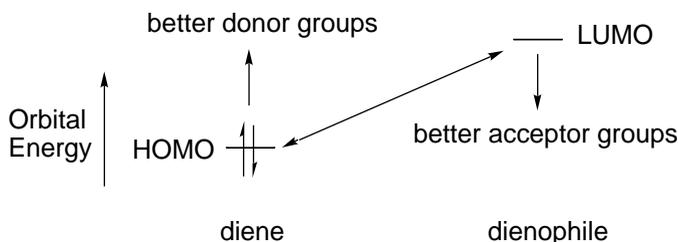
The tutorials in this chapter introduce a number of the basic group operations available in Spartan'04. These include building a group “from scratch”, and processing groups resulting from a conformational search and from varying a torsion angle. Also provided is a simple example of fitting an experimental observable to one or more calculated properties by way of linear regression.

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 (HOMO) on the diene, while acceptor groups lower the energy of the lowest-unoccupied molecular orbital (LUMO) on the dienophile. Thus, the HOMO-LUMO gap is reduced, leading to enhanced stabilization.

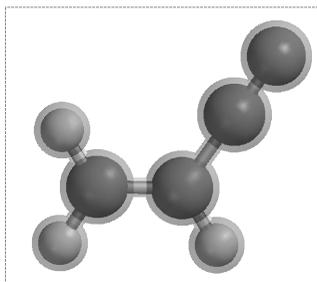


To test such an hypothesis, you will examine the extent to which experimental relative rates of Diels-Alder cycloadditions involving cyclopentadiene and a variety of cyanoethylenes correlate with dienophile LUMO energies.

1. Bring acrylonitrile which you previously constructed onto the screen. Select **Open...** from the **File** menu (or *click* on ) and *double click* on “acrylonitrile_3-21G” in the file browser which results.* Place acrylonitrile onto the clipboard, by first drawing a “selection box”. Position the cursor slightly above and slightly to the left of the molecule then, while holding

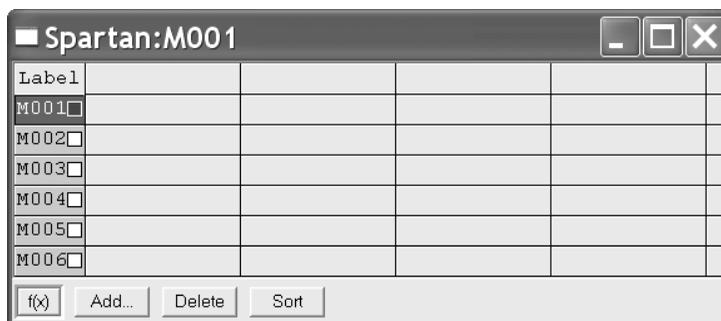
* Make certain that the electrostatic potential map is not displayed. If it is, enter the **Surfaces** dialog (**Display** menu) and *click* on the line “density potential ...” to turn it off.

down on both left and right buttons, *drag* the mouse to a position slightly below and slightly to the right of the molecule. Finally, release both buttons. Acrylonitrile will be surrounded by “dotted lines” (a “selection box”).



- Select **Copy** from the **Edit** menu. Close acrylonitrile (.
2. Enter the builder (). *Click* on **Clipboard** at the bottom of the model kit. Spartan’s clipboard will be accessed and the structure of acrylonitrile will appear in a box at the top of the model kit. (You can manipulate this structure by positioning the cursor inside the box and using the usual mouse/keyboard commands.) *Click* anywhere on screen and acrylonitrile (the contents of the clipboard) will be drawn. *Click* on  to produce a refined structure. *Do not leave the builder.*
 3. Select **New Molecule** from the **File** menu. This requests that a “new molecule” (one which has yet to be built) is to be appended onto the end of a group in which the currently selected molecule (acrylonitrile) is a member. The screen will be cleared. *Click* on **Clipboard** at the bottom of the model kit and *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 .
 4. Repeat this procedure (**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), *click* on  to remove the model kit.

5. The molecules have been put into a single group, allowing calculated properties to be accessed via a spreadsheet. Select **Spreadsheet** from the **Display** menu.



To select individual molecules, *click* on their labels (“M001”, . . .) in the left hand column, or use the and keys at the bottom left of the screen. You may change the default names (to “acrylonitrile”, . . .) by directly typing in new names. *Press* the **Enter** key following each entry.

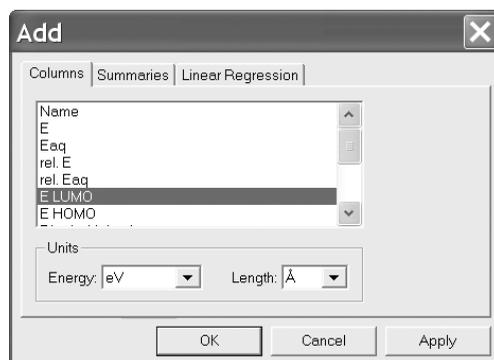
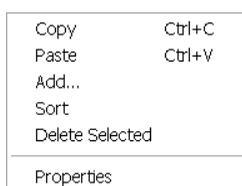
6. Enter the **Calculations** dialog (**Setup** menu), and specify a single-point energy using the Hartree-Fock 3-21G model. Select **AM1** from the menu to the right of “Start from”. This indicates that the 3-21G energy calculation is to be preceded by calculation of geometry using the AM1 model. Make certain that **Global Calculations** is *checked* to ensure that calculations are to be applied to all group members (and not just the selected member).
7. Submit the job. Name it “Diels-Alder dienophiles_3-21G”. While you are waiting for it to complete, enter the experimental relative rates from the table below into the spreadsheet.

Experimental relative rates for Diels-Alder cycloadditions of cyclopentadiene*			
dienophile	log ₁₀ (relative rate)	dienophile	log ₁₀ (relative rate)
acrylonitrile	0	1,1-dicyanoethylene	4.64
<i>trans</i> -1,2-dicyanoethylene	1.89	tricyanoethylene	5.66
<i>cis</i> -1,2-dicyanoethylene	1.94	tetracyanoethylene	7.61

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

First, type a title “Log(rate)=” into the header cell at the top of a “blank” column in the spreadsheet and *press* the **Enter** key. Then enter the rate data in the appropriate cells. *Press* the **Enter** key after each entry. Sort the group according to relative rate. *Click* on the column header “Log(rate)”, and then *click* on **Sort** at the bottom of the spreadsheet.

8. After all calculations are complete, *click* on a header cell at the top of a blank column. Then, *click* on **Add...** at the bottom of the spreadsheet. Alternatively, hold down the right mouse button while the cursor is positioned inside the spreadsheet, and select **Add...** from the menu which results.

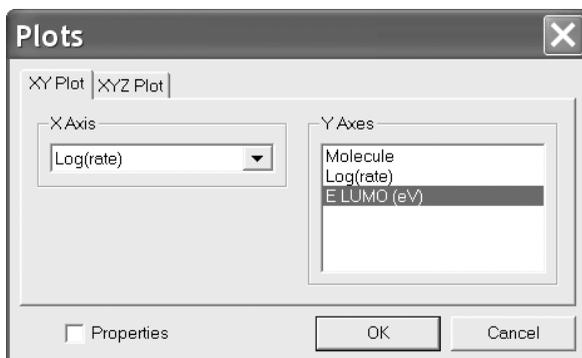


Select **E LUMO** from the list in the dialog which results and **kcal/mol** from the **Energy** menu. *Click* on **OK**.

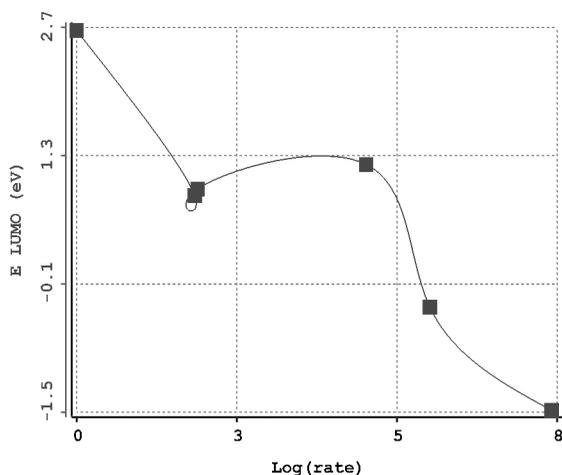
Label	Log(rate)	E LUMO (eV)
acrylonitrile	0.00000000	2.66420798
trans-1,2-dicyanoethylene	1.89000000	0.862469390
cis-1,2-dicyanoethylene	1.94000000	0.935360802
1,1-dicyanoethylene	4.64000000	1.20423522
tricyanoethylene	5.66000000	-0.351445902
tetracyanoethylene	7.61000000	-1.47939639

The spreadsheet has now served its purpose by collecting both calculated (LUMO energy) and experimental (relative rate) data for all six dienophiles. You can, if you wish, now remove it from the screen (*click* on **x** at the top right).

9. Select **Plots...** from the **Display** menu. This leads to the **Plots** dialog.

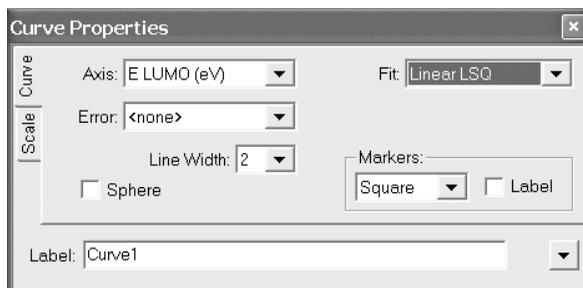


Make certain that the “**XY Plot**” tab at the top of the dialog is selected. Select **Log(rate)** from the list of items in the **X Axis** menu and **E LUMO(eV)** from the **Y Axes** list. *Click* on **OK** to remove the dialog and show the plot.

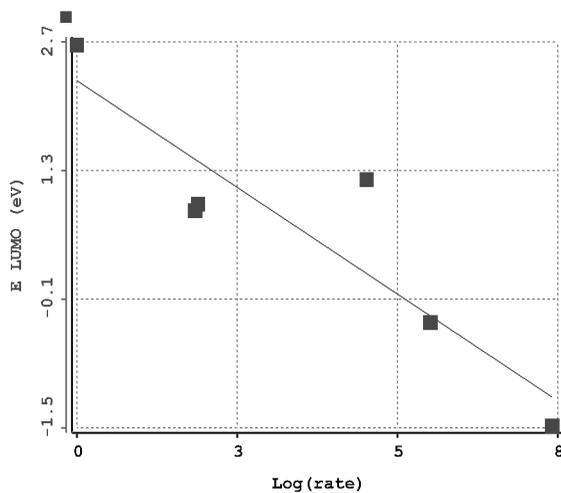


The default curve, a so-called cubic spline, smoothly connects the data points, but is of little value in establishing a correlation. A better representation is provided by a simple linear least-

squares fit. Select **Properties** from the **Display** menu and *click* anywhere on the “curve” which you have just drawn. The **Curve Properties** dialog appears.



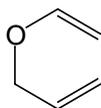
Select **Linear LSQ** from the **Fit** menu. A new plot appears.



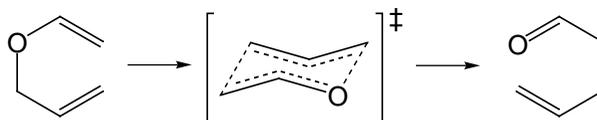
Is there a correlation between relative rates and LUMO energy?

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

Allyl Vinyl Ether



Allyl vinyl ether undergoes Claisen rearrangement, the mechanism for which demands a chair arrangement of the reactant.



Is this the lowest-energy conformer (global minimum) or is additional energy required to properly orient the molecule for reaction? To find out, you need to locate all the conformers of allyl vinyl ether, identify the best chair structure and evaluate its energy relative to that of the actual global minimum. You will first carry out a conformational search using the MMFF molecular mechanics model, and then obtain relative conformer energies using single-point 6-31G* Hartree-Fock calculations based on AM1 equilibrium geometries.

1. Bring up the entry model kit and construct allyl vinyl ether (in any conformation) from a sequence of sp^2 and sp^3 carbons and an sp^3 oxygen. Click on  to produce a refined geometry. Click on .
2. Bring up the **Calculations** dialog and select **Conformer Distribution** from the top menu to the right of “Calculate” and **Molecular Mechanics** and **MMFF** from the two bottom menus. Click on **OK**.
3. Submit the job. Name it “allyl vinyl ether_MMFF”. When completed, it will give rise to a series of low-energy conformers* placed in a new file “allyl vinyl ether_MMFF.Conformer1”. Open this file.** Select **Spreadsheet** from the **Display** menu.

* By default, only conformers within 10 kcal/mol of the global minimum will be kept. This can be changed (see **Conformational Search** in **Appendix C**).

** To avoid confusion, it is a good idea to close the original file “allyl vinyl ether_MMFF”.

Size the spreadsheet such that all rows (corresponding to different conformers) are visible at one time. *Click* on **Add...** at the bottom of the spreadsheet. Select **E** from the list at the top of the dialog which appears, **kcal/mol** from the **Energy** menu and *click* on **OK**. Energies for each of the different conformers will be added to the spreadsheet. Examine the lowest-energy conformer (the top entry). Is it in a “chair conformation” suitable for Claisen rearrangement? If not, identify the lowest-energy conformer which is suitable. You can keep two or more conformers on screen at the same time by *checking* the boxes immediately to the right of “Label” (the leftmost column) in the spreadsheet. To get a clearer idea of structural similarities and differences, align the conformers. Select **Align Molecules** from the **Geometry** (or *click* on the  icon in the **Geometry** toolbar). A message will appear at the bottom left of the screen.

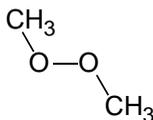
Select atoms .

Click on three (or more) atoms to designate them as alignment centers. Each will be marked by a red circle. If you make a mistake, *click* again (two times) and the circle will disappear. When you are done, *press* the **Align** button at the bottom right of the screen. *Click* on .

4. To obtain a better estimate of conformational energy differences, perform 6-31G* single-point energy calculations using AM1 geometries. Make a copy of “allyl vinyl ether_MMFF.Conformer1” () and name it “allyl vinyl ether_6-31Gs”. Using the copy, delete all conformers except the global minimum and the lowest-energy conformer poised for Claisen rearrangement. Select each conformer to be discarded, and then select **Delete Molecule** from the **File** menu. Alternatively, *click* on the cell in the spreadsheet containing the “label” for the molecule to be deleted, and then *click* on **Delete** at the bottom of the spreadsheet. When you are done, the spreadsheet should contain only two entries.

5. Enter the **Calculations** dialog, and specify calculation of a single-point energy using the Hartree-Fock 6-31G* model. Also, specify **AM1** from the menu to the right of “Start from”. *Check **Global Calculations*** at the bottom of the dialog to specify that the dialog settings apply to both conformers.
6. Submit the job. When completed, examine the conformer energies. How much energy is needed to go from the global minimum to a conformer poised to undergo Claisen rearrangement?
7. Remove all molecules and any remaining dialogs from the screen.

Internal Rotation in Dimethylperoxide



Quantum chemical calculations, in particular, Hartree-Fock molecular orbital calculations and density functional calculations, may be called on to furnish data to parameterize empirical energy functions for use in molecular mechanics and/or molecular dynamics calculations. Most important are data relating to torsional motions, for these are the most difficult to obtain experimentally. Here, the empirical energy function needs to reflect the inherent periodicity. As an example, consider rotation about the oxygen-oxygen bond in a molecule such as dimethylperoxide. This may be described by a truncated Fourier series.

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

Here, ω^{eq} is the ideal dihedral angle and k^{torsion1} , k^{torsion2} and k^{torsion3} are parameters. 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.

In this tutorial, you will generate a potential energy function for rotation in dimethylperoxide using 6-31G* Hartree-Fock calculations (and optionally from B3LYP/6-31G* density functional calculations) and then fit this potential to a truncated Fourier series.

1. Using the entry model kit, construct dimethylperoxide. If the molecule is not already in an *anti* conformation, *click* on  and set the COOC dihedral angle to **180** (180°). **Do not minimize**.
2. Select **Constrain Dihedral** from the **Geometry** menu (or *click* on the  icon from the **Geometry** toolbar). 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. Select **Properties (Display menu)** and *click*

on the constraint marker on the model on screen. This leads to the **Constraint Properties** dialog.



3. Check **Dynamic** inside the dialog. This leads to an extended form of the **Constraint Properties** dialog which allows the single (dihedral angle) constraint value to be replaced by a sequence of constraint values.

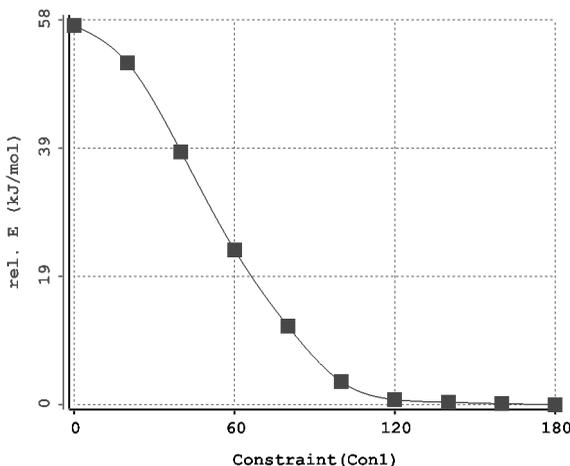


Leave “180” (180°) in the box to the right of **Value**, but change the contents of the box to the right of **to** to “0” (0°). You need to *press* the **Enter** key after you type in the value. **Steps** should be set to “10”. (If it does not, *type* “10” and *press* the **Enter** key.) What you have specified is that the dihedral angle will be constrained first to 180°, then to 160°*, etc. and finally to 0°. *Click* on **✕** to dismiss the dialog.

4. Bring up the **Calculations** dialog and select **Energy Profile** from the top menu to the right of “Calculate”, and **Hartree-Fock** and **6-31G*** from the two bottom menus. *Click* on **OK** and submit the job. Name it “dimethylperoxide_6-31Gs”.

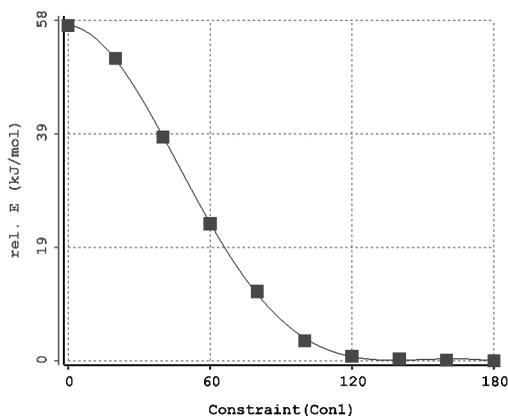
* The difference between constraint values is given by: (final-initial)/(steps-1).

- When the calculations have completed, they will go into a file named “dimethylperoxide_6-31Gs.Profile1”. Open this file. Align the conformers. *Click* on  and, one after the other, *click* on both oxygens and one of the carbons. Then *click* on the **Align** button at the bottom right of the screen. Bring up the spreadsheet (**Display** menu), and enter both the energies relative to the 180° conformer, and the COOC dihedral angles. First *click* on the label (“M001”) for the top entry in the spreadsheet (the 180° conformer), then *click* on the header cell for the leftmost blank column, and finally, *click* on **Add...** at the bottom of the spreadsheet. Select **rel. E** from among the selections in the dialog which results, **kJ/mol** from the **Energy** menu and *click* on **OK**. To enter the dihedral angle constraints, *click* on , *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 .
- Select **Plots...** (**Display** menu). Select **Constraint(Con1)** from the **X Axis** menu and **rel. E(kJ/mol)** from the **Y Axes** list. *Click* on **OK**.



The curve (a so-called cubic spline) smoothly connects the data points. To fit the points to a Fourier series, bring up the **Properties** dialog (**Display** menu) and *click* anywhere on the

plot. Select **Fourier LSQ** from the **Fit** menu and *click* on  to remove the dialog. A new plot appears.



$$\begin{aligned} \text{rel. E (kJ/mol)} = & +57 -27(1-\cos(x)) -13(1-\cos(2x)) -1.1(1-\cos(3x)) \\ & +2.6\sin(x) -1.4\sin(2x) -0.82\sin(3x) \end{aligned}$$

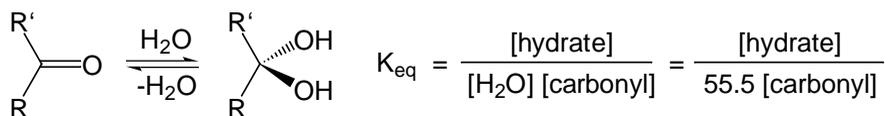
The actual fit expression appears at the bottom of the plot.

7 and 8 optional (cannot be completed with the Essential Edition)

7. Use energies from B3LYP/6-31G* density functional calculations, together with the Hartree-Fock geometries to provide a better “fitting function”. First, make a copy of “dimethylperoxide_6-31Gs.Profile1”. Name it “dimethylperoxide_B3LYP_6-31Gs”. Next, enter the **Calculations** dialog and specify calculation of single-point energies using the B3LYP/6-31G* density functional model. 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.
8. Submit the job. It will require several minutes to complete. When it is done, draw a new energy plot and compare it to the energy plot produced earlier.
9. Remove all molecules and any remaining dialogs from the screen.

Hydration of Carbonyl Compounds

The hydration of carbonyl compounds has been extensively studied primarily because it serves as a model for a number of important reactions, nucleophilic addition to carbonyl compounds among them.



Experimental K_{eq} for hydration of carbonyl compounds*			
	$\log(k_{\text{eq}}/55.5)$		$\log(k_{\text{eq}}/55.5)$
PhCOCH ₃	-6.8	CF ₃ COCH ₃	-0.2
CH ₃ COCH ₃	-4.6	PhCOCF ₃	0.1
PhCHO	-3.8	H ₂ CO	1.6
<i>t</i> -BuCHO	-2.4	CF ₃ CHO	2.7
CH ₃ CHO	-1.7	CF ₃ COCF ₃	4.3

* J.P. Guthrie, Can. J. Chem., **53**, 898 (1975); **56**, 962 (1978).

In this tutorial, you will correlate calculated properties with measured equilibrium constants for carbonyl hydration. The purpose is to illustrate the use of Spartan's linear regression analysis tool.

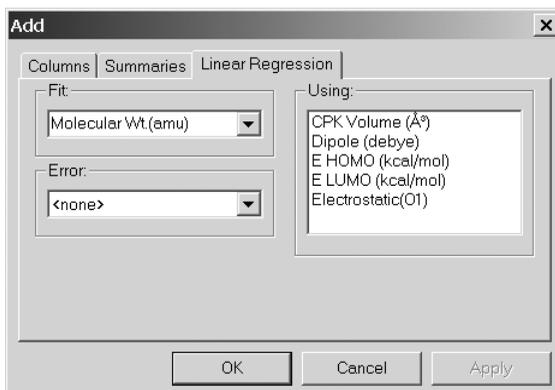
1. Build the compounds* listed above. Use **Carbonyl (Rings menu)** as a starting point for each to ensure consistent atom numbering. Put all in the same list; select **New Molecule** following construction of each molecule, i.e., build and minimize acetophenone, select, **New Molecule**, build and minimize acetone, select **New Molecule**, etc. *Click on* .
2. Enter the **Calculations** dialog and specify calculation of equilibrium geometry using the Hartree-Fock 3-21G model.**

* Keep the phenyl ring and the carbonyl group coplanar for benzaldehyde, acetophenone and trifluoroacetophenone.

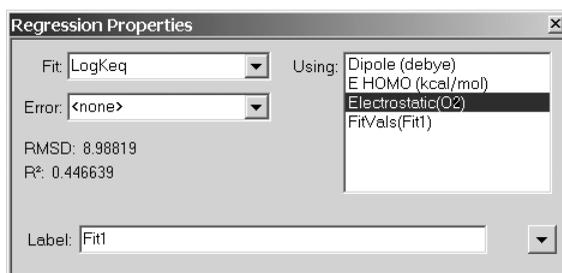
** You can save computer time by specifying calculation of single-point energy using the Hartree-Fock 3-21G model, and then selecting AM1 from the menu to the right of "Start from". This requests a semi-empirical AM1 geometry in place of the 3-21G geometry. As all of these molecules are in SMD, you can save even more time by bringing up the **SMD Preview** dialog (*click on* at the bottom right of the screen), *clicking* on the yellow square to the left of 3-21G and then *clicking* on **Replace All** at the bottom of the dialog. In this case, skip the calculation step as all the results you require are already available.

Make certain that **Global Calculations** is *checked*. *Click* on **Submit**. Name the job “carbonyl compounds_3-21G”.

3. While you are waiting for the calculations to complete, bring up the spreadsheet. *Click* inside the header cell of an empty column, *type* “Log(Keq)” and *press* the **Enter** key. Then enter the experimental equilibrium constants (see box on the previous page) into the appropriate cells. You need to *press* the **Enter** key following each data entry. Sort the list according to the value of Log(Keq). *Click* inside the header cell “LogKeq” and then *click* on **Sort** at the bottom of the spreadsheet. If you like, replace the “labels” in the spreadsheet (“M001”, ...) by correct names (“acetophenone”, ...).
4. After the calculations have completed, *click* inside the header cell for an empty column, and then *click* on **Add...** at the bottom of the spreadsheet. Select (*click* on) the following “properties” in the window at the top of the dialog: **E LUMO**, **E HOMO**, **Dipole**, **CPK Volume** and **Molecular Weight**. *Click* on **OK**.
5. Select **Properties (Display menu)** and *click* on the oxygen atom for whatever compound is displayed. *Click* on **P** to the left of **Electrostatic** (under “Charges”) in the **Atom Properties** dialog (which has replaced the **Molecular Properties** dialog), to place oxygen charges into the spreadsheet.
6. *Click* on **Add...** at the bottom of the spreadsheet, and then *click* on the **Linear Regression** tab at the top of the dialog which results. This brings up the **Add Regression** dialog.



Select **Log(Keq)** from the **Fit** menu and **Electrostatic (O2)*** from the **Using** list. *Click* on **OK**. Two new rows will be added at the bottom of the spreadsheet. With a **Properties** dialog on screen, *click* anywhere on the row in the spreadsheet starting with “Fit1”. The **Regression Properties** dialog appears.



This provides information about the fit of Log(Keq) to the charge on oxygen, in particular, the value of R^2 . This will tend to unity as the quality of the fit improves.

7. Inside the **Regression Properties** dialog, try fitting to different (single) properties in the **Using** list. (The entries toggle “on” and “off” with repeated *clicking*.) Maximize the value of R^2 . Next, try all combinations of two properties. The combination of **E LUMO** and **Electrostatic (O2)** should give the highest value of R^2 . With this combination selected, bring up the **Plots** dialog (**Display** menu) and select **Log(Keq)** from the **X Axis** menu, and **FitVals (Fit1)** from the **Y Axes** list and *click* on **OK**. Next, *click* on the curve (not on the axes) to bring up the **Curve Properties** dialog (which replaces the **Regression Properties** dialog). Select **Linear LSQ** (to replace **Cubic Spline**) from the **Fit** menu. The resulting plot should show good correlation.
8. Close “carbonyl compounds_3-21G” and remove any remaining dialogs from the screen.

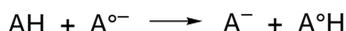
* Your atom numbering may be different, but the reference is to the carbonyl oxygen.

Acidities of Carboxylic Acids

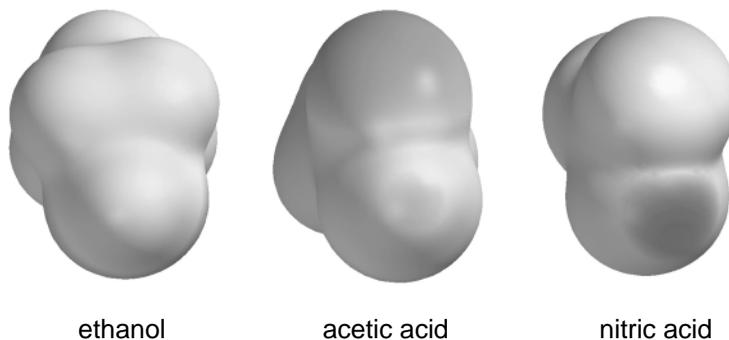
Acid strength is among the most catalogued of molecular properties. It is readily available from calculation, either in terms of absolute deprotonation energy,



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



A reasonable alternative measure of (relative) acid strength may be the value of the electrostatic potential in the vicinity of the “acidic hydrogen” in the neutral acid. This offers the advantage over a reaction energy calculation of having to look at only one molecule. It is clear that electrostatic potential maps uncover gross trends, 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.



In this tutorial, you will explore to what extent electrostatic potential maps may be used to quantify changes in acid strength due to subtle variations in structure. You will also use the tutorial to illustrate how the Spartan Molecular Database of calculated structures, energies and properties may be used to shorten the time required for an investigation.

1. One after the other, build trichloroacetic, dichloroacetic, chloroacetic, formic, benzoic, acetic and pivalic acids. Put all into the same list (**New Molecule** from the **File** menu following the first molecule). *Click* on when you are done.

2. All the molecules which you have built are available in the Spartan Molecular Database. *Click* on  to the left of the name of the presently selected molecule at the bottom of the screen. The **SMD Preview** dialog will appear which displays the structure of the selected molecule on the left and a list of theoretical models for which calculated results are available on the right. *Check* the yellow square to the left of “3-21G” and *click* on **Replace All** at the bottom of the dialog. Structures obtained from Hartree-Fock 3-21G calculations will replace those you have built. You need to calculate a wavefunction for each of the molecules in order to produce electrostatic potential maps.
3. Enter the **Calculations** dialog (**Setup** menu). Check to make certain that a single-point-energy, Hartree-Fock 3-21G calculation has been requested. Also make certain that **Global Calculations** at the bottom of the dialog is checked. *Click* on **OK** to remove the dialog. Enter the **Surfaces** dialog (**Setup** menu). First, make certain that **Global Surfaces** at the bottom of the dialog is checked. *Click* on **Add...** at the bottom of the dialog, select **density** from the **Surface** menu and **potential** from the **Property** menu (**medium** from the **Resolution** menu) in the **Add Surface** dialog which appears and then *click* on **OK**. Leave the **Surfaces** dialog on screen. Submit the job (**Submit** from the **Setup** menu). Name it “carboxylic acids_3-21G”.
4. While you are waiting for the calculations to complete (a few minutes), bring up the spreadsheet (**Spreadsheet** from the **Display** menu). Expand it so that you can see all seven molecules, and that three data columns are available. *Click* inside the header cell for a blank column. *Click* on **Add...** at the bottom of the spreadsheet, select **Name** from the list of entries and *click* on **OK**. The name of each molecule will appear. Next, *click* inside the header cell of the next available data column, *type* “pKa” and *press* the **Enter** key. Enter the individual (experimental) pK_a's into the appropriate cells under this column. You need to *press* the **Enter** key following each entry.

acid	pK _a	acid	pK _a
Cl ₃ CCO ₂ H	0.7	C ₆ H ₅ CO ₂ H	4.19
Cl ₂ CHCO ₂ H	1.48	CH ₃ CO ₂ H	4.75
ClCH ₂ CO ₂ H	2.85	(CH ₃) ₃ CCO ₂ H	5.03
HCO ₂ H	3.75		

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

Finally, *click* inside the header cell of the next available data column and *type* “potential”. *Press* the **Enter** key.

- After all calculations have completed, 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 right of the “Label” column (in the spreadsheet) for each entry. To manipulate them independently of each other, select **Coupled** from the **Model** menu.
- Click* on the line “density . . .” inside the **Surface** dialog to turn on the electrostatic potential map for each molecule. Bring up the **Properties** dialog (**Display** menu) and *click* on the area of “maximum blue” (most positive electrostatic potential) for each molecule in turn. The value of the potential will be displayed to the right of the **Value** in the **Surface Properties** dialog. Enter this value into the appropriate cell of the spreadsheet (in the column titled “potential”). You need to *press* the **Enter** key following each data entry.
- Plot experimental pK_a vs. calculated potential. Bring up the **Plots** dialog (**Display** menu), select **pKa** under the **X Axis** menu and **potential** from the **Y Axes** list, and *click* on **OK**. The data points are connected by a smooth curve (a so-called cubic spline). To get a least squares fit, select **Properties** from the **Display** menu, *click* on the curve, and select **Linear LSQ** from the **Fit** menu in the **Curve Properties** dialog.
- Close “carboxylic acids_3-21G” and remove any remaining dialogs from the screen.

Stereochemical Assignments from ^{13}C NMR (cannot be completed with the Essential Edition)

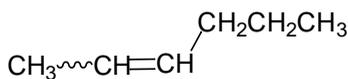
NMR spectroscopy, in particular ^{13}C spectroscopy, is without doubt the method of choice to establish the three-dimensional structure of organic molecules. Only X-ray diffraction provides more definitive results, although the requirement of a crystalline sample severely limits its application. It is now practical to calculate the NMR spectra of “real” organic molecules. The availability of a “virtual NMR spectrometer” will in time offer the organic chemist 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.

Here, you will obtain ^{13}C chemical shifts for *cis* and *trans* stereoisomers of 2-hexene and *endo* and *exo* stereoisomers of 2-methylnorbornane, and compare these to experimental shifts. The Hartree-Fock 6-31G* model will be employed, but you will get all structures from the Spartan Molecular Database. You will establish the extent to which the calculations are able to reproduce differences in chemical shifts as a function of stereochemistry.

1. Build *cis*-2-hexene. Click on at the bottom of the screen (to the left of the molecule name), check the box to the left of the “6-31G*” in the **SMD Preview** dialog which appears and click on **Replace**. *Do not minimize*. Select **New Molecule** from the **File** menu, build *trans*-2-hexene, check the box to the left of “6-31G*” in the preview dialog and click on **Replace**. *Do not minimize*. Click on .
2. Enter the **Calculations** dialog and specify a single-point Hartree-Fock calculation using the 6-31G* basis set. Check **NMR** to the right of “Compute”. Submit the job with the name “2-hexene_6-31Gs”.
3. When completed, examine the ^{13}C chemical shifts, either from the **Atom Properties** dialog or as atom labels (**Configure...** under the **Model** menu and check **Chem Shift** under “Atom” in the dialog which results). Compare them to measured values

with particular attention to the difference in shifts between *cis* and *trans* stereoisomers.

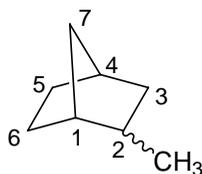
	<i>cis</i>	<i>trans</i>	Δ
C ₁	11.4	16.5	5.1
C ₂	122.8	123.9	1.1
C ₃	129.7	130.6	0.9
C ₄	28.2	34.1	5.9
C ₅	21.4	22.1	0.7
C ₆	12.5	12.5	0.0



Do the calculations distinguish between the two isomers?

- Close “2-hexene_6-31Gs”.
- Build *endo*-2-methylnorbornane. As you did for 2-hexene, replace your structure with the (6-31G*) structure in the Spartan Molecular Database. Select **New Molecule** (**File** menu) and repeat the process for the *exo* isomer. Click on .
- Inside the **Calculations** dialog, specify a single-point Hartree-Fock 6-31G* calculation, and *check* **NMR** (to the right of “Compute”). Submit the job with the name “2-methyl norbornane_6-31Gs”.
- When completed, compare the ¹³C chemical shifts with experimental values with particular attention to differences between *endo* and *exo* stereoisomers.

	<i>endo</i>	<i>exo</i>	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

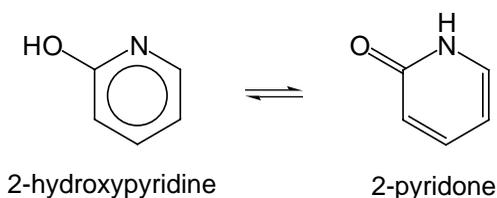


Do the calculations distinguish between the two isomers?

- Close “2-methylnorbornane_6-31Gs”.

Favoring One Tautomer Over Another

2-hydroxypyridine is in equilibrium with its tautomer, 2-pyridone.



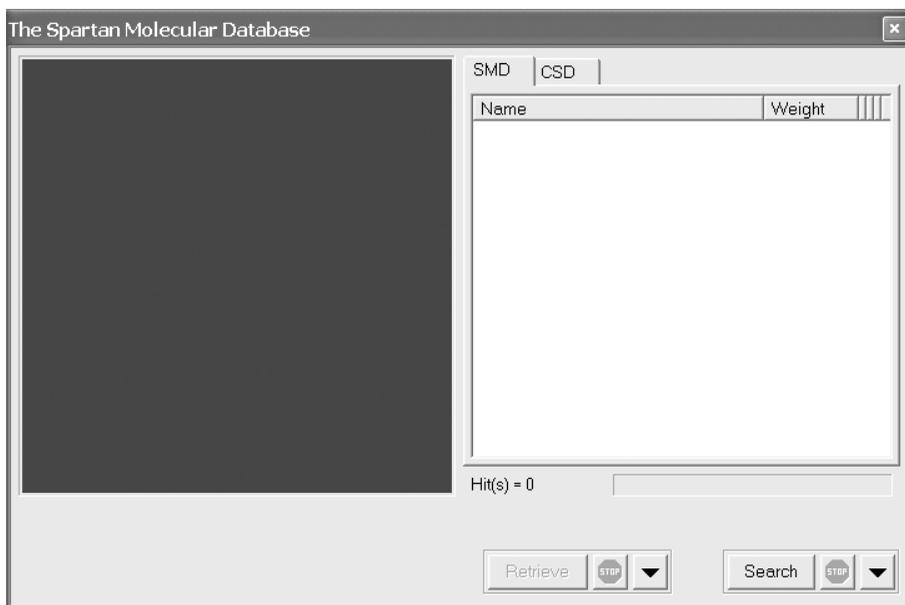
The relative abundance of the two is given by the Boltzmann equation and depends both on their relative energies and on the temperature.

A search of the Cambridge Structural Database uncovers fewer “hits” for derivatives of 2-hydroxypyridine than for derivatives of 2-pyridone. While this does not establish that the latter is a more stable tautomer, it suggests that this is the case.

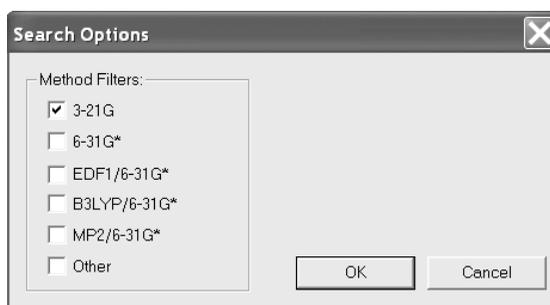
In this tutorial, you will use the Spartan Molecular Database first to establish whether 2-hydroxypyridine or 2-pyridone is lower in energy and then to look for substituents which reverses this preference. No quantum chemical calculations are involved.

1. Build 2-hydroxypyridine. Click on  at the bottom of the screen (to the left of the molecule name) to bring up the **SMD Preview** dialog, check **3-21G** and click on **Replace**. Select **New Molecule** from the **File** menu, build 2-pyridone (start with **Amide** from the **Groups** menu), check **3-21G** in the preview dialog and click on **Replace**. Dismiss the preview dialog (click on ) and then click on .
2. Bring up the spreadsheet (which should contain entries for both 2-hydroxypyridine and 2-pyridone), click on an empty column header and click on **Add...** Select (click on) both **Name** (molecule name) and **rel.E** from the list, choose an appropriate set of units, and click on **OK**. Which molecule is lower in energy according to the calculations? Is your result consistent with or at odds with information in the Cambridge Structural Database (see text box above)?

3. Select 2-hydroxypyridine, *click* on  and then *click* on the **SMD** tab in the **Database** dialog. The **SMD** dialog appears.

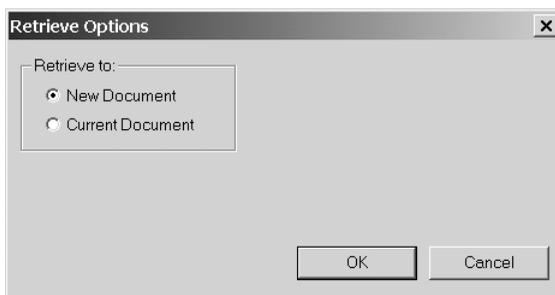


Click on  to the right of the **Search** button at the bottom of the **SMD** dialog to bring up the **Search Options** dialog.



Check 3-21G (only) under “Method Filters” and *click* on **OK**. Next, *click* on the free valence on the 4 position (across the ring from nitrogen). An orange cone will cover the free valence. (If you *click* on the wrong valence, *click* again and then *click* on the correct valence.) What you have done is to request Hartree-Fock 3-21G entries in the Spartan Molecular Database for all 4-substituted 2-hydroxypyridines. *Click* on the **Search**

button at the bottom of the dialog. “Hits” will begin to appear at the right of the dialog. After the search has completed, *click* on ▾ to the right of the **Retrieve** button at the bottom of the dialog to bring up the **Retrieve Options** dialog.



Click on **New Document** under “Retrieve to” and *click* on **OK**. Next, select all entries in the list of hits in the **SMD** dialog by first *clicking* on the top entry and, while holding down on the **Shift** key, *clicking* on the bottom entry. Finally, *click* on the **Retrieve** button.

Click on , and name the file where the hits are stored “substituted 2-hydroxypyridines”. Bring up a spreadsheet for this file and expand to include all of the entries and to have room for one data column. *Click* on an empty column header, *click* on **Add...** at the bottom of the spreadsheet, select **E** from the list of quantities in the resulting dialog (**au** from the **Energy** menu under “Units”) and *click* on **OK**.

- Repeat the process for 2-pyridone, and title the file containing the database hits “substituted 2-pyridones”. When you are done, place both spreadsheets side-by-side on screen and look for common (same substituent) entries. Can you identify substituents which enhance the energetic preferences seen for the parent compound? Can you identify substituents which reverse this preference? Elaborate.
- Close all molecules and any open dialogs.

Chapter 5

Organic Reactions

This chapter outlines and illustrates “strategies” for locating and verifying transition states for organic reactions as well as for exploring changes in product distributions as a function of substituents and reactant stereochemistry.

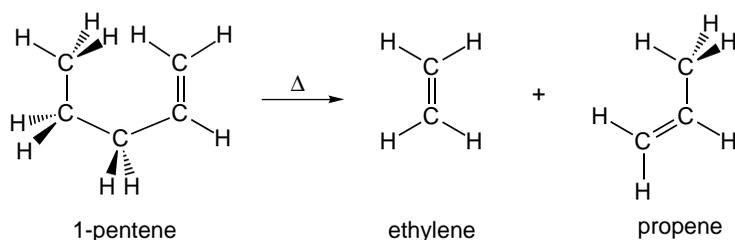
The treatment of chemical reactions adds an entirely new dimension to the application of quantum chemical models. Whereas unique valence structures may generally be written for “normal” molecules and, based on these structures, reasonable guesses at bond lengths and angles may be made, it is often difficult to designate appropriate valence structures for transition states, let alone specify detailed geometrical parameters. This is, for the most part, due to a complete absence of experimental data on the structures of transition states. However, calculated transition-state geometries are now commonplace. Spartan’04 provides both an extensive library of calculated transition states and a facility for matching as closely as possible entries in the library with the reaction at hand.*

Spartan’04 also provides a procedure for “driving” user-defined coordinates. Aside from conformational analysis (see discussion in previous chapter), the major application of this is to “force” reactions, thereby permitting identification of transition states.

The tutorials in this chapter illustrate procedures for “guessing” transition states of organic reactions, and then actually locating and verifying them. They also illustrate a procedure to “drive” a reaction through a transition state. Finally, they address strategies for collecting information on related reactions to assign kinetic product distributions.

* Where a reaction is unknown to Spartan’04’s library, a fallback technique which “averages” reactant and product geometries (similar to the so-called linear synchronous transit method) is invoked.

Ene Reaction of 1-Pentene

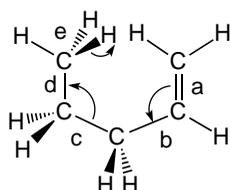


The proposed mechanism of the ene reaction involves simultaneous transfer of a hydrogen atom along with CC bond cleavage. Here, you will obtain the transition state for the ene reaction of 1-pentene from 3-21G Hartree Fock calculations, and you will examine the reaction coordinate for evidence that hydrogen transfer and CC bond breaking occur in concert. Optionally, you will perform B3LYP/6-31G* single-point energy calculations, based on Hartree-Fock 3-21G geometries, to obtain an estimate of the activation energy for the ene reaction. Also, optionally you will produce an intrinsic reaction coordinate which provides a smooth sequence of structures connecting reactant and product through the transition state.

1. Bring up the entry model kit and build 1-pentene in a conformation in which one of the terminal hydrogens on the ethyl group is “poised” to transfer to the terminal methylene group. Minimize (*click* on ) and *click* on .
2. First, save 1-pentene as “1-pentene_B3LYP_6-31Gs” for possible use later (). Also make a copy for immediate use; name it “ene reaction 1-pentene_3-21G”.
3. Select **Transition States** from the **Search** menu (or *click* on the  icon from the **Search** toolbar). *Click* on bond “a” in the figure on the following page and then *click* on bond “b”.

A curved arrow from bond “a” to bond “b” will be drawn (as shown in the figure). Next, *click* on bond “c” and then on bond “d”. A second curved arrow from bonds “c” to “d” will be drawn. Finally, *click* on bond “e” and, while holding down the **Shift** key, *click* on the (methyl) hydrogen to be transferred and on the terminal (methylene) carbon to receive this hydrogen. A third

curved arrow from bond “e” into the “space” between the hydrogen and oxygen will be drawn.



If you make a mistake, you can remove “arrows” using . (You will need to select  to continue.) Alternatively, use the **Delete** key. With all three arrows in place, *click* on  at the bottom right of the screen. Your structure will be replaced by a guess at the ene transition state. 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.

4. Enter the **Calculations** dialog (**Setup** menu), and specify calculation of transition-state geometry using the 3-21G Hartree-Fock model. Select **Transition State Geometry** from the top menu to the right of “Calculate” and **Hartree-Fock** and **3-21G(*)** from the two bottom menus. Also, *check IR* to the right of “Compute”. This requests a vibrational analysis following the optimization*, and is needed both to confirm that you have found a transition state, and to ensure that this transition state smoothly connects reactant and product.
5. Submit the job. When it has completed, animate the motion of atoms along the reaction coordinate. Select **Spectra** from the **Display** menu and *click* on the **IR** tab. *Click* on the top entry in the list in the **IR** dialog which results. It corresponds to an imaginary frequency, and will be designated with an “i” in front of the number. Is the vibrational motion consistent with the reaction of interest and not with some other process?

* Vibrational frequencies need to be calculated using optimized equilibrium or transition-state geometries. Otherwise, their values are meaningless.

6. Controls at the bottom of the **IR** dialog allow for changing both the amplitude of vibration (**Amp**) and the number of steps which make up the motion (**Steps**). The latter serves as a “speed control”. Change the amplitude to “0.3” (*type* “0.3” in the box to the right of **Amp** and *press* the **Enter** key). Next, *click* on **Make List** at the bottom of the dialog. This will give rise to a group of structures which follow the reaction coordinate down from the transition state both toward reactant and product. To avoid confusion, remove the original transition state from the screen. *Click* on “ene reaction 1-pentene_3-21G” (the vibrating molecule) and close it, along with the **IR** dialog.
7. Enter the **Calculations** dialog and specify a single-point energy calculation using the 3-21G Hartree-Fock model (the same level of calculation used to obtain the transition state and calculate the frequencies). Make certain that **Global Calculations** is *checked* before you exit the dialog. Next, enter the **Surfaces** dialog and specify evaluation of two surfaces: a bond density surface and a bond density surface onto which the electrostatic potential has been mapped. *Click* on **Add . . .**, select **density (bond)** for **Surface** and **none** for **Property** and *click* on **OK**. *Click* on **Add . . .** again, select **density (bond)** for **surface** and **potential** for **Property** and *click* on **OK**. Make certain that **Global Surfaces** is *checked*.
8. Submit for calculation. Name it “ene reaction 1-pentene sequence_3-21G”. Once the job has completed, enter the **Surfaces** dialog and, one after the other, select the surfaces which 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 “charge” on the migrating atom. Is it best described as a “proton” (blue color), hydrogen atom (green color) or “hydride anion” (red color)?
9. Close “ene reaction 1-pentene sequence_3-21G” as well as any remaining dialogs.

10 to 14 optional (*cannot be completed with the Essential Edition*)

Methods which account for electron correlation are generally needed to furnish accurate estimates of absolute activation energies. Perform single-point energy calculations using the B3LYP/6-31G* density functional model on both 1-pentene and on the ene reaction transition state (using the 3-21G geometries).

10. Open “ene reaction 1-pentene_3-21G” () and make a copy (). Name it “ene reaction 1-pentene_B3LYP_6-31Gs”.
11. Enter the **Calculations** dialog, and specify a single-point energy using the B3LYP/6-31G* density functional model. Remove the checkmark from **IR**. Submit the job.
12. Open “1-pentene_ B3LYP_6-31Gs” (). Specify a single-point energy calculation using the B3LYP/6-31G* model. Also select **3-21G(*)** from the menu to the right of “Start from”. This designates that a 3-21G equilibrium structure is to be used. Submit the job.
13. Obtain the activation energy (difference in total energies between 1-pentene and the ene reaction transition state).
14. Remove any molecules and dialogs from the screen.

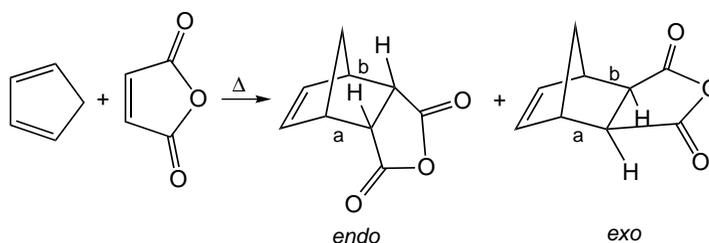
15 and 16 optional (*cannot be completed with the Essential Edition*)

To obtain a reaction coordinate smoothly connecting reactant and product through the transition state, use Spartan’s intrinsic reaction coordinate (IRC) procedure.

15. Open “ene reaction 1-pentene_3-21G” (). Enter the **Calculations** dialog, and *check* **IRC** at the top right. Submit the job. When completed, the results (a list of molecules) will be placed in a file “ene reaction 1-pentene_3-21G.IRC1”. Bring up the file. Using the step (, ) and play () keys at the bottom left of the screen, show the motions of the atoms during the course of reaction.
16. Remove any molecules and dialogs from the screen.

Thermodynamic vs. Kinetic Control

Chemical reactions may yield different products depending on the conditions under which they are carried out. High temperatures and long reaction times favor the most stable (“thermodynamic”) products, while low temperatures and short reaction times favor the most easily formed (“kinetic”) products. For example, the kinetic product in Diels-Alder cycloaddition of cyclopentadiene and maleic anhydride is the *endo* adduct, whereas it seems likely that the less-crowded *exo* adduct is the thermodynamic product.



Here you will first obtain pathways for reactions leading to both *endo* and *exo* adducts using the PM3 semi-empirical model and then (optionally) follow these by single-energy 3-21G Hartree-Fock calculations to get a better estimate of the difference in activation energies.

1. Build the *endo* Diels-Alder adduct of cyclopentadiene and maleic anhydride and minimize (to C_s symmetry).
2. Select **Constrain Distance** from the **Geometry** menu (or *click* on the  icon from the **Geometry** toolbar), and one after the other, *click* on bonds “a” and “b” in the figure above. For each, *click* on the icon  at the bottom right of the screen (it will then turn to ).
3. Select **Properties** from the **Display** menu, and *click* on the constraint marker for bond “a”. The **Constraint Properties** dialog appears, with the value of the constraint for bond distance “a” (1.54Å) given in a box to the right of **Value**. Change this to 1.5Å by *typing* “1.5” inside the box and then *pressing* the **Enter** key. *Check* **Dynamic** inside the dialog. This leads to an

extended form of the **Constraint Properties** dialog, which allows the single constraint value to be replaced by a sequence of constraint values. *Type* “2.7” (2.7Å) into the box to the right of **to** and *press* the **Enter** key. **Steps** should be set to “10”. (If it is not, *type* “10” and *press* the **Enter** key.) What you have now specified is that bond “a” will be constrained first to 1.5Å, then to 1.633Å, then to 1.767Å, etc. and finally to 2.7Å.

You need to repeat the process for bond “b”. *Click* on this bond (the **Constraint Properties** dialog will now refer to the constraint on bond “b”), and *type* “1.5” and “2.7” for **Value** and **to**, respectively. Be certain to *press* the **Enter** key following each. What you have done is to request that bonds “a” and “b” both be constrained from 1.5Å to 2.7Å in 10 equal steps. Close the **Constraint Properties** dialog.

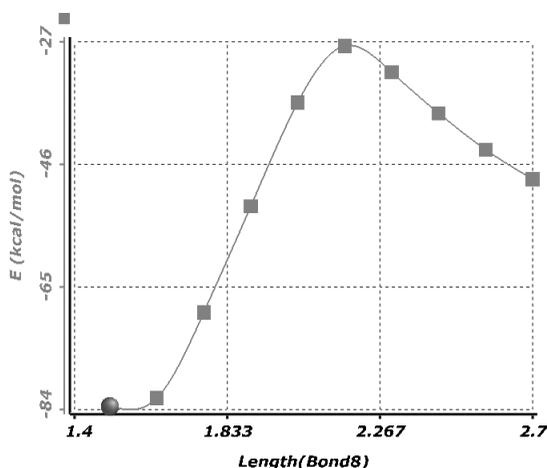
4. Bring up the **Calculations** dialog and select **Energy Profile** from the top menu to the right of “Calculate”, and **Semi-Empirical** and **PM3** from the two bottom menus. *Click* on **Submit** at the bottom of the dialog to submit the job. Name it “cyclopentadiene+maleic anhydride endo_PM3”.
5. When completed the job will give rise to a new file “cyclopentadiene+maleic anhydride endo_PM3.Profile1” containing the 10 steps which make up the energy profile. Open this file.*
6. Bring up the **Spreadsheet**, and *click* on **Add...** at the bottom. Select **E** from among the entries, **kcal/mol** from the **Energy** menu, and *click* on **OK**. Next, *click* on  and *click* on one of the two CC bonds varied in the energy profile.** *Click* on  at the bottom right of the screen. *Click* on . Finally, bring up the **Plots** dialog, and select **Length (Bond8)***** from among

* To avoid confusion, it is a good idea to close the original file “cyclopentadiene+maleic anhydride endo_PM3”.

** Alternatively, you could have selected  (instead of ) , *clicked* on one of the two constraint markers, and then *clicked* on .

*** Most likely the bond you select will not be called “Bond8”.

the items in the **X Axis** menu and **E (kcal/mol)** from the **Y Axes** list. *Click on OK.*



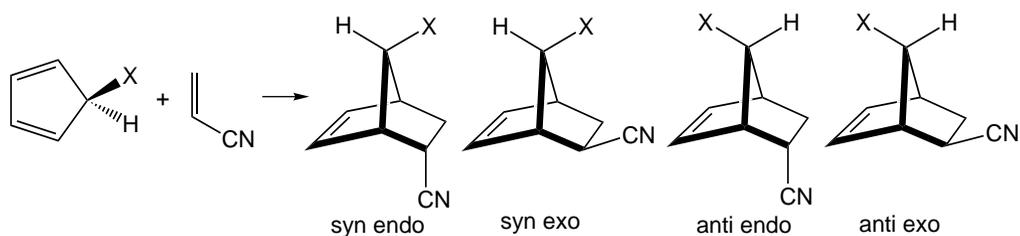
Identify both the reactant and transition state from the plot and estimate the activation energy for the cycloaddition reaction.

- Repeat steps 1 to 6 for the *exo* adduct. Compare the activation energy for *exo* addition to that for *endo* addition (above). What should be the kinetic product?
- Remove all molecules and dialogs from the screen.

9 to 11 optional

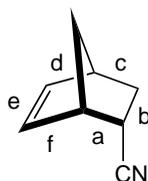
- Open “cyclopentadiene+maleic anhydride endo_PM3. Profile1” (📄) and make a copy (📄). Name it “cyclopentadiene +maleic anhydride endo_3-21G”. Enter the **Calculations** dialog and specify a single-point energy calculation using the Hartree-Fock 3-21G model. Submit. When completed, perform the same spreadsheet and plot operations you did for the PM3 calculations.
- Repeat the above procedure for the *exo* adduct and compare the two activation energies. What is the kinetic product?
- Remove all molecules and dialogs from the screen.

Stereospecific Diels-Alder Reactions

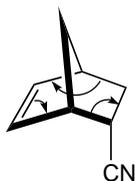


Diels-Alder cycloaddition of 5-substituted cyclopentadienes with acrylonitrile can lead to four stereoproducts, in which the X group is *syn* or *anti* to the dienophile, and the nitrile is *endo* or *exo*. *Anti* products are preferred when X is alkyl (in line with obvious steric dictates), while *syn* products are favored when X is halogen or alkoxy. In general, *endo* adducts are kinetically favored over *exo* adducts (see previous tutorial). In this tutorial, you will first use AM1 semi-empirical calculations to obtain both *syn* and *anti* transition states for *endo* addition of both 5-methylcyclopentadiene and 5-fluorocyclopentadiene and acrylonitrile, and then use Hartree-Fock 3-21G calculations to estimate relative activation energies. As the four transition states are likely to be very similar to the transition state for the “parent” cycloaddition (cyclopentadiene and acrylonitrile), you will first obtain a transition state for the parent reaction, and then to use it as a starting point for locating transition states for the substituted systems.

1. Construct the following substituted norbornene (the product of *endo* addition of cyclopentadiene and acrylonitrile).



2. Click on . Click on bond “a” (see figure above) and then on bond “b”. A curved arrow will be drawn from “a” to “b”. Next, click on bond “c” and then on bond “d”; a second curved arrow from “c” to “d” be drawn. Finally, click on bond “e” and then on bond “f”, leading to a third curved arrow. The model on screen should now appear as follows.



Click on  at the bottom right to produce a guess at the transition state.

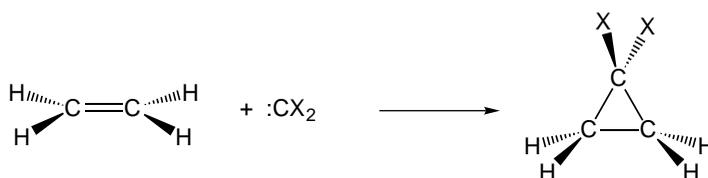
3. Inside the **Calculations** dialog, specify calculation of transition state geometry using the semi-empirical AM1 model. *Check IR* (to the right of “Compute”) to specify calculation of vibrational frequencies. This will allow you to verify that you have indeed located a “reasonable” transition state.
4. Submit the job. Name it “cyclopentadiene+acrylonitrile_AM1”. When it has completed, examine the resulting structure and calculated frequencies. Make certain that there is one and only one imaginary frequency. Animate the motion associated with the imaginary frequency (**Spectra** under the **Display** menu, *click* on the **IR** tab and *check* the box to the left of the imaginary frequency in the dialog which results) to verify that it corresponds to motion along the reaction coordinate.
5. Place the transition-state structure onto the clipboard. Position the cursor slightly above and slightly to the left of the model, then, with both buttons depressed, *drag* the mouse to a position slightly below and slightly to the right of the model, and finally release both buttons. Dotted lines will enclose the model. Select **Copy** from the **Edit** menu. Close “cyclopentadiene+acrylonitrile_AM1” (.
6. Enter the builder (). *Click* on **Clipboard** (at the bottom of the model kit) and then *click* anywhere on screen. The transition-state structure will appear. Add a fluorine to the methylene group of the “cyclopentadiene fragment” of the transition state either *syn* or *anti*. **Do not minimize**. Your starting structure should provide an excellent guess at the transition state for the substituted system.

7. Select **New Molecule** from the **File** menu. The screen will clear. *Click* on **Clipboard** and then *click* anywhere on screen. Add fluorine to the other methylene group position.

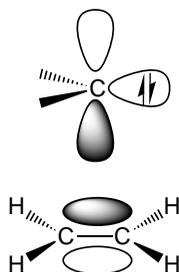
Repeat the process two more times (starting with **New Molecule**), to add methyl both *syn* and *anti* on the methylene group. When you are done (four substituted transition states in total), *click* on .
8. Enter the **Calculations** dialog and specify calculation of transition state geometry using the semi-empirical AM1 model. *Check* **IR** (to the right of “Compute”). Finally, make certain that **Global Calculations** is *checked* before you exit the dialog. Submit the job (name it Diels-Alder stereochemistry_AM1”. When it has completed, verify that all four structures correspond to transition states (using **Spectra** from the **Display** menu).
9. Make a copy of “Diels-Alder stereochemistry” (). Name it “Diels-Alder stereochemistry_3-21G”. Enter the **Calculations** dialog with this copy and specify a single-point energy calculation using the 3-21G Hartree-Fock model. Make certain that you remove the checkmark on **IR** and that **Global Calculations** is *checked* before you exit the dialog.
10. Submit the job. When it completes, bring up the spreadsheet (**Display** menu) and enter the total energies. *Click* on the header cell of a blank column and then on **Add . . .** at the bottom of the spreadsheet. Select **E** from the menu of available quantities and **au** (atomic units) from the **Energy** menu. *Click* on **OK**. Are your results consistent with the observed *syn/anti* selectivity in these reactions?*
11. Remove all molecules and any remaining dialogs from the screen.

* You might find it convenient to have the spreadsheet calculate relative energies. Select (*click* on) the label for one of the fluorine substituted transition states in the spreadsheet, then *click* on **Add...** and select **rel. E** from the menu of available quantities. *Click* on **OK**. Repeat for the methyl substituted transition states.

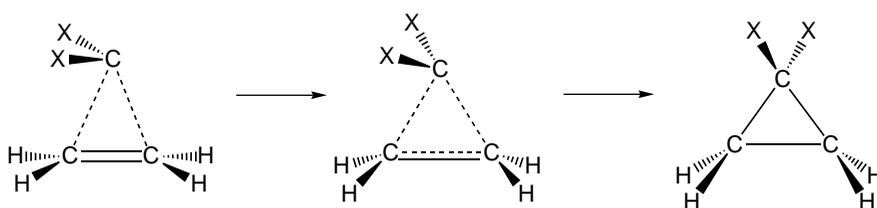
Carbene Additions to Alkenes



Singlet carbenes add to alkenes to yield cyclopropanes. Since a singlet carbene possesses both a high-energy filled molecular orbital in the plane of the molecule, and a low-energy, out-of-plane unfilled molecular orbital, this reaction presents an interesting dilemma. Clearly it would be more advantageous for the low-lying vacant orbital on the carbene, and not the high-lying filled orbital, to interact with the olefin π system during its approach.



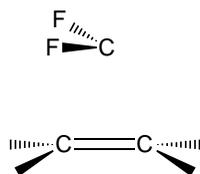
However, this leads to a product with an incorrect geometry, and the carbene must “twist” by 90° during the course of reaction.



In this tutorial, you will use the Hartree-Fock 3-21G model to find the transition state and to analyze the motion of the fragments.

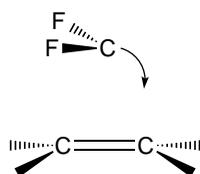
1. Bring up the entry model kit and build ethylene.
2. Select  from the model kit. Click on the **Insert** button at the bottom right of the screen (or press the **Insert** key) and then click anywhere on screen. Next, select  from the model kit and click on two of the free valences on the sp^3 carbon. Next,

click on  and, one after the other, click on the remaining two free valences on the sp^3 carbon. Finally, click on . You are left with two fragments, ethylene and difluorocarbene. Orient the two as to be poised for reaction.*

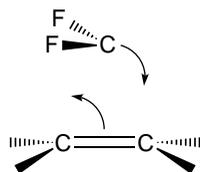


Translations and rotations normally refer to the complete set of fragments, but that they can be made to refer to an individual fragment. Click on a fragment to identify it, and then hold down the **Ctrl** key while manipulations are being carried out.

3. Click on . Click on the carbon on the CF_2 fragment and then, while holding down the **Shift** key, click first on the CF_2 carbon and then on one of the carbons on the ethylene fragment. A curved arrow will be drawn.



Next, click on the CC double bond and then, while holding down the **Shift** key, click on the other ethylene carbon and then on the CF_2 carbon. A second arrow is added to the structure.



With both arrows in place, click on  at the bottom right of the screen. Your structure will be replaced by a guess at the transition state.

* Proper orientation of the two fragments is not crucial in this case, but is primarily to allow the user to associate the “arrows” with the intended reaction. Proper orientation is, however, essential where different stereochemical outcomes are possible.

4. Enter the **Calculations** dialog, and specify calculation of a transition-state geometry using the 3-21G Hartree-Fock model. *Check IR* to the right of “Compute”. This will allow you to examine the motion along the reaction coordinate. *Click* on **Submit** inside the dialog. Name the job “difluorocarbene+ethylene_3-21G”.
5. When the job is complete, examine the geometry of the transition structure. In light of considerations regarding the orientation of filled and empty molecular orbitals on the carbene and the π orbital on ethylene, would you describe your structure as corresponding to an “early” or “late” transition state? Animate the vibrational mode corresponding to the reaction coordinate. Bring up the **IR** dialog (**Spectra** under the **Display** menu and *click* on the **IR** tab). *Click* on the imaginary frequency at the top of the list of frequencies (this corresponds to motion along the reaction coordinate). Does the animation show reorientation of the carbene as it approaches the double bond? When you are finished, turn “off” the animation by again *clicking* on the imaginary frequency.
6. Select **Properties** (**Display** menu) and, in turn, *click* on each of the four hydrogens in the transition state. Change the value in the **Mass Number** menu in the **Atom Properties** dialog from “1” to “2 Deuterium”. When you are done, resubmit the job. When complete, examine the new set of vibrational frequencies. Note that they are uniformly smaller than those for the undeuterated system, and that the largest changes are for vibrational motions where hydrogens are involved.

7 to 10 optional

7. Make a copy of “difluorocarbene+ethylene_3-21G” name it “difluorocarbene+cyclohexene_3-21G”.
8. Bring up the entry model kit with the copy (*click* on ). Select **Freeze Center** from the **Geometry** menu (or *click* on the  icon from the **Geometry** toolbar). One after the other, *click* on all atoms and free valences in your transition state except two

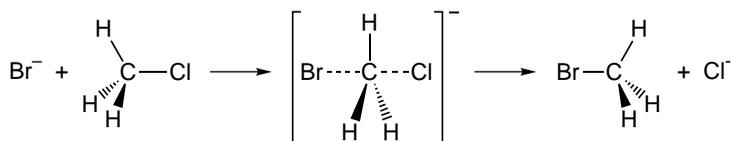
of the free valences on one side of the “ethylene fragment”.* Each of the atoms on which you *clicked* will be given a magenta colored marker, indicating that it is to be “frozen” (not moved during optimization).** Using sp^3 carbon  from the model kit and then , connect the two free valences which you have not “frozen” by a chain of four “methylene groups” to make a cyclohexene ring. *Click* on . Note that the only four methylene groups which you have just added “move” and not the underlying transition state. You have produced an excellent guess at the transition state for difluorocarbene addition to cyclohexene based on your previous transition state for the simpler process.

9. Enter the **Calculations** dialog. It should already specify calculation of transition-state geometry using the 3-21G Hartree-Fock model. Remove the checkmark on **IR** (to the right of “Compute”). *Click* on **Submit**.
10. When completed, compare the geometries of the two transition states (corresponding to addition of difluorocarbene to ethylene and cyclohexene, respectively). To do this, first put the two transition states into the same group. Select **Append Molecule(s)...** from the **File** menu and *double click* on “difluorocarbene+ethylene” in the browser which results. Then bring up the spreadsheet (**Spreadsheet** from the **Display** menu) and *check* each of the boxes to the right of the molecule names. *Click* on  and, one after the other, *click* on the three carbons which make up the “cyclopropane ring”. Finally, *click* on **Align** at the bottom right of the screen, and then *click* on . Are the two transition states very similar as expected?
11. Remove all molecules and any remaining dialogs from the screen.

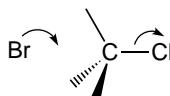
* You could do this more quickly by first *clicking* on , then drawing a selection box around all atoms to be frozen, and then *clicking* inside this box.

** You can remove the “frozen atom” markers from the model by bringing up the **Molecule Properties** dialog (**Display** menu), *clicking* on  at the bottom right of the dialog and then removing the checkmark from **Frozens** in the **Molecule Utilities** dialog which results.

S_N2 Reaction of Bromide and Methyl Chloride



- The S_N2 reaction passes through a transition state in which carbon is in a trigonal bipyramid geometry and the entering and leaving groups are colinear. To build it, first construct methyl chloride. Then *click* on the **Insert** button at the bottom right of the screen (or *press* the **Insert** key), select bromine from the palette of icons in the model kit and *click* anywhere on screen. Two detached fragments, “methyl chloride” and “hydrogen bromide”, appear on screen. *Click* on and then *click* on the free valence on bromine (immediately *click* on to get out of “delete mode”). Alternatively, hold down the **Delete** key and *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). (Recall that translations and rotations normally refer to both fragments, but can be made to refer to a single fragment by first *clicking* on the fragment and then holding down on the **Ctrl** key while carrying out the manipulations.) **Do not minimize**. *Click* on .
- Click* on . *Click* on “bromide” and, while holding down the **Shift** key, *click* again on “bromide” and then on carbon. An arrow will be drawn from “bromide” into the “space” between bromine and carbon. Next, *click* on the CCl bond and then *click* on the chlorine. A second arrow from the carbon-chlorine bond to the chlorine will be drawn.

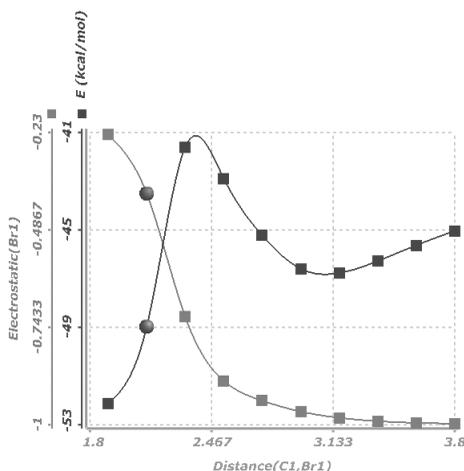


Click on at the bottom right of the screen. Your structure will be replaced by a “guess” at the transition state.

3. Click on  and then 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** key. You have now made a “complex” representing the “reactant”.
4. Click on . 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. Next, bring up the **Properties** dialog and *click* on the constraint marker. The **Constraint Properties** dialog appears. Click on **Dynamic**. Leave the value “3.8” (3.8Å) in the box to the right of **Value** alone, but change the number in the box to the right of **to** to “1.9” (1.9Å) and *press* the **Enter** key. You have requested 10 (the default number) structures with CBr bond lengths from 3.8Å (the starting point) to 1.9Å (the ending point). These should pass through the transition state. Dismiss the **Constraint Properties** dialog.
5. Enter the **Calculations** dialog, and select **Energy Profile, Semi-Empirical** and **AM1** from the appropriate menus to the right of “Calculate”. You need to change **Total Charge** to **Anion**.
6. Submit the job. Name it “bromide+methyl chloride_AM1”. When completed, it will give rise to a sequence of calculations placed in “bromide+methyl chloride_AM1.Profile1”. Open this file, and align the molecules. Click on , then in turn on the three hydrogens, and finally *press* the **Align** button at the bottom right of the screen. Click on .
7. Bring up the **Spreadsheet** and *click* on **Add...** Select **E** from among the quantities listed at the top of the dialog, **kcal/mol** from the **Energy** menu, and *click* on **OK**. Next, enter the CBr distances and bromine charges in the spreadsheet. Click on , select the CBr distance and *click* on  at the bottom right of the screen. Click on . Bring up the **Properties** dialog. Click on bromine and *click* on  to the left of “Electrostatic” under “Charges” in the **Properties** dialog. Finally, bring up the **Plots** dialog, and select **Distance (C1,Br1)** from the **X**

Axis menu, and both **E (kcal/mol)** and **Electrostatic (Br1)** from the **Y Axes** list. *Click* on **OK**.

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



S_N2 reactions involving charged species normally need to be carried out in highly-polar media, e.g., water. Spartan provides two different approaches to account for the solvent: the SM5.4 model of Cramer and Truhlar (see **Appendix A**) in which the solvent is represented by a “reaction field”, and a mixed quantum mechanics/molecular mechanics approach, in which the solute is immersed in a “bath” of solvent and molecular dynamics simulation performed. The first approach is illustrated here while the second is illustrated for zwitterionic and non-zwitterionic forms of triglycine in the next chapter.

8. Add “aqueous phase” data to the spreadsheet. *Click* on an empty column header, *click* on **Add...**, select **E SM5.4** from the list of available quantities (**kcal/mol** from the **Energy** menu), and *click* on **OK**. Bring up the **Plots** dialog and select **Distance (C1,Br1)** from the **X Axis** and **E SM5.4 (kcal/mol)** from the **Y Axes** list. *Click* on **OK**.

9 to 12 optional

9. With “bromide+methyl chloride_AM1_Profile1” enter the **Calculations** dialog. Specify **Single Point Energy** (AM1 should be selected) and *click* on **OK**.
10. Enter the **Surfaces** dialog. *Click* on **Add...** Select **density (bond)** from the **Surface** menu and **none** from the **Property** menu and *click* on **OK**. Again *click* on **Add...** and again select **density (bond)** from the **Surface** menu, but this time **potential** from the **Property** menu. *Click* on **OK**.
11. Submit the job. When completed, *click* on the line “density...” inside the **Surfaces** dialog. *Click* on  at the bottom left of the screen to animate the display. Note, the smooth way in which bonds are broken and formed during the course of reaction. *Click* on  at the bottom of the screen when you are done.
12. Reenter the **Surfaces** dialog. Turn “off” display of the bond density (*click* on the line “density...”), and turn “on” display of the electrostatic potential mapped onto the bond density (*click* on the line “density potential...”). *Click* on . Relate the migration of negative charge during reaction as indicated by colors in the electrostatic potential map to the “charge” plot you constructed in step 5 above. Recall, that colors near red indicate maximum negative potential.
13. Remove all molecules and any remaining dialogs from the screen.

Chapter 6

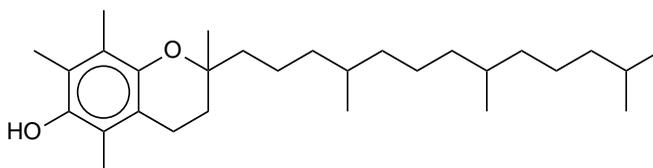
Biologically Interesting Molecules

This chapter illustrates applications involving “biologically interesting” molecules, introduces the peptide model kit and shows how a structure from the Protein Data Bank (PDB) may be brought into Spartan’04 for further analysis.

At present time, calculations on “real” biopolymers (proteins and RNA/DNA strands) are limited to molecular mechanics models. However, large classes of organic molecules of biological interest, among them steroids, prostaglandins and vitamins, are amenable to investigation using quantum chemical models. The first three tutorials give examples of such applications, and the last of these also provides a bridge between small molecules and biopolymers.

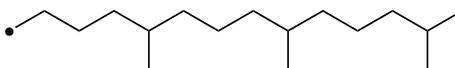
Polypeptides and polynucleotides are considered in the last two tutorials. The peptide model kit, intended primarily to construct small polypeptide strands in “idealized” geometries, is used to build helical polyglycine, and comparisons are made between zwitterionic and non-zwitterionic forms both in and out of water. The structures of a small molecule - DNA complex and a protein-RNA complex, obtained from the protein databank (PDB), are used in the two final tutorials, the first as the basis of a graphical modeling study, and the second to illustrate display of hydrogen bonds.

Vitamin E



Vitamin E may play an active role in defending cells from attack by reacting quickly with oxidizing agents to give stable products that can then be safely excreted. While the mechanism of the vitamin's action is not completely certain, it seems likely that it might directly transfer a hydrogen to another free radical leading to its "destruction" and to the formation of a stable "Vitamin E radical". Graphical models can help to account for this biological function, as well as suggest why Vitamin E incorporates a long hydrocarbon chain.

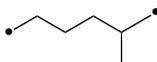
1. Build vitamin E. Start with **Benzene** from the **Rings** menu. Add a sequence of three sp^3 carbons (>C-) and an sp^3 oxygen (>O-) to the ring and then join them (O) to form the bicyclic skeleton. Click on E to produce a refined (intermediate) structure.
2. Add the saturated carbon chain (the " \bullet " is a free valence).^{*} Don't worry about its conformation.



Finally, add the four methyl groups and the hydroxy group at the appropriate ring positions. Click on E to produce a final structure.

3. Enter the **Calculations** dialog (**Setup** menu) and specify calculation of equilibrium geometry using the AM1 semi-empirical model. Click on **OK**. Next, enter the **Surfaces** dialog

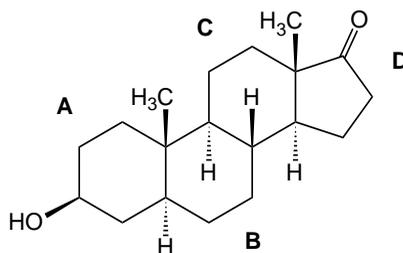
* You could save time by first building the five-carbon fragment (the " \bullet 's" are free valences),



then placing it on the clipboard, and finally using this fragment (instead of sp^3 carbon) as the building block. You need to add one sp^3 carbon at the end.

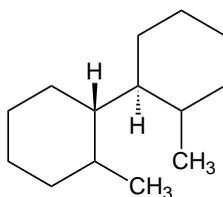
- (**Setup** menu). *Click* on **Add...** and select **density** from the **Surface** menu and **potential** from the **Property** menu. Submit the job; name it “vitamin E_AM1”.
4. When completed, examine the electrostatic potential map. Inside the **Surfaces** dialog, *click* on the line “density potential . . .”. Note that the potential map suggests that the greater portion of the molecule (the hydrocarbon chain) is non polar. This facilitates its incorporation into lipids.
 5. Make a copy of “vitamin E_AM1” (*click* on ). Name it “vitamin E radical_AM1”. Select **Delete** from the **Build** menu (or *click* on ) and *click* on the hydroxyl hydrogen. **Do not minimize**. You already have an excellent starting structure.
 6. Enter the **Calculations** dialog and change **Multiplicity** from **Singlet** to **Doublet**. *Click* on **OK**. Enter the **Surfaces** dialog. First, remove the request for the electrostatic potential map (*click* on the line: “density potential . . .” and then *click* on **Delete** at the bottom of the dialog). Next, make a request for a spin density surface. *Click* on **Add...**, select **spin** from the **Surface** menu and **none** from the **Property** menu, and *click* on **OK**. Submit the job.
 7. When completed, enter the **Surfaces** dialog and *click* on the line: “spin . . .”. Note that the unpaired electron is not localized on oxygen, but rather is delocalized over the benzene π system. This is why vitamin E forms a stable radical and is able to act as an effective “radical scavenger”.
 8. Remove all molecules and any remaining dialogs from the screen.

Androsterone



Androsterone illustrates the steps involved in building a complex organic molecule with fused rings and several stereocenters. It also provides a good opportunity to compare space-filling models and electron density surfaces as measures of molecular size and shape.

1. Click on . Select **Cyclohexane** from the **Rings** menu, and click anywhere on screen.
2. **Cyclohexane** is still selected in the **Rings** menu. Make certain that the associated icon (at the top of the model kit) indicates “eq” rather than “ax” (meaning that attachment is to be made using an *equatorial* ring position). If not, click on the icon and it will switch from “ax” to “eq”. Click on one of the *equatorial* free valences of the cyclohexane ring on screen. The two six-membered rings will be joined through their *equatorial* valences.
3. Rotate around the bond connecting the two cyclohexane rings such that the *axial* free valences on the connecting carbons are *antito* each other. This bond was the last bond formed and should be encircled by a red marker. (If it is not, click on the bond.) Then *drag* the mouse up and down while holding down both the **Alt** key and the left button). Orient the molecule such that the *equatorial* free valences on the cyclohexane carbons one position removed from those which are already bonded are in front of you and “poised” to form a third cyclohexane ring (in a chair geometry).
4. Select sp^3 carbon  from the model kit and, click on *equatorial* free valences facing each other on both of the six-membered rings you have just joined. The resulting structure should be as follows.



Click on  and, one after the other, *click* on free valences on the two methyl groups you have just added which are in closest proximity. This will lead to a third six-membered ring. *Click* on . All three six-membered rings should now be in chair geometries and the stereochemistry should be as in the figure above. If not, you need to start over (select **Clear** from the **Edit** menu), or “undo” the last operation (select **Undo** from the **Edit** menu).

5. *Click* on C(sp³)  in the model kit. *Click* on *equatorial* free valences on two appropriate positions of one of the external six-membered rings (the “C ring”). Two methyl groups will be added, from which the “D ring” is to be formed.
6. sp³ carbon is still selected. *Click* on a free valence on one of the methyl groups added in the previous step to make it an ethyl group. By appropriate bond rotations, position the “methyl” and “ethyl” groups such that two free valences are in proximity.
7. *Click* on . One after the other, *click* on the two free valences which have been made nearly coincident in the previous step. A bond will be drawn forming a five-membered ring. *Click* on ; another refined (intermediate) structure will appear. All that now remains is to add a carbonyl group on the “D ring”, and to place the hydroxy and methyl substituents.
8. *Click* on C(sp³)  in the model kit. *Click* on the appropriate *axial* free valence involving the “C” and “D” rings, and then on the proper *axial* free valence involving the “A” and “B” rings.
9. *Click* on the O(sp³)  in the model kit. Add hydroxy to the appropriate *equatorial* position on the “A ring”, and to the carbon on the “D ring” which is to become the carbonyl carbon.

Click on . Click on free valences on carbon and on oxygen associated with the hydroxy group just added to the “D ring”. A (distorted) carbonyl group will be formed. Click on  and then on .

10. Androsterone incorporates several chiral centers. To assign them as R or S, select **Configure...** (**Model** menu) and *check* **R/S** under “Atom” in the dialog which appears. Click on **OK**. R/S labels are attached to each of the chiral centers. (You can remove them by selecting **Labels** from the **Model** menu.)
11. Select **Calculations...** from the **Setup** menu. Inside the dialog, specify calculation of an equilibrium geometry at the AM1 semi-empirical level. Exit the dialog and submit the job. Name it “androsterone_AM1”. Once completed, examine the output. Note the large number of geometrical variables and the small number of optimization cycles required.

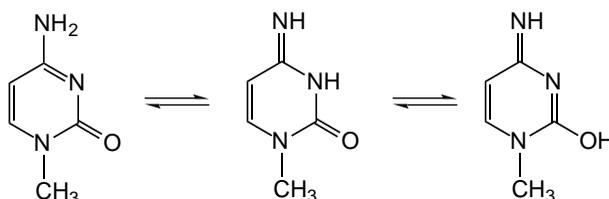
12 to 14 optional

Compare the volume of a space-filling model to that obtained from an electron density surface.

12. Select **Properties** (**Display** menu). This leads to the **Molecule Properties** dialog. Note the surface area and the volume of a space-filling (CPK) model.
13. Select **Surfaces** (**Setup** or **Display** menu). Click on **Add...**. Select **density** from the **Surface** menu and **none** from the **Property** menu, and *click* on **OK**.
14. Submit the job. When it has completed, enter the **Surfaces** dialog and *click* the line “density . . .”. Enter the **Properties** dialog, and *click* on any portion of the density surface. Both the surface area and the volume of the electron density surface appear. How do these compare with the corresponding quantities based on the CPK model?
15. Remove androsterone and any remaining dialogs from the screen.

Tautomers of Nucleotide Bases

Protons bound to heteroatoms in heterocyclic compounds are likely to be very mobile in solution and, where two or more heteroatoms are present in a structure, different isomers (tautomers) may be in equilibrium. As a case in point, consider the nucleotide base cytosine (where a methyl group has replaced the sugar-phosphate backbone).



The existence of a low-energy tautomer could have far-reaching consequences, given that cytosine is one of the nucleotide bases and its valence structure is key to hydrogen bonding in DNA. In this tutorial, you will examine the possible tautomers of 1-methylcytosine for evidence of low-energy structures.*

1. Bring up the entry model kit () and build 1-methylcytosine. Start with **Amide** from the **Groups** menu. Select planar trigonal nitrogen (instead of pyramidal nitrogen) for the external amino group. Minimize and *click* on .
2. Note that the word “Tautomer” appears at the bottom right of the screen. This indicates that tautomers exist for the structure you have built. Select **Tautomers** from the **Search** menu (or *click* on the  icon in the **Search** toolbar). Step through the tautomers using the  and  keys at the bottom right of the screen. To put the tautomers in a group, *click* on  to the right of the step keys, and then *click* on **OK** in the dialog which results.
3. Enter the **Calculations** dialog with this group.** Specify a single-point energy calculation using the 3-21G Hartree-Fock

* Note, however, that were the energy of an alternative tautomer only 3 kcal/mol higher than that for the “normal” structure, this would translate into a relative abundance of only about 1% at room temperature. Thus, any alternative tautomers would need to be very close in energy to the lowest-energy tautomer to have noticeable effect.

** 1-cytosine which you built remains on screen. Close it.

model. Also, select **AM1** from the menu to the right of “Start from” to indicate that semi-empirical geometries will be employed.* Make certain that **Global Calculations** is *checked* before you *click* on **Submit** at the bottom of the dialog. Name the job “1-methylcytosine tautomers_3-21G”.

4. After the three calculations have completed, bring up the spreadsheet and *click* on the line corresponding to the “normal” structure for 1-methylcytosine (the one that you originally built). Next, *click* on the header cell corresponding to the leftmost blank column, then *click* on **Add...**, then select **rel. E** from the available properties and **kcal/mol** from the **Energy** menu, and finally, *click* on **OK**. Tautomer energies (relative to the “normal” form) appear in the spreadsheet. Are either of the alternatives close in energy to the normal form of 1-methylcytosine?

5 and 6 optional (cannot be completed with the Essential Edition)

To get a better estimate of relative tautomer energies, perform single-point calculations using the localized MP2 (LMP2) model.

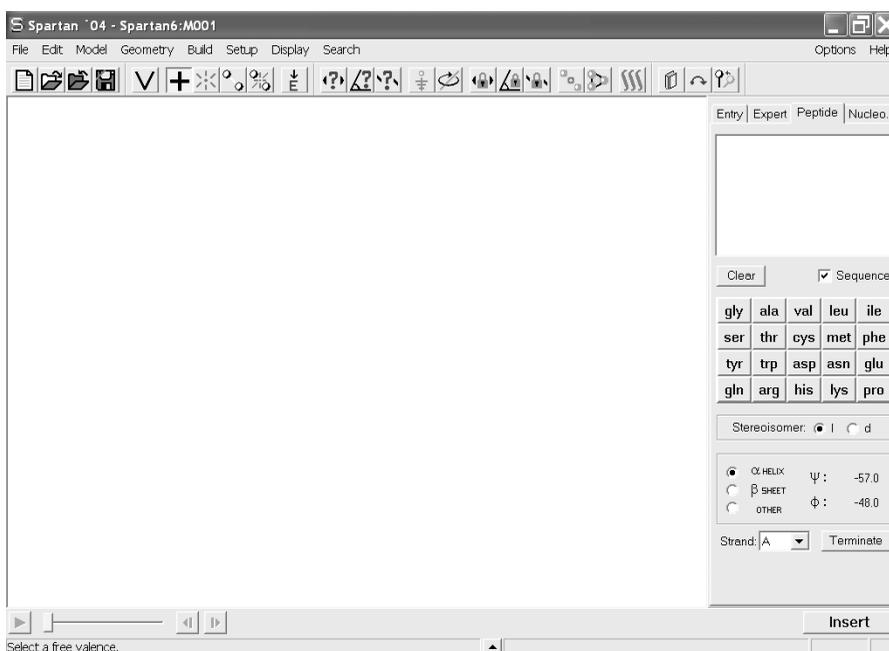
5. Make a copy of “1-methylcytosine tautomers_3-21G” (📄). Name it “1-methylcytosine tautomers_LMP2_6-31Gs”. Enter the **Calculations** dialog with this copy and specify **Single Point Energy** from the menu to the right of “Calculate” and **Møller Plesset, MP2 and 6-31G*** from the three bottom menus. *Check Localized* to the far right of “Calculate”. Also, reset the menu to the right of “Start from” to **Initial**. Finally, make certain that **Global Calculations** is *checked*. Submit the job.
6. When it completes, bring up the spreadsheet (it should contain the relative tautomer energies). Does the use of the correlated LMP2 model change any of the earlier conclusions regarding the likelihood of alternative tautomers?
7. Close whatever molecules and dialogs that remain on screen.

* This is done to save computer time. If you wish to use 3-21G geometries instead, select **Equilibrium Geometry** (instead of **Single Point Energy**) from the menu to the immediate right of “Calculate” and **Initial** (instead of **AM1**) from the menu to the right of “Start from”.

Polyglycine

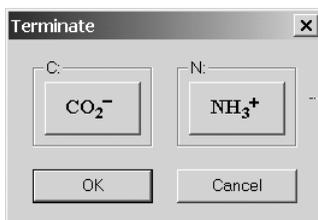
Triglycine and (optionally) decaglycine will be used to illustrate construction of simple amino acid sequences using Spartan'04's peptide model kit, as well as to investigate the role of aqueous media in altering the equilibrium between “neutral” and zwitterionic forms and to show the utility of electrostatic potential maps in conveying information about overall charge distribution.

1. Bring up the peptide model kit by *clicking* on , and then *clicking* on the **Peptide** tab at the top of the entry model kit.



2. Make certain that **Sequence** is checked, and then *click* three times on “gly” (glycine) from the selection of amino acid codes. The sequence “gly-gly-gly” will appear in the box at the top of the model kit.
3. **alpha Helix** near the bottom of the model kit should be selected. If it is not, *click* on it. The backbone ψ and ϕ angles which define an α helix will appear at the right. *Click* anywhere on screen. Triglycine will appear, although it will not be properly terminated.

4. First consider the non-zwitterionic structure. *Click* on **Terminate** in the model kit. The **Terminate** dialog will appear allowing you to specify “C” and “N” terminating groups.



Select **CO₂H** for the C terminating group (*click* on the icon to cycle between groups), and **NH₂** for the N terminating group. *Click* on **OK**.

Amino acids replace atomic fragments, functional groups, rings and ligands as the basic building blocks in the peptide model kit, and these other building blocks are missing. Therefore, most modifications of peptides, aside from modifications in sequence of amino acids and in overall conformation, need to be carried out using either the entry or expert model kits.

5. Select **Freeze Center** from the **Geometry** menu (or *click* on ). *Click* on **Freeze Heavy** at the bottom right of the screen. This indicates that all heavy (non-hydrogen) atoms are not to be moved during molecular mechanics minimization.* *Click* on  to produce a refined structure (subject to the restriction that heavy atoms are kept in place).
6. Select **New Molecule** from the **File** menu. *Click* anywhere on screen. *Click* on **Terminate** inside the model kit and this time select **CO₂⁻** and **NH₃⁺** for “C” and “N” terminating groups, respectively. *Click* on **OK**. *Click* on  and then *click* on **Freeze Heavy** at the bottom of the screen. Finally, *click* on .
7. Dismiss the model kit by *clicking* on . Both forms of triglycine now occupy the same group. Enter the **Calculations** dialog and specify a single-point energy calculation using the

* This is necessary to maintain the idealized helix structure.

Hartree-Fock 3-21G model. Do not change **Total Charge** (from **Neutral**) for the zwitterionic form of triglycine. Even though its Lewis structure incorporates formal “+” and “-” charges, the molecule is neutral. Also make certain that **Global Calculations** is *checked*. Click on **Submit** at the bottom of the dialog. Name the job “triglycine_3-21G”.

8. After the calculations complete, bring up the spreadsheet, *click* on the header cell of an empty column, and *click* on **Add...** at the bottom of the spreadsheet. Select **E** from the list of available properties at the top of the dialog which appears, and **kcal/mol** from the **Energy** menu, and then *click* on **OK**.

Which form of triglycine, zwitterion or non-zwitterion, is favored in the gas phase?

9 to 10 optional (*cannot be completed with the Essential Edition*)

9. Make a copy of “triglycine_3-21G” (). Name it “triglycine in water_3-21G”. Enter the **Calculations** dialog with this copy, and again specify a single-point energy calculation using the Hartree-Fock 3-21G model. Select **Water** for **Solvent** (to the right of “Compute”). Submit the job. When completed (two calculations), bring up a spreadsheet and enter the energies of the two forms.

Which form of triglycine, zwitterion or non-zwitterion, is favored in water? Rationalize any changes in relative energies over the gas-phase results.

10. Remove “triglycine in water_3-21G” and remaining dialogs from the screen.

11 to 15 optional

An electrostatic potential map for the zwitterionic form of a bigger polypeptide, decaglycine, clearly shows charge separation to “explain” why such a structure is not favored in the gas phase.

11. Bring up the peptide model kit.* *Click* seven times on “gly” (glycine) from the selection of amino acid codes. A sequence of ten glycines has now been requested. *Click* anywhere on screen. *Click* on **Terminate** in the model kit and select CO_2^- and NH_3^+ for “C” and “N” terminating groups, respectively, and then *click* on **OK**. *Click* on  and then *click* on **Freeze Heavy** at the bottom of the screen. *Click* on , and then *click* on  to dismiss the model kit.
12. Enter the **Calculations** dialog and specify a single-point energy AM1 calculation. *Check* **Converge** (near the bottom right of the dialog). Semi-empirical calculations on molecules of this complexity often have trouble converging and this option invokes a number of special convergence techniques.
13. Bring up the **Surfaces** dialog and request calculation of an electrostatic potential map. *Click* on **Add...**, select **density** from the **Surface** menu and **potential** from the **Property** menu, and *click* on **OK**.
14. Submit the job. Name it “decaglycine zwitterion_AM1”. Execution will take several minutes due primarily to calculation of the graphic. When completed, again enter the **Surfaces** dialog. *Click* on the line “density potential . . .”. Examine the electrostatic potential map. Recall that colors near red correspond to areas on the surface which are negatively charged (attracted to a point-positive charge), while colors toward blue designate regions of positive charge. Intermediate colors (greens) represent neutral regions. What do you conclude about the environment in which decaglycine wishes to exist?
15. Remove decaglycine and any remaining dialogs from the screen.

* The following instructions assume that this section follows the building of triglycine, i.e., that the box at the top of the peptide model kit already contains a sequence of three glycines. If you are starting from scratch, first make certain that **Sequence** is checked, then *click* ten times on “gly”, then *click* on **α Helix** and finally *click* anywhere on screen.

Propamidine DNA Complex

Small molecules are known to be able to insert themselves into the grooves of DNA. Binding may lead to changes in the structure of the DNA strand (for example, changes in the spacing and orientation of base pairs) and may act to inhibit DNA replication.

This tutorial serves to illustrate how “small molecules” may be manipulated and examined in the presence of “big molecules”. You will first examine the structure of a known complex, specifically that of propamidine binding in the “minor groove” of a dodecamer. This complex originates from the Protein Data Bank (PDB)*, but the PDB file originally brought into Spartan’04 has been parsed into two components of a list (the short strand of DNA and propamidine). Additionally, water molecules have been eliminated. Finally, an electrostatic potential map has been obtained for propamidine. The parsed file (read only) has been written on the distribution media under the name “propamidine DNA complex”**. **

1. Locate and open “propamidine DNA complex” and make a copy with the same name in your working directory. Then, bring up the spreadsheet and reduce it to minimal size in order to see only the names of the individual molecules “DNA strand” and “propamidine”. *Check* both boxes to the right of the molecule names such that both are simultaneously displayed on screen.
2. At the outset, both molecules are displayed as ball-and-spoke models, and it is difficult to locate propamidine inside the DNA strand. Select propamidine (*click* on its name in the spreadsheet) and then select **Space Filling** from the **Model** menu. The two components are now clearly distinguished and you can see how closely they interlock.

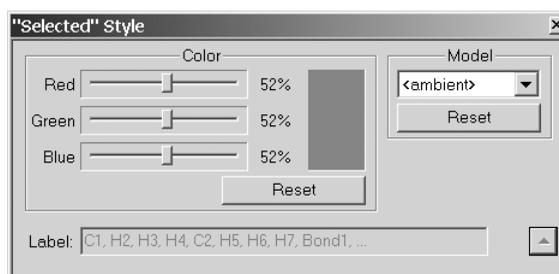
Experiment with different model styles for each of these models. To see how tight the fit really is, display both as space-filling models. Another interesting display is to represent propamidine

* PDB designation 102D. C.M. Nunn and S. Neidle, to be published.

** Under the directory: Program Files/Wavefunction/Spartan04vXYZ/Tutorials

as a space-filling model and the DNA strand using “ribbons”. Select **Hide** and then **Ribbons** from the **Model** menu.

3. Another way to differentiate the components is by color. Bring up both as space-filling models and, while holding down the **Alt** key, *click* on any portion of the propamidine model. The whole model will be selected (indicated by all atoms being tinted “gold”). Select **Properties** from the **Display** menu, giving rise to the “**Selected**” **Style** dialog.



“Paint” propamidine such that it can be easily distinguished from the DNA strand and *click* anywhere on the (propamidine) model to lose the gold tint. Experiment with different colorations. When you are done, reselect propamidine, and *click* on **Reset** inside the “**Selected**” **Style** dialog.

4. Display the DNA strand as a space-filling model and propamidine as a tube or ball-and-spoke model. Select propamidine and then bring up the **Surfaces** dialog (**Setup** or **Display** menu). Note that an electrostatic potential map has been requested but is marked “Pending” (meaning that it has yet to be calculated). Make certain that **Global Surfaces** at the bottom of the dialog is unchecked. Submit the job. When completed, turn “on” the electrostatic potential map by *checking* the yellow box in the dialog. These kinds of displays may be used to supplement conventional models and provide insight into the possible relevance of charge-charge interactions on binding.
5. Remove “propamidine DNA complex” and any remaining dialogs from the screen.

Hydrogen Bonding in Biopolymers

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

This tutorial shows how different molecular models may be employed to visualize an unusual protein-RNA complex*. In particular, it illustrates the display of hydrogen bonds. No calculations are involved.

1. Locate and open “protein RNA complex”** and make a copy. The structure, which comes up as a ribbon display (only), determined from NMR, and several “alternative” conformers have been provided. Step through them ( and ) to see where they are similar and where they differ.
2. Select **Configure...** from the **Model** menu and *click* on the **Ribbons** tab. Select **By Residue** under “Coloring” in the **Configure Ribbons** dialog and *click* on **OK**. The model is now colored according to amino acid/nucleotide base. *Click* on the various “color bands” to see what they are.
3. Select **Hydrogen Bonds** (**Model** menu). Single “dotted lines” represent hydrogen bonds throughout the “protein part” of the complex, and “sets” of dotted lines in the “RNA” part. The latter form the connections between nucleotide bases and the number of lines in each set actually allows you to identify what the bases are.
4. Select **Tube** (**Model** menu). Also, *uncheck* **Hydrogens** from this menu. You can now see in greater detail the structure of the complex and the positions of the hydrogen bonds.
5. Close “protein RNA complex”.

* PDB designation 1A1T. R.N. de Guzman, Z.R. Wu, C.C. Stalling, L. Pappalardo, P.N. Borer and M.F. Summers, *Science*, **279**, 384 (1998).

** Under the directory: Program Files/Wavefunction/Spartan04vXYZ/Tutorials

Chapter 7

Inorganic and Organometallic Molecules

This chapter shows how to construct inorganic and organometallic molecules using Spartan'04's expert model kit. It also describes quantum chemical models suitable for use where transition metals are involved.

The majority of organic molecules are made up of a relatively few elements and obey conventional valence rules. They may be easily built using the entry model kit. However, many molecules incorporate other elements, or do not conform to normal valence rules, or involve ligands. Most important among them are inorganic and organometallic compounds involving transition metals. These need to be constructed using the expert model kit.

Transition-metal inorganic and organometallic compounds may also require different quantum chemical methods from those which are satisfactory for organic molecules. In particular, Hartree-Fock models have proven not to be suitable where transition metals are involved. The PM3 semi-empirical model, which has been parameterized for most transition metals, generally provides a good account of equilibrium geometries, as do density functional models. The latter are also believed to provide a satisfactory account of the thermochemistry of reactions involving transition-metal systems, although there is very little experimental data with which to compare.

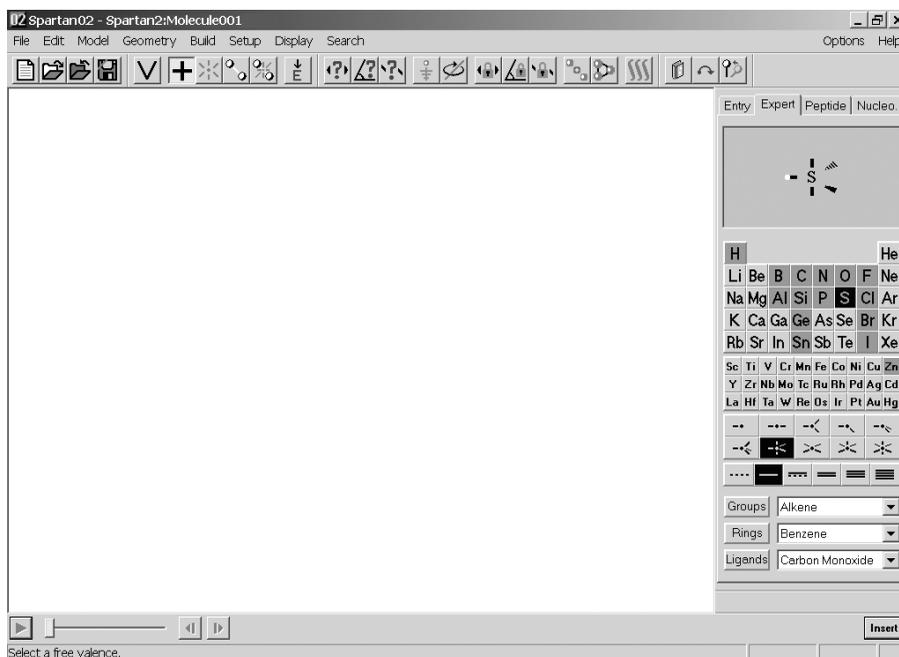
The tutorials in this chapter illustrate construction of inorganic and organometallic molecules, as well as the selection of suitable quantum chemical models.

Sulfur Tetrafluoride



Sulfur tetrafluoride cannot be constructed using Spartan'04's entry 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 expert model kit.

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



The expert model kit comprises a *Periodic Table** followed by a selection of “atomic hybrids”, then bond types, and finally

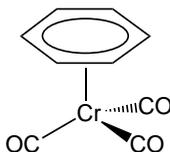
* Not all methods are available for all elements listed. Elements for which a specific method (selected in the **Calculations** dialog) are available will be highlighted in the *Periodic Table* if **Element Overlay** in the **Miscellaneous Preferences** dialog (**Preferences...** under the **Options** menu; see **Chapter 16**) is turned “on”. Note also that elements beyond those listed in the *Periodic Table* may be specified. For a discussion, see **Atom Properties** under the **Display** menu (**Chapter 14**).

- Rings, Groups** and **Ligands** menus (the first two of which are the same as found in the entry model kit).
2. Select (*click* on) **S** in the *Periodic Table* and the five coordinate trigonal bipyramid structure  from the list of atomic hybrids. *Click* on screen. A trigonal bipyramid sulfur will appear.
 3. Select **F** in the *Periodic Table* and the one-coordinate entry  from the list of atomic hybrids. One after the other, *click* on both *axial* free valences of sulfur, and two of the three *equatorial* free valences.
 4. It is necessary to delete the remaining free valence (on an *equatorial* position); otherwise it will become a hydrogen. *Click* on  and then *click* on the remaining *equatorial* free valence.
 5. *Click* on . *Click* on  to remove the model kit.
 6. Select **Calculations...** from the **Setup** menu. Specify calculation of equilibrium geometry* using the Hartree-Fock 3-21G model.**
 7. Submit the job. Name it “sulfur tetrafluoride_3-21G”. When completed, select **Properties (Display** menu) and *click* on an atom, e.g., sulfur. The charge on that atom will appear in the (**Atom Properties**) dialog. Are the charges consistent with covalent or ionic bonding?
 8. Remove sulfur tetrafluoride and any remaining dialogs from the screen.

* 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.

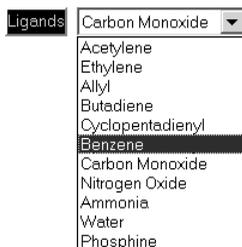
** The 3-21G(*) basis set, which incorporates a set of unoccupied d-type functions, is used in place of 3-21G for the sulfur atom.

Benzene Chromium Tricarbonyl



Comparison of electrostatic potential maps for this system and that of free benzene will allow you to classify $\text{Cr}(\text{CO})_3$ as an electron donor or an electron acceptor “substituent”.

1. Click on  and bring up the expert model kit. Select **Cr** from the *Periodic Table* and the four-coordinate tetrahedral structure  from the list of atomic hybrids. Click anywhere on screen.
2. Click on **Ligands** in the model kit, select **Benzene** from the menu of available ligands.



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

3. Select **Carbon Monoxide** from the **Ligands** menu, and click on the remaining (three) free valences on chromium. Click on  to produce a refined structure.
4. Select **New Molecule** from the **File** menu. The screen will blank. Build benzene and click on . Click on .
5. Select **Calculations...** (**Setup** menu). Specify calculation of equilibrium geometry with the semi-empirical PM3 model. Make certain that **Global Calculations** (at the bottom of the dialog) is checked. You want the calculations to apply to both benzene chromium tricarbonyl and benzene. Click on **OK**.

6. Select **Surfaces** (**Setup** or **Display** menu). *Click* on **Add...** Specify **density** from the **Surface** menu, and **potential** from the **Property** menu, and *click* on **OK**. Make certain that **Global Surfaces** is checked.
7. Submit the job (two separate calculations). Name it “benzene chromium tricarbonyl_PM3”. When completed bring up the spreadsheet (**Spreadsheet** from the **Display** menu), and *check* the box to the right of the label for both entries. This allows the two molecules to be displayed simultaneously on screen. If **Coupled** (**Model** menu) is *checked*, remove the checkmark by selecting it. This allows the two molecules to be moved independently. Orient each molecule so that you can clearly see the benzene face (exposed face in the case of the organometallic).
8. Inside the **Surfaces** dialog, *click* on the line “density potential . . .”. Compare electrostatic potential maps for both free and complexed benzene, with attention to the “exposed face” on benzene.* Is the effect of the Cr(CO)₃ group to donate or to 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?

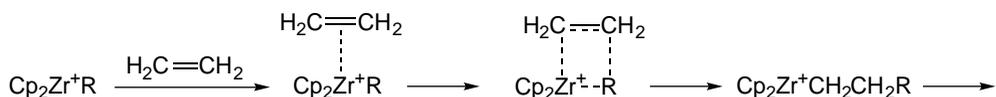
9 optional (*cannot be completed with the Essential Edition*)

9. Repeat the two calculations using density functional theory. Make a copy of “benzene chromium tricarbonyl_PM3” (); name it “benzene chromium tricarbonyl_BP_6-31Gs”. Inside the **Calculations** dialog, specify a single-point energy calculation using the BP/6-31G* model. Submit. When completed, examine the electrostatic potential maps. Are they qualitatively similar to those from the PM3 calculations?
10. Remove all molecules and any remaining dialogs from the screen.

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

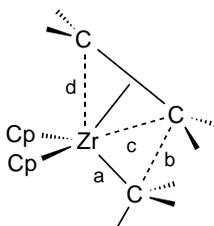
Ziegler-Natta Polymerization of Ethylene

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



In this tutorial, you will use PM3 calculations to obtain a transition state for insertion of ethylene into $\text{Cp}_2\text{ZrCH}_3^+$ and, (optionally), estimate the activation energy using density functional calculations.

- Bring up the expert model kit. Select **Zr** and , and *click* on screen. Select **C** ( is still selected), and *click* on one of the free valences on zirconium. Select **Cyclopentadienyl** from the **Ligands** menu and, one after the other, *click* on two of the free valences on zirconium. Select **Ethylene (Ligands menu)** and *click* on the remaining free valence on zirconium.
- Orient the methyl and ethylene as shown below.



- Constrain the four distances a, b, c, d to 2.35Å, 2.05Å, 2.60Å and 2.35Å, respectively. *Click* on , and repeat the following steps for each of the four “bonds”. *Click* on the bond (or pair of atoms) and then *click* on  at the bottom right of the screen. The icon will change to . Type in the appropriate distance and *press* the **Enter** key. When you are done, *click* on .
- Bring up the **Calculations** dialog, and specify calculation of equilibrium geometry using the PM3 model. You will need to change **Total Charge** to **Cation**. *Check Constraints* to the right of “Subject to”. *Click* on **Submit** at the bottom of the dialog and name the job “Cp2ZrMe cation+ ethylene_PM3”.

5. When the job has completed, again bring up the **Calculations** dialog. Change **Equilibrium Geometry** to **Transition State Geometry**. Remove the checkmark on **Constraints** and *check IR* to the right of “Compute”. *Click* on **Submit**.
6. When the job has completed, bring up the **IR** dialog (**Spectra** from the **Properties** menu and *click* on the **IR** tab) and *click* on the imaginary frequency. Would you describe the process as “concerted” or occurring in discrete steps?

7 to 9 optional (cannot be completed with the Essential Edition)

7. Perform single-point BP/6-31G* density functional calculations to obtain an estimate for the energy barrier for ethylene insertion. Make a copy of “Cp2ZrMe cation+ethylene_PM3” (); name it “Cp2ZrMe cation+ethylene_BP_6-31Gs”. Enter the **Calculations** dialog with this copy, and specify calculation of a single-point energy using the BP/6-31G* density functional model. *Check Pseudopotential* at the far lower right of “Calculate” to specify use of a pseudopotential for Zr associated with the 6-31G* basis set. Remove the checkmark on **IR** (to the right of “Compute”). **Total Charge** should still be set to **Cation**. *Click* on **Submit**.
8. Build both ethylene and Cp₂ZrCH₃⁺ (name them “ethylene_BP_6-31Gs” and “Cp2ZrMe cation_BP_6-31Gs”, respectively). For Cp₂ZrCH₃⁺, start with three-coordinate trigonal Zr, and then add two cyclopentadienyl ligands and a four-coordinate tetrahedral carbon. For each, enter the **Calculations** dialog, and specify a single-point energy with the BP/6-31G* density functional model. Select **PM3** from the menu to the right of “Start From”. For “Cp2ZrMe cation_BP_6-31Gs” (only) *check Pseudopotential*, and set **Total Charge** to **Cation**.
9. Submit both jobs. When they (and the transition-state calculation) have completed, calculate an activation energy for the insertion reaction.
10. Remove all molecules and any remaining dialogs from the screen.

Section III

Features and Functions

This section describes the functions available under the menus incorporated into Spartan'04, and is intended to serve as a general reference to the program. Available molecular mechanics and quantum chemical methods are enumerated, but no commentary is provided as to their performance or computational requirements. Similarly, available graphical displays are enumerated but no description of their use is provided. These issues are treated in detail in “**A Guide to Molecular Mechanics and Quantum Chemical Calculations**”.

Chapter 8

The File Menu

*This section describes operations under the **File** menu. This provides model kits for building new molecules as well as access to the file system to read and write Spartan files. It also provides input and output of a variety of commonly-employed “external” file types, including input of 2D structures (drawings). Operations under this menu also allow construction of custom databases and provide printing of text and on-screen graphics.*

The **File** menu controls reading and writing of the file system, provides initial access to model kits for molecule building, and allows for printing of text and graphical displays.

New	Ctrl+N
Open...	Ctrl+O
Close	
Save	Ctrl+S
Save As...	
New Molecule	
Delete Molecule	
Append Molecule(s)...	
Print...	Ctrl+P
Print Setup...	
Exit	

New (📄)

Brings up the entry model kit and clears the screen. Use of the entry and other model kits is discussed in **Chapter 12**.

Open... (📁)

Opens a file which contains all information associated with a particular molecule (or list of molecules). Displays the molecular structure(s), as well as any graphical surfaces and/or plots which were displayed

prior to the last save operation. **Open...** leads to a file browser from which a single molecule (or list of molecules) needs to be selected.

Spartan can read several different types of files. These include several file types which are “native” to Spartan.

.spartan	Spartan’04 document
.spinput	Spartan input (included in .spartan)
.sparchive	Spartan archive (included in .spartan)
.spproparc	Spartan property archive (included in .spartan)
.sxf	Spartan exchange (use with molecule viewers)
.col	Spartan collection (use with molecule viewers)

It can also read several “non-native” files containing 3D structure information,

.mac	MacroModel
.mol	SYBYL Mol
.mol2	SYBYL Mol2
.pdb	PDB

files containing 2D information (chemical structures),

.sdf	MDL SDF
.skc	MDL SKC
.tgf	MDL TGF

and files containing 1D information.

.smi	SMILES
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Note that the Cartesian coordinates from any of these files may be replaced by coordinates generated on the basis of atomic connectivity alone. This is especially useful for “2D” input (structure drawing), where the Z coordinate in the original file may be zero. Coordinate replacement is accomplished using the **Replace Coords.** button in the **Molecule Properties** dialog (**Display** menu; see **Chapter 14**).

In addition, several graphics file formats are supported.

.bmp	bitmap
.jpg	JPEG
.avi	AVI
.png	PNG

Except for .spartan files, these are all normally hidden from view, and may be seen by selecting “All Files” under the **Files of type** menu at the bottom of the browser.

Close

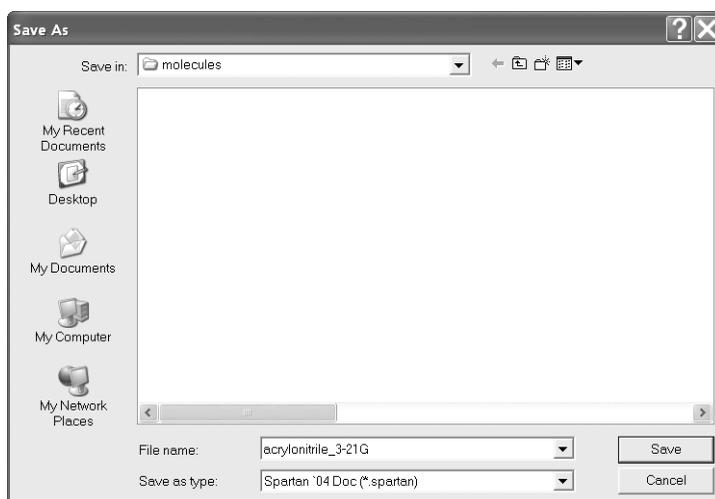
Closes the selected molecule (or list of molecules to which the selected molecule belongs), as well as the spreadsheet and any associated graphical surfaces and/or plots and molecule specific dialogs. A prompt for a name is provided if the molecule has not previously been saved. Notification is also provided if a previously-saved molecule has been altered and verification requested that any changes are to be saved.

Save

Saves the selected molecule (or list of molecules to which the selected molecule belongs) *exactly as it appears on screen*, that is, rendered in terms of a specific structure model and optionally with one or more graphical surfaces, spectra and/or plots displayed. Opening the molecule will bring it on screen exactly as it was last saved. If the molecule has previously been named, **Save** does not lead to any further requests or informative dialogs. Otherwise, **Save** behaves as **Save As...** (see below).

Save As...

Saves the selected molecule (or list of molecules to which the selected molecule belongs) *exactly as it appears on screen*, that is, rendered in terms of a specific structure model and optionally with one or more graphical surfaces, spectra and/or plots displayed under a user-specified name. Files may be either be saved in “native” Spartan’04 format (the default) or in any of the formats listed under **Open**. Selection is made under the **Save as type** menu in the **Save As** dialog.



Save As can also be used to create custom databases of molecular structures, energies and properties, supplementing the **Spartan Molecular Database** provided with Spartan'04 (see **Chapter 15**). In this case, the “.spentry” suffix needs to be specified. Full details relating to database preparation are provided in **Appendix H**.

New Molecule

Brings up the entry model kit and clears the screen. This function is identical to **New**, except that the resulting molecule is appended to the end of the list associated with the molecule which is presently selected.*

Delete Molecule

Deletes from a list of molecules the molecule (or molecules) which is (are) presently selected.

* Examples are provided in the tutorials *Dienophiles in Diels-Alder Cycloadditions* and *Hydration of Carbonyl Compounds* in **Chapter 4**, *Stereospecific Diels-Alder Reactions* in **Chapter 5**, *Polyglycine* in **Chapter 6** and *Benzene Chromium Tricarbonyl* in **Chapter 7**.

Append Molecule(s)...

Appends a file which contains all information associated with a particular molecule (or list of molecules) onto the end of a list of molecules associated with the molecule which is presently selected.*

Append Molecule(s)... leads to a file browser from which one or more molecules (or lists of molecules) needs to be selected.**

Print...

Causes whatever is presently displayed on screen to be printed (according to the specifications made in the **Print Setup** dialog; see below). An output file as well as the contents of a spreadsheet may also be printed. To print output, bring up and select an output window (**Output** under the **Display** menu) and select **Print Output...** (which has replaced **Print...**) from the **File** menu. To print the contents of the spreadsheet, bring up and select a spreadsheet (**Spreadsheet** under the **Display** menu) and select **Print Spreadsheet...** (which has replaced **Print...**) from the **File** menu.

* An example is provided in the tutorial *Carbene Additions to Alkenes* in **Chapter 5**.

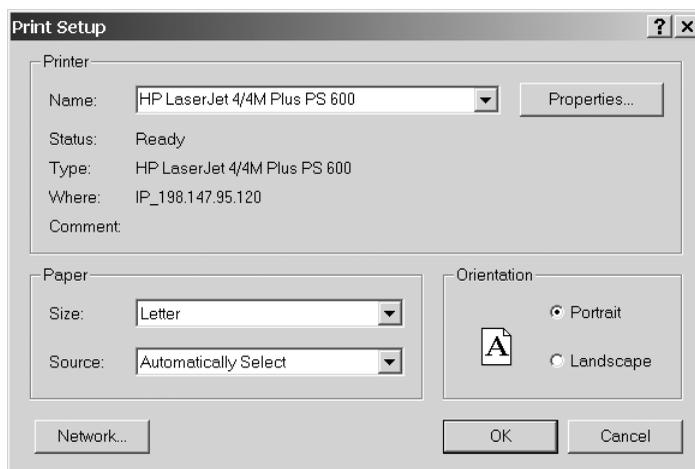
** Alternatively, molecules may be appended onto existing lists either by copy/paste operations using the clipboard or by *dragging* from an external (to Spartan'04) window. Both require that the destination list and its associated spreadsheet be open on screen.

Copy a molecule open on screen into the clipboard by first selecting (*clicking* on) it, and then selecting **Copy** from the **Edit** menu. Alternatively, *click* on its entry ("molecule name") in its spreadsheet, 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. (Note, however, that the clipboard holds only a single "copy", and that any subsequent copy operation overwrites the first.) 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 list), and then selecting **Paste** from the **Edit** menu.

Copy a molecule from an external (to Spartan'04) window, by first selecting the molecule, and then *dragging* it from the external window onto the open spreadsheet (associated with the destination list) inside of Spartan'04. Several molecules can be selected (and *dragged*) at once using the **Shift** and **Ctrl** keys in the usual manner.

Print Setup...

Results in a dialog specific to the available printer.



Specification usually involves designation of paper size, layout and orientation, in addition to degree of enlargement. Color printers may require additional information.

Exit

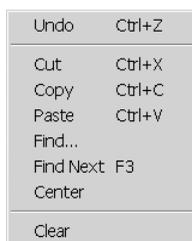
Exits Spartan'04, i.e., clears the screen and closes all molecules in the window. A prompt for a name is provided for each molecule which has not previously been saved.

Chapter 9

The Edit Menu

*This section describes operations under the **Edit** menu. These provide for “undoing” commands, copying screen images to and from the clipboard, finding text and graphics, centering molecules on screen and clearing the screen of the selected molecule.*

Entries under the **Edit** menu serve a variety of functions.



Undo	Ctrl+Z
Cut	Ctrl+X
Copy	Ctrl+C
Paste	Ctrl+V
Find...	
Find Next	F3
Center	
Clear	

Undo

This function “undoes” the last operation (only) from the **Build** menu: **Add Fragment, Delete, Make Bond, Break Bond, Minimize**. Also, “undoes” **Clear** from the **Edit** menu and  from **Transition States (Search menu)**. **Undo** may also be used to undo replacement of a molecule or a set of molecules from the Spartan Molecular Database (see **Chapter 15**). Otherwise, **Undo** is unavailable (dehighlighted).

Cut, Copy, Paste

These three functions transfer items to and from the clipboard. **Cut** moves the selected item to the clipboard. The selected item is deleted. **Copy** copies the selected item to the clipboard. The selected item is unaffected. **Paste** transfers the contents of the clipboard to the designated location. The contents of the clipboard are unaffected. Only one snapshot at a time may be placed in the clipboard; selecting **Cut** or **Copy** again will replace a previous snapshot with a new image.

There are four important uses of the clipboard within Spartan'04.

- (i) Transferring on-screen graphics into other applications such as Microsoft Word® and PowerPoint®.
- (ii) Transferring data from a spreadsheet into other applications such as Microsoft Excel®.
- (iii) Temporary storage of a molecular structure for use in molecule building. This is illustrated in the tutorial *Vitamin E* in **Chapter 6**.
- (iv) Making lists and/or transferring molecules between lists.

Cut and **Copy** operations for the first three require drawing a “selection box”. To do this, first position the cursor slightly above and slightly to the left of the item to be transferred. Then, while holding down both buttons, *drag* the mouse to a location slightly below and slightly to the right of the item to be transferred. Finally, release both buttons.

Further discussions relating to use of the clipboard in molecule building is provided in **Chapter 12** and for list operations in **Chapter 14**.

Find..., Find Next

Find locates a text string defined in the **Find** dialog if an **Output** window 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 the selected molecule on screen, i.e., places the center of geometry at the center of the screen.

Clear

Clears (deletes) all structures and other information for the selected molecule, and brings up a model kit (if one is not already present). If the molecule had previously been saved, no information is actually removed from the file system until the molecule is again saved.

Chapter 10

The Model Menu

*This section describes structure models available under the **Model** menu: wire, ball-and-wire, tube, ball-and-spoke and space-filling (CPK) models, with or without hydrogens, with or without hydrogen bonds indicated and with or without atom labels, as well as ribbon displays for polypeptides and polynucleotides, with or without labels and with or without hydrogen bonds indicated. It also describes functions for configuring atom labels to display element name, R/S chirality, mass number, charge or chemical shift, and for specifying color coding and display style for ribbon labels, as well as for turning “on” and “off” a variety of other labels. Finally, it describes functions which allow model style to be applied globally (to all members in a list) and for models to be manipulated in concert.*

Designation of model display style and model attributes are by way of the **Model** menu.



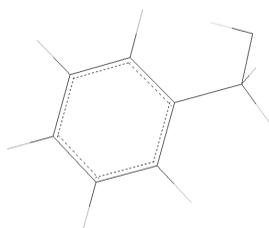
Only one model style (**Wire**, **Ball and Wire**, **Tube**, **Ball and Spoke**, **Space Filling** or **Hide**) may be selected. The selected model is designated by a “•” in front of its entry in the menu. **Global Model**, **Coupled**, **Hydrogens**, **Labels**, **Ribbons** and **Hydrogen Bonds** operate as “toggle” switches. A “✓” in front of the entry in the menu indicates that it is turned “on”.

All of the available structure models, as well as any graphical surfaces, 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 **Miscellaneous Preferences** dialog under **Preferences...** in the **Options** menu (see **Chapter 16**). Both structure models and graphical displays may be presented in 3D stereo. This is also controlled from the **Miscellaneous Preferences** dialog, or from the keyboard (see **Keyboard Functions** in **Chapter 2**).

Wire

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

Wire Model



The bonds are drawn in two colors, one for each of the atoms making up the bond. Default atom colors are given in **Table 10-1**. These apply globally (to all atoms of given type), and may be changed using **Colors** under the **Options** menu (see **Chapter 16**). Colors of individually selected atoms may be set using the **Atom Style** dialog (under **Properties** in the **Display** menu; see **Chapter 14**). All models use the same color scheme for atoms, and provide for the same mechanism of changing colors globally or individually.

Ball and Wire

This display represents atoms by small balls and bonds by wires.

Ball-and-Wire Model

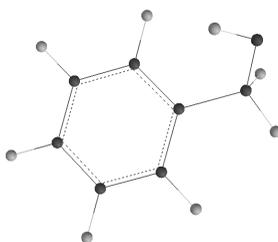


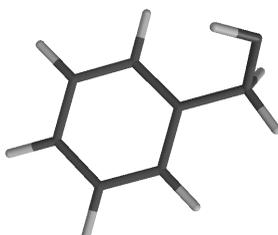
Table 10-1: Default Atom Colors

main group		main group (con't)	
Hydrogen	white	Bromine	orange
Lithium	tan	Rubidium	red
Beryllium	green	Strontium	red
Boron	tan	Indium	tan
Carbon	gray	Tin	gray
Nitrogen	blue-gray	Antimony	tan
Oxygen	red	Tellurium	tan
Fluorine	green	Iodine	tan
Sodium	yellow		
Magnesium	blue	transition metals	
Aluminum	purple	Scandium-Zinc	green
Silicon	gray	Yttrium-Cadmium	green
Phosphorus	tan	Lanthanum-Mercury	green
Sulfur	sky blue		
Chlorine	tan	noble gases	
Potassium	red	Helium	orange
Calcium	red	Neon	orange
Gallium	orange	Argon	orange
Germanium	gray	Krypton	orange
Arsenic	orange	Xenon	yellow
Selenium	orange		

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

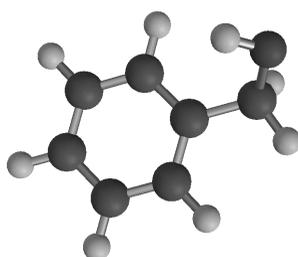


Tube Model

Tubes may either be cylinders or be “split” to represent multiple bonds depending on whether **Split Tubes** in the **Miscellaneous Preferences** dialog (**Preferences...** under the **Options** menu; see **Chapter 16**) is “off” or “on”. As in the wire representations, the bonds are drawn in two colors.

Ball and Spoke

In this display, atoms are represented by balls (the size and color of which depends on atom type), and bonds by spokes.



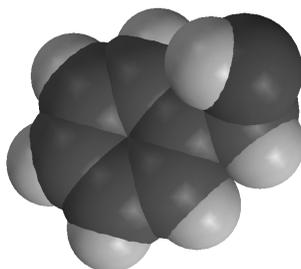
Ball-and-Spoke Model

Spokes may either be cylinders or be “split” to represent multiple bonds depending on whether **Split Tubes** in the **Miscellaneous Preferences** dialog (**Preferences...** under the **Options** menu; see **Chapter 16**) is “off” or “on”. Bond (spoke) color is gray by default but it may be changed using **Colors** under the **Options** menu (see **Chapter 16**). Colors of individually selected bonds may be set using the **Bond Style** dialog (under **Properties** in the **Display** menu; see **Chapter 14**).

Space Filling

This represents the molecule as a composite of spheres, the size and color of which depend on the atom type. Also known as CPK models, space-filling models portray overall molecular size, the sphere radii being chosen as approximating van der Waals contact distances. These radii may be changed in the **VDW Radii Preferences** dialog under **Preferences...** in the **Options** menu (see **Chapter 16**).

Space-Filling Model



The volume and surface area displayed in the **Molecule Properties** dialog (available under **Properties** in the **Display** menu; see **Chapter 14**) correspond to a space-filling model.

Hide

This removes the structure model from the screen where its display may lead to unnecessary crowding, e.g., proteins. A model may be restored by selecting it from the **Model** menu. Caution: **Hide** may result in “loss of a molecule”. It can be “recovered” using the **Page Up** or **Page Down** keys (see **Keyboard Functions** in **Chapter 2**) until its name appears in the window title bar, followed by switching on a model.

Spartan'04 allows different parts of a molecule to be rendered in terms of different model styles and colors. This is useful as a means to focus attention on specific “interesting” regions while drawing attention away from “less-interesting” regions. Regions may be individual atoms and/or bonds or any collection of atoms and/or bonds connected or not. They are selected in the usual manner, either by *clicking* on an individual atom or bond or, with the aid of the **Shift**, **Ctrl** and **Alt** keys, by *clicking* on a set of atoms and/or bonds, or by defining a selection box. Discussion has already been provided in **Chapter 2**.

Once a region has been defined, control of model style and color is by way of the “**Selected**” **Style** dialog under **Properties** in the **Display** menu. This is described in **Chapter 14**, and an example is provided in the tutorial *Propamide DNA Complex* in **Chapter 6**.

Global Model

If *checked*, this signifies that all molecules in a list will share attributes. These include presentation of hydrogens, atom and other labels, hydrogen bonds and ribbon displays. Global model style is controlled from the **Molecule Preferences** dialog (**Preferences...** under the **Options** menu; **Chapter 16**) **Global Model** acts in a toggle manner, i.e., repeated selection switches between “global” and “local” display.

Coupled

If *checked*, this signifies that all molecules in a list selected for simultaneous display will be moved together. **Coupled** is turned “on” following molecule alignment (see **Align Molecules** under the **Geometry** menu; **Chapter 11**). **Coupled** acts in a toggle manner, i.e., repeated selection couples and decouples the molecules.

Hydrogens

If *checked*, this signifies that hydrogens are to be included in the model. Hydrogen removal is useful to simplify the displays of large molecules e.g., polypeptides. Note that some structures, e.g., from the Cambridge Structural Database or from PDB files, may lack hydrogens. These then need to be “grown” before they can be displayed (see discussion under **Molecule Properties** in **Chapter 14**). **Hydrogens** acts in a toggle manner, i.e., repeated selection turns “on” and “off” the display of hydrogens.

Labels

If *checked*, this signifies that labels associated with atoms, ribbons and bonds as well as with other attributes (points, planes, constraints and frozen markers) specified in **Configure...** (see below) are to be displayed in the model. **Labels** acts in a toggle manner, i.e., repeated

selection turns “on” and “off” display of labels. **Labels** is automatically turned “on” following selection of **Apply** or **OK** in the **Configure** dialog (see below).

Ribbons

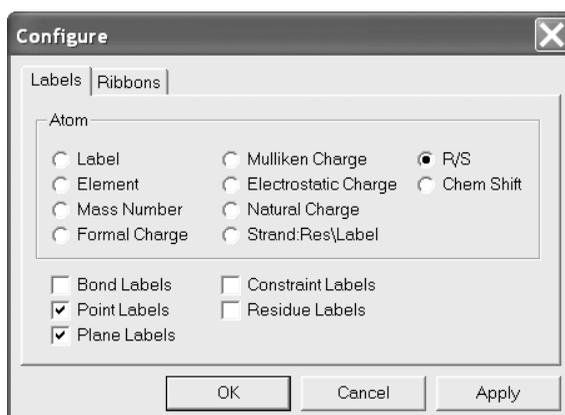
If *checked*, this signifies that ribbons are to be displayed along with the selected model. (If only ribbons are desired, e.g., in proteins, select **Hide** for the model.) **Ribbons** acts in a toggle manner, i.e., repeated selection turns “on” and “off” display of ribbons.

Hydrogen Bonds

If *checked*, this signifies that hydrogen bonds are to be drawn as part of the model. Hydrogen bonds are defined as non-bonded contacts between a nitrogen, oxygen, phosphorous or sulfur and a hydrogen attached to nitrogen, oxygen, phosphorous or sulfur separated by a distance ranging from 1.6 to 2.1 Å and making an X–H--Y (X, Y = N, O, P, S) angle of $>120^\circ$. **Hydrogen Bonds** acts in a toggle manner, i.e., repeated selection turns “on” and “off” display of hydrogen bonds.

Configure...

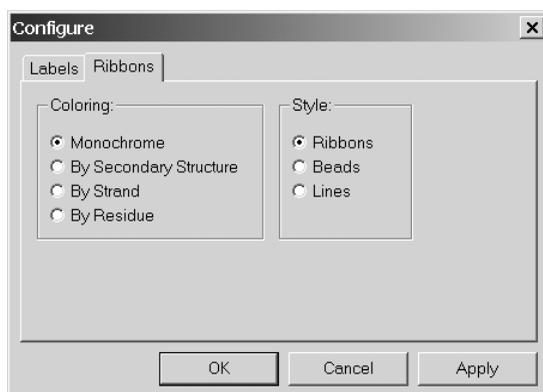
This selects the types of labels attached to atoms and ribbons, as well as turns “on” and “off” labels on bonds, points, planes and constraint markers. (Atom and ribbon labels are turned “on” and “off” using **Labels** and **Ribbons** controls, respectively; see above.) Upon initial entry, the **Configure Labels** dialog will appear.



Atom labels may be selected from among the following (only one selection is allowed): **Labels** (the default, a unique element/number combination, may be changed; see **Atom Properties** in **Chapter 14**), **Element**, **Mass Number**, **R/S** (chirality), **Mulliken Charge**, **Electrostatic Charge**, **Natural Charge**, **Chem Shift**, or **Strand:Residue:Label** (polypeptides and polynucleotides).

Check boxes allow turning “on” **Bond Labels**, **Point Labels**, **Plane Labels**, **Constraint Labels** and **Residue Labels**.

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



Ribbon coloring may be selected from among the following (only one selection is allowed): **Monochrome**, **By Secondary Structure**, **By Strand** or **By Residue**. Ribbon style may be selected from among the following (only one selection is allowed): **Ribbons**, **Beads** or **Lines**.

The 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 and leaves the dialog on screen. Note, that **Labels** (from the **Model** menu) will be turned “on” following either *clicking* on **OK** or on **Apply**.

Chapter 11

The Geometry Menu

*This section describes functions available under the **Geometry** menu. These provide information about geometrical parameters (bond lengths, angles and dihedral angles), as well as provision for defining points and planes, for setting geometrical constraints, for freezing atomic centers, for altering default bond and ring assignments and introducing NOEs in conformational searching and for aligning molecules in a list.*

Information about the geometry of the selected molecule, as well as provision for setting geometrical parameters, is available under the **Geometry** menu. Functions under this menu also provide for defining points and planes, for setting up geometrical constraints, for altering default bond and ring assignments for conformational searching as well as incorporating NOE data, and for aligning molecules in a list.

Measure Distance
Measure Angle
Measure Dihedral
Freeze Center
Set Torsions
Constrain Distance
Constrain Angle
Constrain Dihedral
Define Point
Define Plane
Align Molecules

All functions under the **Geometry** menu require selection of one or more atoms, points, or bonds, or a previously-defined constraint. This is accomplished by *clicking* on the atom or bond or constraint. As atoms are selected, each will be identified by a small gold sphere. As bonds are selected, the two atoms connected by the bond will be identified by small gold spheres. Selection of a distance constraint

results in two atoms being identified by gold spheres, an angle constraint in three atoms identified, and a dihedral constraint in four atoms being identified.

Measure Distance (⌘?)

This obtains and displays the distance (in Ångstroms) between two atoms, whether or not they are bonded, or the length of a bond (in Ångstroms). Selection results in a message at the bottom left of the screen.

Select two atoms, a bond, ...

Clicking on two atoms (points) displays the distance.

Distance(C1,C2) = 1.500 Å

Alternatively, *clicking* on a bond or on a distance constraint displays the bond or constraint length.

Length(Bond1) = 1.531 Å

Measure Distance may also be used for distances involving user-defined points (see **Define Point** in this chapter) and/or user-defined planes (see **Define Plane** in this chapter). In addition, it may be used to alter the distance between atoms (as long as both atoms 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. The distance (length) may be entered into the spreadsheet by *clicking* on to the right of its display.

Note that the altered distance will not be maintained during optimization. If this is what is desired, **Constrain Distance** should be used (see discussion following).

Measure Angle (⌘?)

This obtains and displays the angle (in degrees) involving three atoms, or two connected bonds or a constraint. Selection results in a message at the bottom left of the screen.

Select three atoms, two bonds, ...

Clicking on three atoms, or on two adjacent bonds, or on an angle constraint, displays the angle at the bottom right of the screen.

Angle(C3,C2,C1) = 109.47°

Measure Angle may also be used for angles involving user-defined points (see **Define Point** in this chapter) and/or user-defined planes (see **Define Plane** in this chapter). In addition, it may be used to alter an angle. This applies only where all three atoms are contiguous and are not incorporated into the same ring. The angle may be changed by altering the contents of the box to the right of **Angle (A,B,C) =**, and then *pressing* the **Enter** key. The angle may be entered into the spreadsheet by *clicking* on  to its right.

Note that the altered angle will not be maintained during optimization. If this is what is desired, **Constrain Angle** should be used (see discussion following).

Measure Dihedral

This obtains and displays the dihedral angle (in degrees) involving four atoms, three connected bonds or a dihedral constraint. Note that the dihedral angle is defined as the angle between the plane made by the first three atoms (or the first two bonds) specified, and the plane made by the last three atoms (or the second two bonds) specified. Selection results in a message below the menu bar at the bottom left of the screen.

Select four atoms, three bonds, ...

Clicking on four atoms, or on three adjacent bonds, or on a constraint, displays the dihedral angle at the bottom right of the screen.

Dihedral(C3,C2,C1,H4) = 180.00°

Measure Dihedral may also be used for dihedral angles involving user-defined points (see **Define Point** in this chapter) and/or user-defined planes (see **Define Plane** in this chapter). In addition, it may be used to alter a dihedral angle. This applies only where no more than two atoms are incorporated into a single ring. The dihedral angle may be changed by altering the value inside the box to the right of

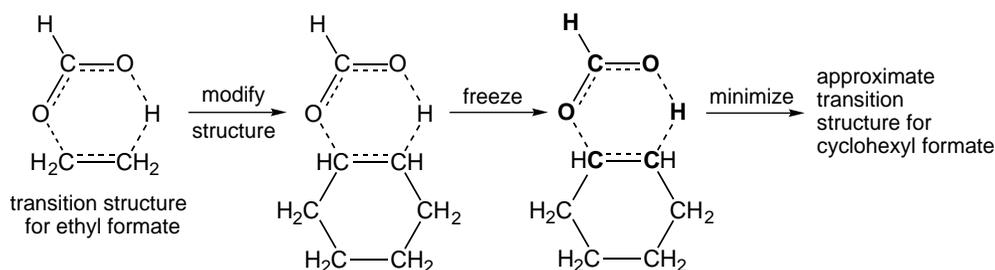
Dihedral (A,B,C,D) = , and then *pressing* the **Enter** key. The dihedral angle may be entered into the spreadsheet by *clicking* on  to its right.

Note that the altered dihedral angle will not be maintained during optimization. If this is what is desired, **Constrain Dihedral** should be used (see discussion following).

Freeze Center

This allows “freezing” of one or more atoms during structure minimization (in build mode) or (optionally) during equilibrium or transition-state geometry optimization, or during a conformational search, or generation of an energy profile using methods under the **Calculations** dialog. Freezing inside the **Calculations** dialog needs to be explicitly indicated (see **Chapter 13**).

Atom freezing is especially useful in a number of situations, among them “guessing” transition-state geometries for reactions which are closely related to those for which transition states are already available. For example, a good guess at the transition state for pyrolysis of cyclohexyl formate might 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.

Select atom to freeze.

Clicking on an atom, or on a free valence**, “freezes” it; *clicking* again “thaws” the atom (or free valence). Buttons at the bottom right

* An example of this is presented in the tutorial *Carbene Additions to Alkenes* in **Chapter 5**.

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

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**).

Another important use of frozen atoms is in conjunction with data resulting from a search of the Cambridge Structural Database (see **Databases** under the **Search** menu; **Chapter 15**). Hydrogen positions are more often than not poorly located in X-ray structures, and X–H bond lengths are commonly as much as 0.1 to 0.2 Å shorter than they should be. Structures incorporating such bond lengths are clearly inappropriate for energy and property calculations and may also be problematic as starting geometries in quantum chemical calculations. One solution is to “freeze” all heavy (non-hydrogen) atoms (**Freeze Heavy**) and then to carry out molecular mechanics minimization using either **Minimize** from the **Build** menu (see discussion in **Chapter 12**) or from the **Calculations** dialog under the **Setup** menu (see discussion in **Chapter 13**).

Frozen atoms are indicated by magenta colored markers (). Whether or not these are included with the model (outside of “Freeze Center” mode) for an individual molecule is controlled from the **Molecule Utilities** dialog available under the **Display** menu (see **Chapter 14**). Global settings are controlled from the **Molecule Preferences** dialog under **Preferences...** in the **Options** menu (see **Chapter 16**).

Set Torsions ()

Spartan’04 automatically identifies bonds and rings for conformational searching and specifies default step sizes. **Set Torsions** allows these defaults to be altered. Selection results in flexible bonds each being marked by a gold cylinder, and flexible rings each being marked by a gold circle around one or more atoms, and a message appears at the bottom left of the screen.

Select bonds or ring atoms.

Clicking on a bond or an atom contained in a ring selects it for rotation. In the case of a ring, “rotation” means that the atom is to be “puckered-up” and “puckered-down” (restricted rotation). The default rotation is provided in a box to the right of **Fold** at the bottom right of the screen. This is typically 2 or 3 for a single bond (step size of 180°

and 120°, respectively) and 3 for a flexible ring. A value of “1” indicates that the bond (ring) is not to be rotated (rotation by 360°). Other integer values may be entered into the box, followed by *pressing* the **Enter** key. The original (default) settings may be retrieved by *clicking* on **Defaults** at the bottom right of the screen.

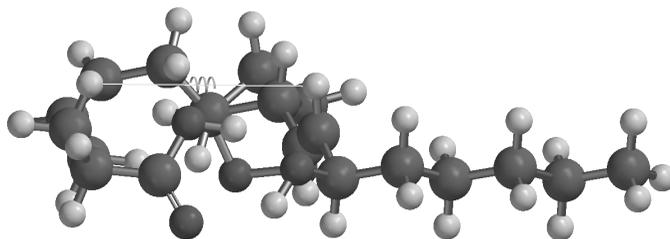
Six-membered rings are treated as special cases with only the two “chair” conformers examined. This is indicated by two circles on opposite atoms. Other conformers can be generated by selecting additional ring atoms.

◀ and ▶ buttons at the bottom right of the screen are available to “step through” the possible single-bond conformers. Any conformer can be selected in lieu of the initial structure. Alternatively, the full set of conformers may be generated by *clicking* on ▾ (to the right of the step keys), and then *clicking* **OK** in the dialog which results. Note, that duplicate conformers have not been removed.

Set Torsions is also used to specify non-bonded distances which need to be kept below a threshold value. These follow for NOE (Nuclear Overhauser Effect) measurements and may be referred to as NOE conditions or simply NOEs. NOEs are specified by *clicking* on two (non-bonded) atoms while holding down the **Shift** key. In response, a message appears at the bottom of the screen.

NOE(H2,H7) = 

Clicking on  changes it to  and enters the default value for the NOE threshold into the box. This value can be changed. A line is drawn between atoms which are to be kept within the threshold value.



Once set, NOEs are used in conformational searching without further user intervention.

Constrain Distance 

Constrain Angle 

Constrain Dihedral 

These allow introduction of one or more geometrical constraints during structure minimization (in “build mode”), and (optionally) during equilibrium or transition-state geometry optimization using any of the available methods under the **Calculations** dialog (**Chapter 13**). The introduction of constraints is useful in a number of situations:

- (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” geometrical parameters, e.g., very long bonds, as for example required in the construction of transition states* and intermolecular complexes.

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

Select two atoms, a bond, ...

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

Constraint(C1,C2) = 

Clicking on  changes it to  and shows the current distance.

Constraint(C1,C2) = 

* An example of this is provided in the tutorial *Ziegler-Natta Polymerization of Ethylene* in **Chapter 7**.

This (constraint) distance can now be changed by altering the contents of the box and then *pressing* the **Enter** key. 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 “off” the constraint and returns the icon to the . Finally, the value of the constraint, which may be different from the value of the current distance, may be entered into the spreadsheet by *clicking* on  to its right.

This sequence of operations (bond identification followed by turning “on” and “off” the constraint) can 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 only upon energy minimization in build mode () , but are optional using methods under the **Calculations** dialog (**Chapter 13**).

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

Constraints may also be modified as well as posted to the spreadsheet from the **Constraint Properties** dialog (available under **Properties** in the **Display** menu; see **Chapter 14**). In addition, a sequence of constraints may be defined (from some initial value to some final value in a given number of steps). This allows generation of an energy profile along a predefined set of coordinates* (see **Calculations** in **Chapter 13**).

Whether or not constraint markers are included with the model (outside of “Constraint Distance, etc. mode”) for an individual molecule is controlled from the **Molecule Utilities** dialog available under the **Display** menu (see **Chapter 14**). Global settings are controlled from the **Molecule Preferences** dialog (**Preferences...** under the **Options** menu; see **Chapter 16**).

* Examples of this are provided in the tutorial *Internal Rotation in Dimethylperoxide* in **Chapter 5**, and the tutorials *Thermodynamic vs. Kinetic Control* and *S_N2 Reaction of Bromide and Methyl Chloride* in **Chapter 6**.

Define Point, Define Ligand 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.

Select atoms. Repeat to terminate.

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

Selecting **Define Point** (or *clicking* on ) while holding down on the **Shift** key, followed by *clicking* on the appropriate atoms, leads to a “ligand point”. This 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 12**) for a discussion.

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

Whether or not points are included with the model for an individual molecule is controlled from the **Molecule Utilities** dialog available under the **Display** menu (see **Chapter 14**). Global settings are controlled from the **Molecule Preferences** dialog (**Preferences...** under the **Options** menu; see **Chapter 16**).

Define Plane ()

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

Select three atoms.

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 point.

Whether or not planes are included with the model for an individual molecule is controlled from the **Molecule Utilities** dialog available under the **Display** menu (see **Chapter 14**). Global settings are controlled from the **Molecule Preferences (Preferences...** under the **Options** menu; see **Chapter 16**).

Align Molecules ()

This allows for alignment of molecules in a list by best matching the coordinates (and optionally atom type) of selected atoms. Selection results in a message at the bottom left of the screen.

Select atoms.

Atoms may be selected by *clicking* on them, at which time they are marked by a red circle. *Clicking* a second time also selects the atom (marking them with two concentric circles) but instructs the alignment procedure to ignore the atom type (atomic number). *Clicking* a third time deselects (and unmarks) the atom. Selected atoms are marked by a single red circle if atom type is to be considered, and by two concentric red circles if atom type is to be ignored. At least three (non-colinear) atoms need to be selected for alignment to be meaningful, and it is recommended that no more than five atoms be selected. Following selection of atoms, *clicking* on the **Align** button at the bottom right of the screen aligns the molecules. Note that atom selection is not lost, and molecules can be “realigned” by again selecting **Align Molecules** and *clicking* on **Align**.

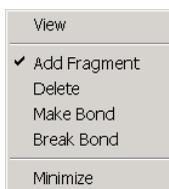
Note that the motions of different molecules in a list are automatically coupled following molecule alignment. They can be decoupled by selecting **Coupled** from the **Model** menu (see **Chapter 10**).

Chapter 12

The Build Menu

*This section describes functions available under the **Build** menu. These include model kits and associated tools for building organic, inorganic and organometallic molecules as well as polypeptides and polynucleotides, in addition to a molecular mechanics procedure for preliminary structure refinement.*

Functions required for building and refining molecules are collected under the **Build** menu.

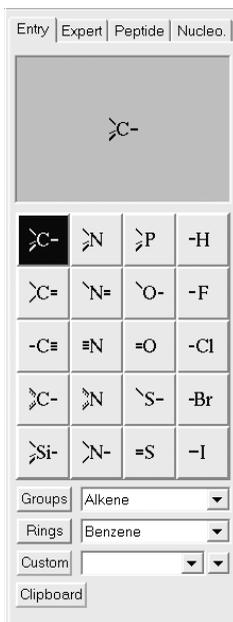


Selection of **Add Fragment** results in display of one of four model kits: an entry model kit for most organic molecules, an expert model kit for organic molecules not easily represented in terms of classical valence structures, as well as inorganic and organometallic molecules, and specialized model kits for polypeptides and polynucleotides. The entry and expert model kits utilize “atomic fragments”, functional groups and rings (and ligands in the expert 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. Once selected, a model kit remains on screen until **View** is selected.

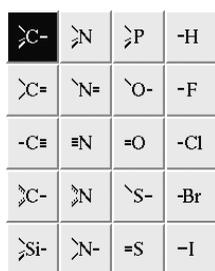
Molecule construction in all four model kits proceeds much in the same manner as a chemist would assemble a structure from a model kit, i.e., pieces are taken from the “kit” one at a time and added sequentially to the molecule under construction.

Entry Model Kit

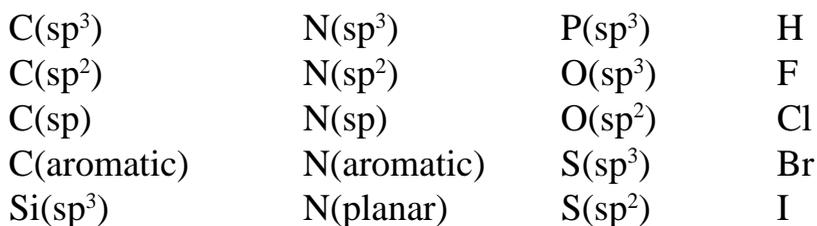
Spartan'04's entry model kit contains a suite of molecule building/editing tools specifically designed to construct most organic molecules.



In the center of the model kit are a selection of “atomic fragments” displayed as icons.



From left to right and then top to bottom, these correspond to:



An “atomic fragment” is chosen by *clicking* on its icon, following which this icon is displayed at the top of the dialog. Once selected, the atomic fragment can be used to initiate building, to add alongside of an existing structure or appended onto an existing molecular fragment. To initiate building, *click* anywhere on screen. To add alongside of an existing structure, first *click* on **Insert** at the bottom right of the screen (or *press* the **Insert** key), and then *click* anywhere on screen. To bond to an existing fragment, *click* on a free valence. Selection of bond type, i.e., single, double, triple or aromatic, in the case of atomic fragments with multiple bond types, e.g., sp² carbon, occurs automatically depending on the nature of the free valence selected.

Three menus inside the entry model kit provide access to a number of pre-built fragments corresponding to common functional groups (**Groups**) and rings (**Rings**), and to additional libraries of functional groups, rings and ligands (as well as any user-defined structures) stored in the file system (**Custom**). The entry model kit also has access to the clipboard (**Clipboard**).

(i) **Groups**

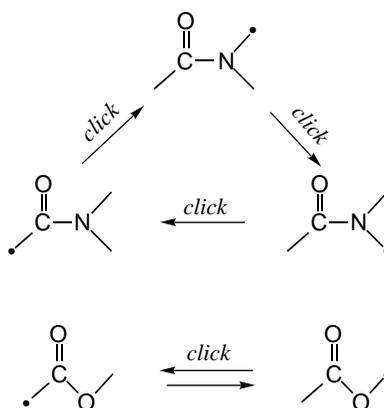
Clicking on **Groups** brings up a menu of available functional groups, and results in an icon of one group from this menu being displayed at the top of the model kit.



A different group may be selected from the menu (its icon will be displayed). Once selected, a functional group may then be used to initiate building by *clicking* anywhere on screen, to add alongside of an existing structure on screen by *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key), and then *clicking*

anywhere on screen, or to add to an existing structure by *clicking* on the appropriate free valence.

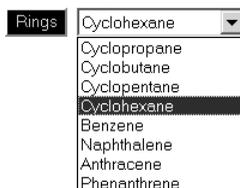
The amide and carboxylic acid groups have two different types of atoms with free valences. The amide group actually has three different free valences, one on carbon and two on nitrogen. The free valence which will be used to connect these groups to a molecule under construction is marked with a “•” (in the icon). The marked position circulates among the possible positions with repeated *clicking* on the icon.



Additional functional groups are found in a library accessible from **Custom** (see discussion following).

(ii) Rings

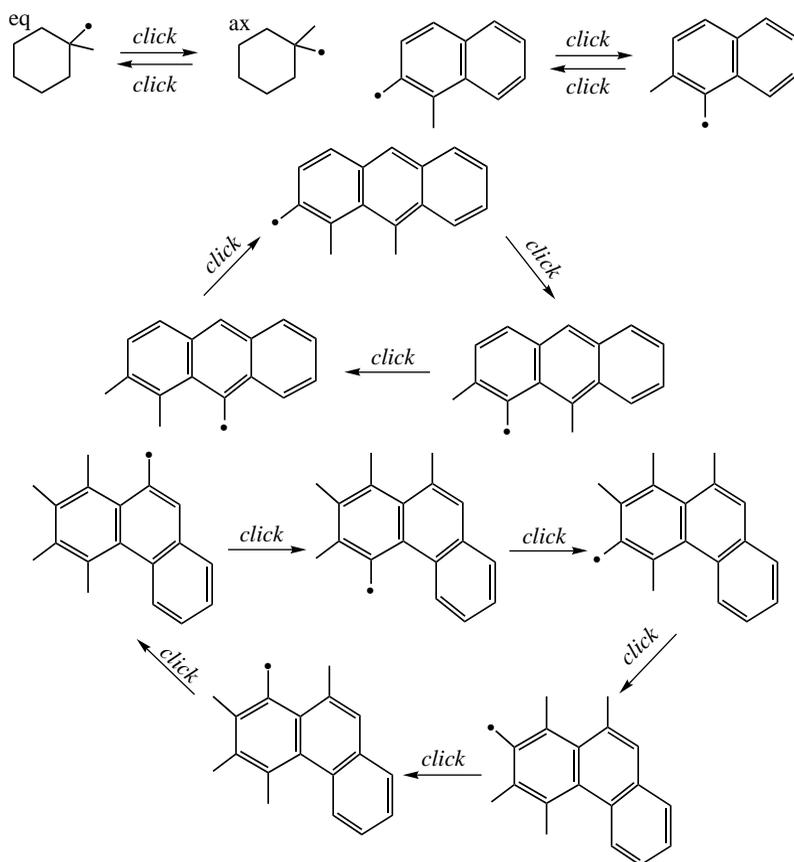
Clicking on **Rings** brings up a menu of available rings, and results in an icon of one ring from this menu being displayed at the top of the model kit.



A different ring may be selected from the menu (and its icon displayed). Once selected, a ring may then be used to initiate building by *clicking* anywhere on screen, to

add alongside of an existing structure on screen by *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key), and then *clicking* anywhere on screen, or to add to an existing structure by *clicking* on the appropriate free valence.

Cyclohexane, naphthalene, anthracene and phenanthrene rings have more than one kind of free valence. The free valence which is used to connect these rings to the molecule under construction is marked with a “•” (in the icon). As with groups, the marked position circulates among the available positions with repeated *clicking* on the icon. Selection of an *axial* or *equatorial* free valence in the cyclohexane ring is indicated by the label “ax” or “eq” appearing alongside the icon.



Note that all rings in this menu are hydrocarbons. Heteroatoms may be substituted using the atom

replacement feature available in conjunction with the entry and expert model kits (see discussion of **General Molecule Building Functionality** following).

Additional rings are found in a library accessible from **Custom** (see discussion following).

(iii) **Custom**

Custom is used to select any molecule or molecular fragment which has been previously saved in Spartan'04's file system for use in molecule building. To access the file system, *click* on the rightmost down arrow key to the right of the **Custom** menu. This gives rise to the usual file browser. Select (*click* on) an entry and *click* on **Open** (or *double click* on the entry). The selected molecule is identified by its name (or by "M001", etc. if no name has previously been supplied) in the menu immediately to the right of **Custom**. Select it and a ball-and-wire model will appear 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 containing the model). Once selected, the molecule or molecular fragment may be used to initiate building by *clicking* anywhere on screen, to add alongside of an existing structure by *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key), and then *clicking* anywhere on screen, or to add to an existing structure by *clicking* on the appropriate free valence. In the latter case, the attachment point (on the molecule in the clipboard) needs to be identified by *clicking* on the appropriate free valence.

Only one entry from the file system is allowed, and selection of a new entry will overwrite the previous entry. However, in the event that the selected entry is a list of molecules, each of the individual members (as identified by their names or by "M001", "M002", etc.), may be

selected in turn (by selecting different entries from the menu to the right of **Custom**).

Upon installation, Spartan'04 is setup for **Custom** to point to a directory "Program Files/Wavefunction/Spartan04vXYZ/Library". This contains (among other things) a selection of "rings" and "ligands".

(iv) **Clipboard**

Clicking on **Clipboard** accesses the clipboard (see **Cut** and **Copy** under the **Edit** menu in **Chapter 9** for discussion of adding to the clipboard). A ball-and-wire model of whatever is on the clipboard is displayed 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 containing the model). Once selected, the molecule or molecular fragment may be used to initiate building by *clicking* anywhere on screen, to add alongside of an existing structure by *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key), and then *clicking* anywhere on screen, or to add to an existing structure by *clicking* on the appropriate free valence. In the latter case, the attachment point needs to be identified by *clicking* on the appropriate free valence in the clipboard.

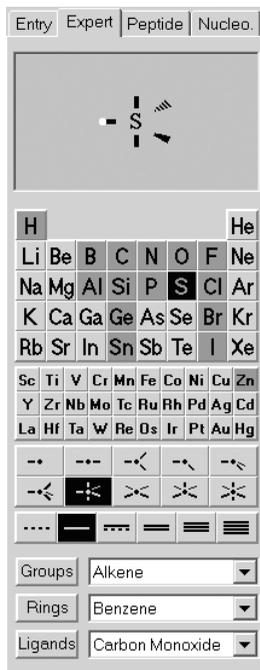
An "empty" clipboard will be signaled by:



Expert Model Kit

Spartan'04's expert model kit allows construction of a much wider class of molecules (including inorganic and organometallic species) than permitted using the entry model kit. Structures which violate conventional bonding rules may also be constructed, as this model kit purposefully provides no checking. The expert model kit is reached by *clicking* on the tab marked **Expert** which is located at the top of the entry (or peptide or nucleotide) model kit. (Return to the entry, peptide

or nucleotides model kit is accomplished by *clicking* on the **Entry**, **Peptide** or **Nucleotide** tab, respectively, in the expert model kit).



At the top of the model kit is a *Periodic Table* covering the first four rows of main-group elements, and all three rows of transition metals.* Main-group elements appear at the top and transition metals at the bottom.

H							He		
Li	Be	B	C	N	O	F	Ne		
Na	Mg	Al	Si	P	S	Cl	Ar		
K	Ca	Ga	Ge	As	Se	Br	Kr		
Rb	Sr	In	Sn	Sb	Te	I	Xe		
Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn
Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd
La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg

If **Element Overlay** (**Miscellaneous Preferences** dialog under **Preferences...** in the **Options** menu; see **Chapter 16**) is *checked*, elements which are available for the selected level of calculation (**Calculations** dialog under the **Setup** menu; see **Chapter 13**) will be highlighted. Immediately below is a selection of atomic hybrids.

* The remaining elements may be specified using the **Atom Properties** dialog under the **Display** menu (see **Chapter 14**) although computational models may not be available.



Following this, is a selection of bond types.



Further down the model kit below the buttons marked **Groups**, **Rings** and **Ligands** (the first two of which are the same as found in the entry model kit).

Selection of atom type is effected 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. Once fully specified, the “atom” (atom type + atomic hybrid) can be used to initiate building, to add alongside of an existing structure or to append onto an existing molecular fragment. To initiate building, *click* anywhere on screen. To add alongside of an existing structure, first *click* on **Insert** at the bottom right of the screen (or *press* the **Insert** key), and then *click* anywhere 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.



All atoms are initially connected with single linkages. Bond types (partial single, single, aromatic, double, triple or quadruple) may be changed by first selecting the appropriate bond type from those available, then *clicking* on the bond to be changed, and then *clicking* again to institute the change, i.e., *double clicking* on the bond. Bond types have no impact on quantum chemical calculations, but do affect molecular mechanics calculations (including structure minimization in the builder; see discussion following).

Unlike the entry model kit, no valence checking is performed in the expert model kit. The user is free to construct any arrangement of atoms. Note, that molecular mechanics parameters may be poor, and “unreasonable” minimized geometries may result.

Three fragment collections are located inside the expert model kit:

(i) **Groups**

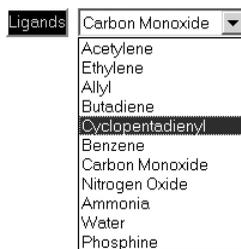
This contains the same groups as in the entry model kit.

(ii) **Rings**

This contains the same rings as in the entry model kit.

(iii) **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 for 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 at the top of the model kit.



A different ligand may be selected from the menu (and its icon displayed), and then used to initiate building by *clicking* anywhere on screen, to add alongside an existing structure on screen, by *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key), followed by *clicking* anywhere on screen, or may be added to an existing structure by *clicking* on the appropriate free valence.

Additional ligands are found in a library accessible from **Custom** in the entry model kit. Ligands may also be built with the help of **Define Point** under the **Geometry** menu (**Chapter 11**).

Peptide Model Kit

Spartan'04 provides a model kit for construction of polypeptides. It is reached by *clicking* on the tab marked **Peptide** which is located at the top of the entry, expert and nucleotide model kits. (Return to the entry, expert or nucleotide model kit is accomplished by *clicking* on the **Entry**, **Expert** or **Nucleotide** tab, respectively, in the peptide model kit.)



At the middle of the peptide model kit are icons designating the amino acids (specified by their usual three-letter codes).

gly	ala	val	leu	ile
ser	thr	cys	met	phe
tyr	trp	asp	asn	glu
gln	arg	his	lys	pro

An amino acid is selected by *clicking* on its three-letter code, following which either an icon of the amino acid is displayed in the box at the top of the model kit, or the three-letter code for the amino acid is appended to the sequence of codes in the box. 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 entry or expert 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.

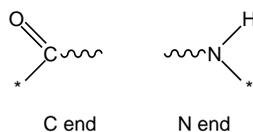
Peptide construction (**Sequence** “on”) is accomplished in three steps:

- (i) Specification of an 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 can 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 can be changed back to l by *checking l*). d amino acids are indicated by “.d” following the code in the box.

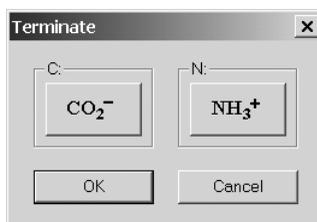
The sequence can be altered by changing the text in the box. Existing amino acid codes can be deleted or changed or new codes can be added. The entire sequence can be specified in this way if desired. Specification of a non-existent code will result in an error message. The sequence can be cleared by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

- (ii) Specification of 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.

- (iii) Termination. The peptide is not yet terminated, and the two ends are still set up for addition of further amino acids, i.e.,



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

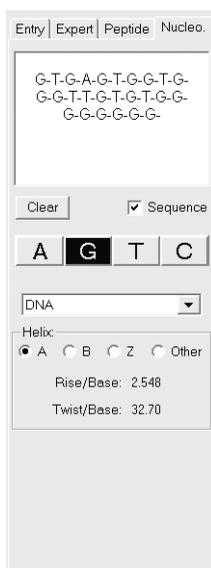


C and N terminating groups may be selected by repeated *clicking* on the C and N icons, respectively. Selection will rotate among the available terminating groups. *Clicking* on **OK** removes the dialog and terminates the polypeptide. *Clicking* on **Cancel** or on  removes the dialog but does not terminate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

The peptide (or single amino acid) may now be used either to initiate building, by *clicking* anywhere on screen or added alongside of an existing structure, by first *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key), followed by *clicking* anywhere 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'04 provides a model kit for construction of polynucleotides. It is reached by *clicking* on the tab marked Nucleotide which is located at the top of the entry, expert and peptide model kits. (Return to the entry, expert or peptide model kit is accomplished by *clicking* on the **Entry**, **Expert** or **Peptide** tab, respectively, in the nucleotide model kit.)



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

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

Immediately below 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 G U C

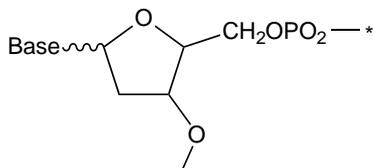
A nucleotide base is selected by *clicking* on its letter, following which either an icon of the base is displayed in the box at the top of the model kit, or the letter for the base is appended to the sequence of letters in the box. Nucleotide bases replace “atoms”, functional groups, rings and ligands 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 entry or expert 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:

- i) Specification of 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 can be altered by editing the contents of the box. Existing base codes can be deleted or changed or new codes added. The entire sequence can be specified in this way if desired. The sequence can be cleared, by *clicking* on **Clear**.
- ii) Specification of helical structure. Once sequencing is complete, a helical structure may be specified by *clicking* on **A**, **B** or **Z**. These correspond to “standard” A, B and Z 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) can now be used to either initiate building, by *clicking* anywhere on screen, added alongside of an existing structure, by first *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key) followed by *clicking* on screen, or joined 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

Bond Rotation/Bond Stretching

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 desired bond. The selected bond is marked by a red cylinder. (The bond connecting the last “atom”, functional group or ring added to the molecule is automatically selected.)
- (ii) Simultaneously *pressing* the **Alt** key and the left mouse button while *dragging* the mouse, for bond rotation, or the **Alt** key and the right mouse button for bond stretching.

Atom/Fragment Replacement

Another function of the mouse is atom replacement. *Double clicking* on an atom (not a free valence) while an atomic fragment in the entry model kit or an atom icon in the expert model kit is highlighted, replaces this atom by the selected atom icon. Atom replacement

functions differently in the entry and expert model kits. In the entry model kit, free valences are adjusted to accommodate the replacement, e.g., replacement of sp^3 carbon by sp^3 oxygen results in two free valences being removed. Atom replacements which violate valence rules or which would disrupt substituents are not permitted. In the expert model kit, atom replacement merely 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 presently available in the peptide and nucleotide model kits.

Chirality Inversion

Finally, *double clicking* on a chiral atom with the **Ctrl** key depressed inverts the chirality of the atom ($R \rightarrow S$ or $S \rightarrow R$). This function is available in all four model kits, but may not be used in some ring systems where its use might lead to unacceptable structures. Where there is only a single chiral center, chirality inversion has the effect of changing enantiomer.

View (V)

This exits build mode, and removes the model kit from the screen (if it was previously displayed). Selection permits display of more than a single molecule on screen. Features available in build mode which actually alter molecular geometry are unavailable.

Initial entry into build mode is by way of **New** under the **File** menu (see **Chapter 8**). **Add Fragment**, **Delete**, **Make Bond**, **Break Bond** and **Minimize** are for modifying existing structures.

Add Fragment (+)

This allows access to the libraries of atomic fragments, functional groups, rings and ligands* as well as the clipboard. If a model kit is already on screen, *clicking* on an atomic fragment, atom, etc., icon, or on the **Groups**, **Rings**, **Ligands**, **Custom** or **Clipboard** button

* Replaced by amino acids in the peptide model kit and nucleotide bases in the nucleotide model kit.

leads to “add fragment” mode. If a model kit is not on screen, selection of **Add Fragment** results in a model kit being placed on screen. This accomplished, a fragment may be used to initiate building by *clicking* anywhere on screen, to add alongside an existing structure on screen by *clicking* on **Insert** at the bottom right of the screen (or *pressing* the **Insert** key) followed by *clicking* anywhere 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.

Delete (✕)

This allows both atom and/or free valence removal from a structure, as well as deletion of points, planes and/or constraints.* Selection results in a message at the bottom left of the screen.

Select object to delete.

Subsequent *clicking* on an atom, free valence, a point, a plane or a constraint 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. See **Using the Mouse in Chapter 2** for a discussion of how to manipulate detached fragments independently or in concert.

Selection of **Delete** does not bring up a model kit nor does it remove a model kit which is present on screen.

Atom deletion can be terminated by selection of any other function.

Deletion may also be accomplished by holding down on the **Delete** key while *clicking* on the atom, free valence, etc.

* **Delete** is also used to delete spectral plots (see **Spectra** under the **Display** menu, **Chapter 14**) as well as individual curves in a plot or entire plots (see **Plots** under the **Display** menu, **Chapter 14**).

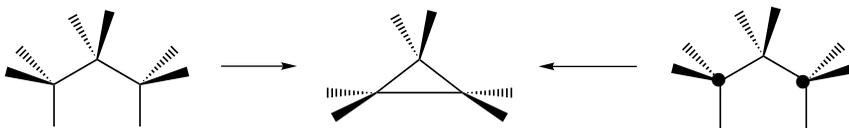
Make Bond ()

This allows bonding between free valences and/or atoms on different centers. Selection results in a message at the bottom left of the screen.

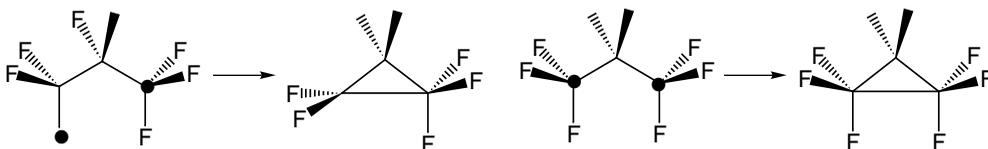
Select two free valences.

Subsequent *clicking* on two free valences (on two 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. If the two atoms involved in the selection are already bonded, this will result in the bond order being increased by one, i.e., single \rightarrow double, double \rightarrow triple. An atom cannot be bonded to itself, and any attempt to do so will lead to an error message.

Where available, free valences are consumed as a result of bond formation, irrespective of whether free valences or atoms are selected.



Note, however, that in the absence of available free valences a bond will still be made between atoms.



This is particularly useful for constructing hypervalent arrangements. Note that free valences can be “protected” without altering the molecule by adding hydrogens to them ( from the entry model kit).

Selection of **Make Bond** does not bring up a model kit nor does it remove a model kit which is already present on screen.

Bond creation can be terminated by selection of any other function.

Break Bond ()

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

Select bond to break.

Subsequent *clicking* on a bond will result in its breaking; the free valences on the respective atoms will automatically be restored. Note that bond breaking may result in detached fragments. See **Using the Mouse in Chapter 2** for a discussion of how to manipulate detached fragments independently or in concert.

Selection of **Break Bond** does not bring up a model kit nor does it remove a model kit which is present on screen.

Bond deletion can be terminated by selection of any other function.

Minimize ()

The molecular geometry resulting from building may be refined using molecular mechanics based on the MMFF force field. Selection results in a message at the bottom left of the screen.*

Minimizer is active.

The strain energy as it is commonly known, displayed at the bottom right of the screen, is continually updated during the minimization process. At any time, minimization may be stopped 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 in Chapter 11**) are enforced during minimization. Also, any frozen atoms (see **Freeze Center in Chapter 11**) remain “frozen”. NOEs are not taken into account.

With a model kit already on screen, **Minimize** reverts back to **Add Fragment** following completion. With no model kit on screen, **Minimize** does not revert to **Add Fragment**.

* Outside of “build mode”, and if there are results which will be destroyed as a result of structure minimization, selection leads to a warning message.

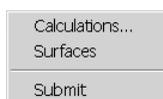
Chapter 13

The Setup Menu

*This chapter describes functions available under the **Setup** menu. These specify molecular mechanics calculations, semi-empirical calculations, Hartree-Fock molecular orbital calculations, and correlated calculations, including local density calculations, density functional calculations, Møller-Plesset calculations and coupled cluster calculations for ground-state species, and configuration interaction calculations, local density calculations and (time dependent) density functional calculations for excited-state species. Tasks include calculation of energy, equilibrium structure and conformation, transition-state structure and constructing energy profiles, although not all tasks are available for some methods. A wide variety of all-electron Gaussian basis sets are supported for Hartree-Fock and correlated calculations as are pseudopotentials for calculations on molecules incorporating heavy elements.*

*Functions under the **Setup** menu also permit inclusion of solvent by way of molecular dynamics, specify calculation of IR, NMR and UV/visible spectra, calculation and printing of a variety of molecular properties, and designation of 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. Also provided under the **Setup** menu is a facility for submitting jobs for calculation.*

The **Setup** menu provides access to dialogs for specifying molecular mechanics and quantum chemical calculations, as well as specifying graphical displays and for submitting jobs for calculation.



Calculations...

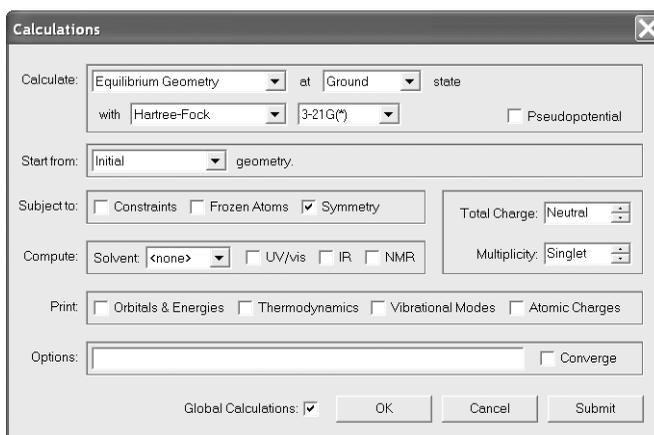
Calculations modules perform: molecular mechanics calculations using the SYBYL and MMFF force fields; MNDO (MNDO/d where second-row and heavier elements are involved), AM1 and PM3 semi-empirical calculations, including PM3 calculations on transition-metal inorganic and organometallic systems; Hartree-Fock molecular orbital calculations; local density calculations; BP, BLYP, EDF1 and B3LYP density functional calculations; Møller-Plesset calculations through fourth order and localized MP2 (LMP2) calculations; coupled cluster calculations; configuration interaction calculations (for excited-state species). A wide selection of basis sets is available, ranging from the STO-3G minimal basis set (Hartree-Fock models only), to the 3-21G split-valence basis set (Hartree-Fock models only), to 6-31G*, 6-31G** and cc-pVDZ polarization basis sets to the more extensive 6-311G*, 6-311G**, cc-pVTZ and cc-pVQZ basis sets. In addition, pseudopotentials for “heavy elements” are available. All basis sets, except for STO-3G and 3-21G may be supplemented with additional polarization functions and/or diffuse functions.

The “Essential Edition” of Spartan’04 for Windows permits calculations on ground-state species only, and with molecular mechanics, semi-empirical and Hartree-Fock models only. STO-3G, 3-21G, 6-31G* and 6-311G* basis sets only, with extensions for additional polarization functions and/or diffuse functions are supported. These and other differences are dealt with at the end of this section.

Discussion of molecular mechanics and quantum chemical methods in general, and of the specific methods available in Spartan’04 is provided in “**A Guide to Molecular Mechanics and Quantum Chemical Calculations**”. This guide also provides a brief discussion of ways in which the different methods may be effectively and efficiently combined, and a description of graphical models and modeling techniques.

Quantum chemical calculations, in particular, also result in a variety of atomic and molecular properties as well as infrared, UV/visible and NMR spectra. These are available for selected models. Finally, solvent effects on molecular energies and properties may be obtained by way of a procedure in which the system is “immersed” in a box of solvent and a molecular dynamics simulation performed.

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



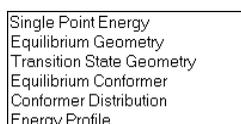
This contains a number of pull-down menus, buttons and text boxes:

(i) **Calculate**

This section contains a series of menus and check boxes which, taken together, specify the task to be accomplished, the electronic state (“ground” or “excited”) the type of calculation, method and basis set to be employed and details specific to each calculation type.



Specification of **Task** is by way of a pull-down menu:



Single Point Energy applies to all methods. **Equilibrium Geometry**, **Equilibrium Conformer**, **Conformer Distribution** and **Energy Profile** apply to all methods except MP3, MP4, CCSD, CCSD(T), G3(MP2), G3, CIS(D) and excited-state density functional methods. **Transition State Geometry** applies to all methods except molecular mechanics methods and MP3, MP4, CCSD, CCSD(T), G3(MP2), G3, CIS(D) and excited-state density functional methods. Additionally, MP2 methods based on localized orbitals are available for single-point energy calculations only. Finally, note that **Equilibrium Conformer** and **Conformer Distribution** revert to **Equilibrium Geometry** in the event that the molecule has only a single conformer.

Specification of **State** (electronic state) is by way of a pull-down menu. The default setting **Ground** may be changed to **Excited** by *clicking* on  to the right of the box and back again to **Ground** by *clicking* on . Different methods are available to handle ground and excited state species. Hartree-Fock, Møller-Plesset as well as a variety of advanced correlated methods are available only for ground-state species, while configuration interaction methods are available only for excited-state species. Density functional methods are available for both ground and excited state species. **State** is ignored for molecular mechanics and semi-empirical calculations.

Specification of **Type of Calculation** is by way of a pull-down menu. Selections in the menu depend on electronic state. For ground-state species:

Molecular Mechanics
Semi-Empirical
Hartree-Fock
Density Functional
Møller Plesset
Advanced Correlated

For excited-state species:

Density Functional
Config. Interaction

All calculation types except for Hartree-Fock require specification of additional information:

Molecular Mechanics	MMFF SYBYL
Semi-Empirical	AM1 PM3 MNDO
Density Functional	BP BLYP EDF1 B3LYP local
Møller-Plesset	MP2 MP3 MP4
Advanced Correlated*	CCSD CCSD(T) G3(MP2) G3
Configuration Interaction	CIS CIS(D)

Except for molecular mechanics and semi-empirical methods, either restricted or unrestricted methods can be used. By default, singlets are described using restricted methods and non-singlets are described using unrestricted methods. The default selections may be overridden using the **Scf** keyword (see **Appendix C**).

Except for molecular mechanics and semi-empirical methods, a basis set needs to be specified.** For Hartree-Fock methods:

STO-3G 3-21G(*) 6-31G* 6-31G** 6-31+G* 6-311G* 6-311+G**

* A number of other advanced correlated methods are available, and may be entered directly into the **Options** box: CCSD(2), OD, OD(T), QCCD, QCCD(2), QCISD, QCISD(T) and G2.

** A number of other basis sets are available, and may be entered directly into the **Options** box: 6-31G or 6-311G followed by: (d), (d,p), (2d), (2d,2p), (2df, 2pd), (3d, 3p), (3df, 3pd); 6-31G or 6-311G with “++” inserted before G; cc-pVDZ and cc-pVQZ.

3-21G refers to use of the 3-21G representation for first row, main-group elements as well as for transition metals, but use of the 3-21G^(*) basis set which incorporates a set of d-type functions for second-row and heavier main-group elements.

For all other methods:

6-31G*
6-31G**
6-31+G*
6-311G*
6-311+G**
cc-pVTZ

The combination of a method, e.g., B3LYP, and a basis set, e.g., 6-31G*, constitutes a **theoretical model** or more simply a **model**. The nomenclature is to separate method and basis set by a “/”, e.g., B3LYP/6-31G*. By convention, specification of Hartree-Fock (HF) as a method is optional and specification of basis set alone refers to Hartree-Fock models, e.g., both HF/6-31G* and 6-31G* refer to combination of the Hartree-Fock method and the 6-31G* basis set. Methods without basis sets, e.g., MMFF (molecular mechanics) and PM3 (semi-empirical) are themselves models.

An additional control, **Localized**, appears only where a single-point energy using the MP2 model has been requested. If *checked*, **Localized** signifies that an MP2 calculation is to be based on Hartree-Fock orbitals that have been localized. This reduces computation time by a small amount (the reduction becomes greater with increasing molecular size), but leads to significant reduction in required memory and disk. The resulting method is referred to as localized MP2 or LMP2.

An additional control, **Density**, appears only where a single-point energy using either MP2 or CIS models has been requested. If *checked*, **Density** signifies that the post-Hartree-Fock density matrix is to be evaluated (in addition to the energy). This leads to a significant increase in computation time, but is required if properties

(dipole moments, charges, etc.) or graphical surfaces are to be based on the post-Hartree-Fock wavefunction (rather than on the Hartree-Fock wavefunction). Post-Hartree-Fock density matrix evaluation is required (and is performed automatically) for equilibrium and transition-state geometry determination. The control is not available for localized MP2 models.

If *checked*, **Pseudopotential** signifies that a pseudopotential is to replace the all-electron basis set for heavy elements. In effect, this limits description of heavy elements to valence electrons only.* Pertains to Hartree-Fock, density functional, Møller-Plesset and advanced correlated (except G3(MP2) and G3) calculations only, and only for third-row and heavier elements. Does not pertain to STO-3G and 3-21G basis sets. For availability and description of pseudopotentials in Spartan'04, consult the on-line help facility (**Chapter 17**).

An additional control, **IRC** (Intrinsic Reaction Coordinate), appears when a transition-state geometry has been requested using Hartree-Fock, density functional or MP2 models. If *checked*, **IRC** signifies that the resulting transition state will be used to generate a pathway (an intrinsic reaction coordinate) leading first to reactant and then to product. (It is advisable, although not necessary, to compute the IR spectrum prior to calculation of an intrinsic reaction coordinate.) The full sequence of steps: reactant → transition state → product, will be placed in a file “xxx.IRCn” where “xxx” is the name given to the molecule and “n” is a number (1, 2...). The default number of steps in the sequence (40) may be changed using the keyword “IRCSteps” (see **Appendix C**). **IRC** is not presently available for semi-empirical models. **IRC** is not available in the Essential Edition.

* Some pseudopotentials also take account of electrons occupying the shell immediately below the valence shell.

(ii) **Start from**

Spartan'04 allows calculations from one model to be preceded by equilibrium geometry calculations at another (simpler) model, for example, Hartree-Fock calculations to be preceded by semi-empirical geometry calculations. (This feature does not apply to transition-state geometry calculations.) Available choices depend on the method selected:

molecular mechanics

not available

semi-empirical

Initial MMFF MMFF Conformer

Hartree-Fock

Initial MMFF AM1 PM3 3-21G(*) MMFF Conformer

density functional, Møller-Plesset,
advanced correlated

Initial MMFF AM1 PM3 3-21G(*) 6-31G* MMFF Conformer

In addition, geometry optimization may be preceded by a search for the lowest-energy MMFF conformer. In this case, selection leads to an additional menu specifying the level of calculation to be employed for geometry optimization. The contents of this menu depend on the method selected:

molecular mechanics

not available

semi-empirical

not available

Hartree-Fock

MMFF AM1 PM3 3-21G(*)

density functional, Møller-Plesset,
advanced correlated

MMFF AM1 PM3 3-21G(*) 6-31G*

(iii) **Subject to**

Spartan'04 allows calculations to be carried out in the presence of geometrical constraints or with atoms which have been frozen in place. In addition, Spartan'04 attempts to make full use of symmetry.

If *checked*, **Constraints** signifies use of any previously defined constraints on distances, angles and dihedral angles into equilibrium and transition-state geometry optimization, conformation searching and generation of energy profiles. Does not apply to single-point energy calculations. See **Chapter 11** for information about constraining geometrical parameters.

NOE data are not treated as constraints by Spartan, but rather as “post-calculation filters” in establishing conformer distributions.

If *checked*, **Frozen Atoms** signifies that the coordinates of any atoms that have previously been “frozen” will not be moved during equilibrium and transition-state geometry optimization, conformation searching and generation of energy profiles. Does not apply to single-point energy calculations. See **Chapter 11** for information about freezing atoms. See also discussion in **Chapter 15** regarding the freezing of heavy atoms in structures resulting from a search of the Cambridge Structural database.

If *checked*, **Symmetry** signifies that molecular symmetry is to be employed wherever possible to simplify the calculation. By default **Symmetry** is *checked*.

(iv) **Compute**

Entries under this section request calculation of a number of “important” spectral quantities, as well as solvent

effects using a molecular dynamics model*. Other quantities such as the dipole moment and LogP** which are “less costly” are calculated automatically, whereas calculation of still others may be requested from the **Options** box (see discussion following).

Solvent (*not yet implemented as of version 1.01*)

This accesses a menu which either specifies **none** (gas-phase calculation) or the name of a solvent into which the system is to be immersed, in preface to a molecular dynamics calculation.

The mixed mechanics/quantum mechanics molecular dynamics procedure employed by Spartan'04 to estimate solvent effects on energies and properties comprises the following steps:

1. “Immerse” the system (“substrate”) in a box of the selected solvent such as to maintain the normal density (of the solvent) at room temperature. The box typically contains on the order of 200-300 solvent molecules.
2. Perform a “preliminary” molecular dynamics simulation using “gas-phase” substrate charges, dipole moment, etc. This simulation, as well as the “full” simulation performed in step 4, assumes that both the substrate and the solvent are rigid, and that only intermolecular geometrical variables are explored. Solvents with two or more conformers are treated as (Boltzmann-weighted) collections of the different conformers.
3. Calculate a solvent term to be added to the one-electron Hamiltonian (of the substrate) based on electrostatic

* For gas-phase calculations, the aqueous solvation energy is estimated using the SM5.4 procedure of Cramer, Truhlar and co-workers (C.C. Chambers, G.D. Hawkins, C.J. Cramer and D.G. Truhlar, *J. Phys. Chem.*, **100**, 16385 (1996)). This is added to the “gas phase” total energy and written to the output. This sum is also available in the spreadsheet (see **Chapter 14**).

** LogP is estimated both according to the method of Ghose, Pritchett and Crippen (*J. Computational Chem.*, **9**, 80 (1988)), and of Villar (*J. Computational Chem.*, **6**, 681 (1991); *Int. J. Quantum Chem.*, **44**, 203 (1992)), and written to the output. Both Ghose-Crippen and Villar LogP values may also be brought into the spreadsheet (see **Chapter 14**).

interactions involving the solvent charges and averaged over 20-50 molecular dynamics configurations. Perform a quantum chemical calculation on the substrate using this additional term and obtain a new set of atomic charges, a new dipole moment, etc.

4. Perform a “full” simulation using the new set of charges, etc.
5. As in step 3, calculate a solvent term to be added to the one-electron Hamiltonian and, using this term, perform a quantum chemical calculation on the substrate.

The result is a wavefunction appropriate for the substrate immersed in solvent, from which a total energy* as well as molecular properties and graphical surfaces may be obtained. These take the place of the corresponding gas-phase quantities in the molecule archives, and all references to these archive (from dialogs, the spreadsheet, etc.) refer to the “solvated” system.

Solvent calculations are presently restricted to water and are applicable to all calculation methods which produce a wavefunction. Molecular mechanics calculations, in particular, are excluded.

UV/vis

If *checked*, specifies that a single-point excited-state calculation will be performed (following a ground-state calculation) and that state-to-state energy differences will be reported.

UV/vis calculations are presently restricted to Hartree-Fock models (when the CIS model is used for the excited state) and to local density and density functional models (where the corresponding time-dependent density functional models are used for the excited state).

* The total energy also includes a van der Waals term to account for direct solute-solvent interactions. This is based on an average of representative molecular dynamics configurations.

IR

If *checked*, calculates vibrational frequencies and corresponding normal modes of vibration. These are then available in the output (**Output** under the **Display** menu, see **Chapter 14**) along with selected thermodynamic properties (entropies* and free energies). Vibrational modes may be animated and an IR spectrum displayed from the **IR** dialog accessible from **Spectra** under the **Display** menu (see **Chapter 14**).

Second derivatives required for frequency calculation are evaluated analytically for molecular mechanics, semi-empirical, Hartree-Fock, local density and density functional models. Other models involve numerical differentiation of analytical first derivatives.

NMR

If *checked*, specifies that NMR chemical shifts will be calculated. These are then available in the output (**Output** under the **Display** menu, see **Chapter 14**) as well as from the **Atom Properties** dialog (**Display** menu). ¹³C (proton decoupled) and ¹H (shifts only) spectra may be displayed from the **NMR** dialog accessible from **Spectra** under the **Display** menu (see **Chapter 14**). In both cases, line intensities are assumed to be proportional to the number of equivalent carbons or hydrogens. Coupling constants are not presently available and only Hartree-Fock models are supported.

(v) **Total Charge**

Total charge. The default setting **Neutral** may be changed either by *clicking* on  to the right of the box, and selecting **Anion**, **Dianion**, **-3**, etc. from the menu which appears, or by replacing any menu entry by a

* Note that the vibrational contribution to the entropy goes to ∞ as frequency goes to 0. This is a consequence of the linear harmonic oscillator approximation and is incorrect. Vibrational entropy contributions from frequencies below 300 cm^{-1} should be treated with caution.

numerical value. **Total Charge** is ignored for molecular mechanics calculations.

(vi) **Multiplicity**

Spin multiplicity. The default setting **Singlet** may be changed either by *clicking* on  to the right of the box, and selecting instead **Doublet** or **Triplet** from the menu which appears, or by replacing any menu entry by a numerical value. Multiplicity is 1 for singlets, 2 for doublets, 3 for triplets, 4 for quartets, etc. **Multiplicity** is ignored for molecular mechanics calculations.

(vii) **Print**

Entries under this section, request printing of a number of common quantities. Printing of additional quantities may be requested from the **Options** box (see below).

Orbitals & Energies

If *checked*, writes the molecular orbitals and orbital energies to the output. HOMO and LUMO energies are also available from the **Molecule Properties** dialog under the **Display** menu (see **Chapter 14**), as well as in the spreadsheet (**Chapter 14**).

Thermodynamics

If *checked*, writes thermodynamic quantities to the output. Requires that vibrational frequencies (**IR** under “Compute”) have been calculated. Selected thermodynamic quantities are also available in the spreadsheet (**Chapter 14**).

Vibrational Modes

If *checked*, writes vibrational frequencies and normal modes to the output. Requires that vibrational frequencies (**IR** under “Compute”) have been calculated.

Atomic Charges

If *checked*, writes Mulliken, natural and electrostatic-fit charges to the output. Atomic charges are also available

from the **Atom Properties** dialog (**Display** menu; **Chapter 14**) and in the spreadsheet (**Chapter 14**).

(viii) **Options**

Additional features affecting calculations are invoked using keywords entered into the box to the right of **Options**. Keywords may be either single words or expressions. Keyword=N indicates an integer argument, and keyword=F indicates a real argument. **Appendix C** contains a listing of commonly-used keywords. A more complete up-to-date listing is found under on-line help.

(ix) **Converge**

If *checked*, invokes procedures to assist in convergence. Use of **Converge** will generally increase computation time. **Converge** does not apply to molecular mechanics calculations.

(x) **Global Calculations**

If *checked*, signifies that settings in the **Calculations** dialog are to be applied to all members of the list.

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 right. (**Submit** and **OK** will be deactivated 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.

The **Calculations** dialog in the Essential Edition of Spartan'04 for Windows differs primarily in the "Calculate" section.



"task" ▾
with "type of calculation" ▾ "method" ▾ "basis set" ▾

The **Task** menu is the same but the **Type of Calculation** menu is restricted to molecular mechanics, semi-empirical and Hartree-Fock models.

Molecular Mechanics
Semi-Empirical
Hartree-Fock

The **Basis Set** menu (Hartree-Fock models only) is identical except that pseudopotentials are not available.

Additionally, intrinsic reaction coordinate (**IRC**) calculations, molecular dynamics solvent calculations (**Solvent** under “Compute”) and UV/visible and NMR spectra (**UV/vis** and **NMR** under “Compute”) are not available in the Essential Edition. IR spectra (**IR** under “Compute”) are available, but the required second-derivative calculations are performed numerically rather than analytically and are significantly slower.

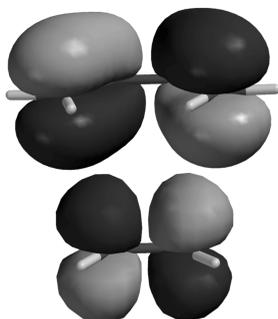
Surfaces

Spartan’04 provides for graphical display of the molecular orbitals, the electron density, the spin density for open-shell systems (the difference in electron densities arising from the α and β spin manifolds), the electrostatic potential (the energy of interaction of a point positive charge with the nuclei and electrons of a molecule), and the local ionization potential (a measure of the ease with which electrons are detached from a region of space). These may be represented as a surface of constant value (an isosurface), and displayed as an “arrangement of dots”, a mesh, or a fully-lighted opaque or translucent solid. Some examples of graphical output in orthogonal projection are reproduced in grayscale in **Figure 13-1**. Surfaces (like other graphical objects) may also be rendered in perspective (see **Chapter 10**) and in stereo (see **Chapter 2**).

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 which have received widespread attention are those based on the electron density surface (depicting overall molecular size and shape). For example, the electrostatic potential may be mapped onto a surface of electron density, yielding an electrostatic potential map, which portrays both steric and electrostatic characteristics. Mapping is via the use of color; colors toward blue represent one extreme value of a property and colors toward red represent the other extreme.

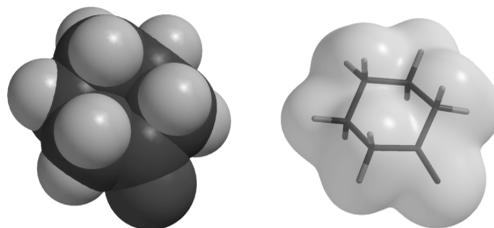
Figure 13-1: Examples of Graphical Displays Available in Spartan'04

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



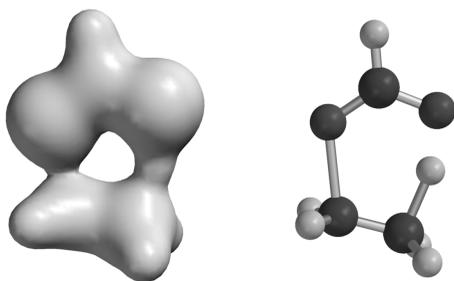
showing interaction of the HOMO of 1,3-butadiene and the LUMO of ethylene.

Space-filling model and electron density surface (0.002 electrons/au³) of cyclohexanone,



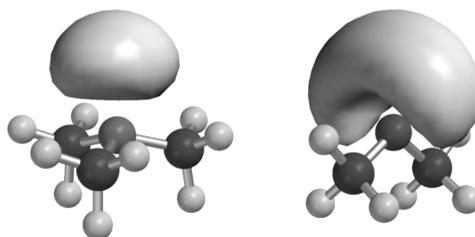
showing overall molecular size and shape.

Electron density surface (0.08 electrons/au³) of transition structure for pyrolysis of ethyl formate,



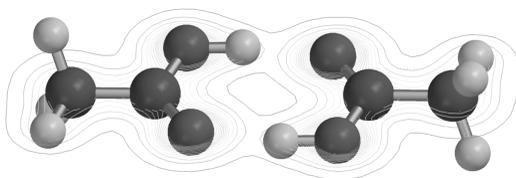
showing bonding in the transition state.

Electrostatic potential surfaces (-10 kcal/mol) of trimethylamine (left) and dimethyl ether (right),



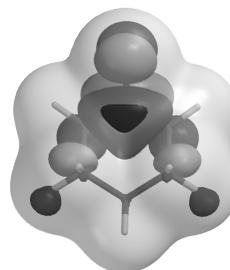
showing the lone pairs on nitrogen and oxygen, respectively.

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.

Finally, calculated quantities may also be displayed as two dimensional contour plots (“slices”). Unlike surfaces and maps, these can be manipulated (translated and rotated) independently of the molecular skeleton. An example of a slice display is provided in **Figure 13-1**.

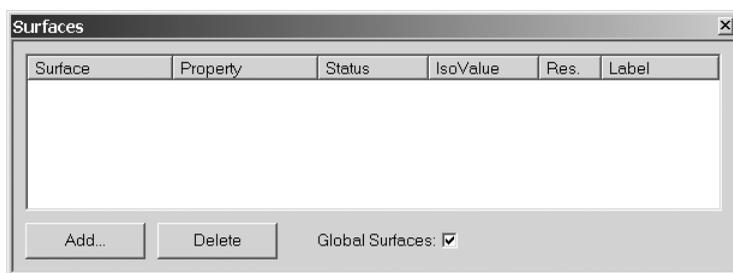
Several different surfaces, maps and slices may be simultaneously displayed. This allows visual comparison of different surfaces, of different properties or both. In addition, any of the usual structure representations (skeletal, ball-and-wire, tube, ball-and-spoke and space-filling models) may be displayed along with the encoded surfaces. The total graphical display can become very complex, and selective use of meshes and/or translucent solids (as opposed to opaque solids) may be needed to facilitate visualization.

Discussion of the utility of graphical models for describing molecular structure and chemical reactivity, including numerous examples, is provided in “**A Guide to Molecular Mechanics and Quantum Chemical Calculations**”.

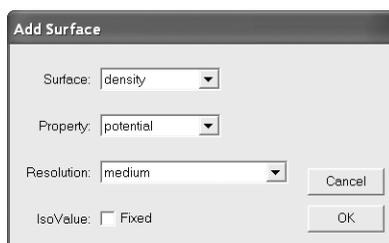
The following are among the most useful graphical surfaces and property maps:

HOMO	demarks electron-rich areas such as lone pairs
LUMO	demarks regions susceptible to nucleophilic attack
density	demarks chemical bonds and indicates overall molecular size and shape
spin density	demarks location of unpaired electrons (radical sites)
electrostatic potential map	quantifies electron-rich/electron-poor regions, for example, as related to acid and base sites
LUMO map	quantifies regions accessible to nucleophilic attack, for example, regio and stereochemical differences
local ionization potential map	quantifies regions accessible to electrophilic attack, for example, regio and stereochemical differences

Selection of **Surfaces** from the **Setup** menu results in display of the **Surfaces** dialog.

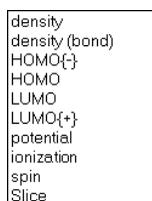


The box at the top of the dialog identifies graphical surfaces for later calculation and display. The **Add...** button at the bottom of the dialog is used to specify new graphical surfaces. *Clicking* on it leads to the **Add Surface** dialog which contains three menus and a check box:



(i) **Surface**

Available surface types appear in a menu to the right of **Surface**.



Available surfaces are the electron density at isosurface values which provide indication of overall molecular size (**density**) and of location of chemical bonds (**density (bond)**), the molecular orbitals (**HOMO{-}**, **HOMO**, **LUMO**, **LUMO{+}**, **SOMO**), the electrostatic potential (**potential**), the local ionization potential (**ionization**) and the spin density (**spin**).

The local ionization potential does not go to zero far removed from the molecule. This makes its use as a surface problematic, although it does not affect its value as a property mapped onto a density surface.

Selection of “**HOMO{-}**” and “**LUMO{+}**” results in display of a box alongside of the entry, e.g.

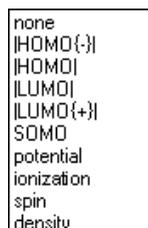


This contains a decrement value from the HOMO and increment value from the LUMO, allowing any molecular orbital to be specified.

Selection of **Slice** designates that the surface will be a 2D plane (a slice) cut through the graphic defined by **Property** (see below).

(ii) **Property**

Properties available for mapping onto surfaces appear in a menu to the right of **Property**.



Available properties are the electron density (**density**), the molecular orbitals (**HOMO{-}**, **HOMO**, **LUMO**, **LUMO{+}**, **SOMO**), the electrostatic potential (**potential**), the local ionization potential (**ionization**) and the spin density (**spin**). **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.

In addition, a “spin button” will be displayed in the event that **Multiplicity** (in the **Calculations** dialog) is set to a

value other than **Singlet**, or if “Scf=unrestricted” has been specified under **Options** in the **Calculations** dialog. Then it will be available (highlighted) only if **HOMO{-}**, **HOMO**, **LUMO** or **LUMO{+}** has been selected for **Surface** or for **Property**. *Clicking* on the button toggles it between **Alpha** and **Beta**. **Alpha** designates that the molecular orbital either to be displayed as a surface or mapped as a property onto a surface will come from the α spin manifold; **Beta** designates that the molecular orbital will come from the β spin manifold.

(iii) **Resolution**

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

low (8x Faster)
medium
intermediate (4x Slower)
high (8x Slower)

Medium resolution generally is of sufficient quality for routine work, low resolution is used to get rough images very quickly, while intermediate and high resolution may be employed to obtain graphics suitable for publication. Both calculation time and disk storage requirements increase significantly with increasing resolution.

(iv) **IsoValue**

This allows a fixed (single-valued) isosurface to be generated in place of a three-dimensional grid of points (from which different isosurfaces, slices and/or property maps can be constructed). While this is less flexible, it is entirely sufficient in the majority of cases, in particular, in dealing with property maps which are nearly always based on a density surface representing overall molecular size and shape. Fixed isosurfaces and property maps based on fixed isosurfaces are much less costly than non-fixed isosurfaces (maps), both in terms of computer time and disk space.

Checking the box to the left of **Fixed** leads to display of the isovalue (0.002 in the case of density). This value may be changed. **Fixed** may not be specified in conjunction with **Slice** as a **Surface**.

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

The process (*clicking* on **Add...**, surface and property selection, *clicking* on **OK**) may be repeated as required.

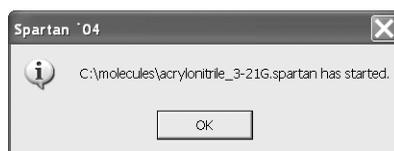
An existing graphic may be deleted from the list by first highlighting (*clicking* on) it and then *clicking* on **Delete**.

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

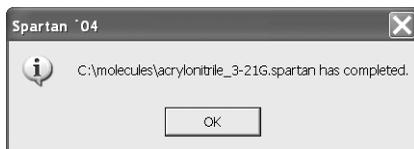
Following setup of a molecular mechanics or quantum chemical calculation, and/or request for generation of graphics files, the required calculations are actually performed using **Submit** under the **Setup** menu. If the job has not previously been named, selection of **Submit** triggers a request for a name (see **Save As...**; **Chapter 8**). After a name has been provided (or if a name already exists) a dialog appears indicating that the job has actually been submitted.*



* Actually, the job is submitted to a job queue and will be submitted for execution only when released from this queue. See **Monitor** under the **Options** menu (**Chapter 16**) for discussion.

*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.



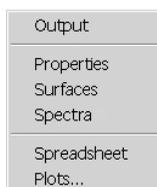
*Click on **OK** to remove it.*

Chapter 14

The Display Menu

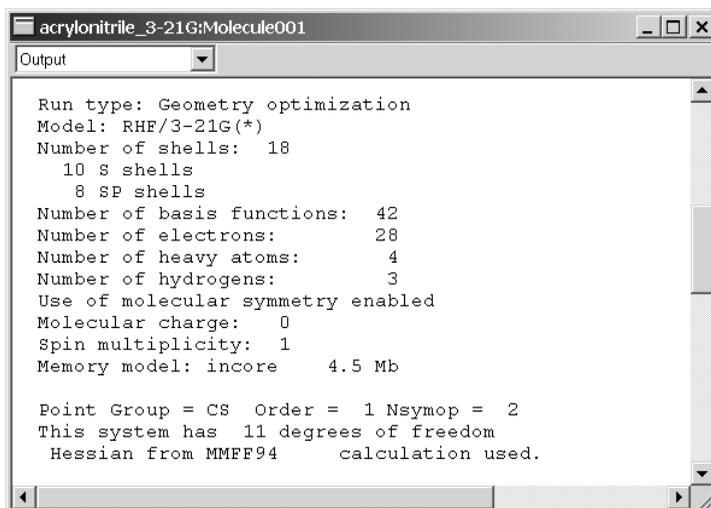
*This chapter describes functions available under the **Display** menu. These provide for text, dialog, spreadsheet and graphical displays following molecular mechanics or quantum chemical calculations. Functions are also available to query a variety of on-screen objects (molecules, atoms, surfaces, etc.), to display infrared and NMR spectra, to animate vibrational motions and to prepare 2D and 3D plots from spreadsheet data.*

A variety of output from molecular mechanics and quantum chemical calculations is accessible by way of the **Display** menu.

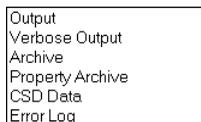


Output

Selection of **Output** opens a window.



A menu at the top left of the window selects the type of output for display.



Output provides normal output, **Verbose Output** provides extended output, **Archive** and **Property Archive** provide the contents of Spartan'04's archive and property archive files*, respectively, **CSD Data** provides the literature reference and other information for data in the Cambridge Structural Database (CSD), and **Error Log** documents execution errors.

The contents of the window may be scrolled in the usual manner and may be “paged up” or “paged down” by *clicking* above or below the scroll bar. The contents may be printed by selecting **Print Output...** from the **File** menu (which has replaced **Print...** when an output window is selected), or copied to the clipboard by selecting **Copy** from the **Edit** menu when an output is selected. **Find...** and **Find Next** functions from the **Edit** menu are also available.

An output window is associated with each molecule (or each list of molecules), and as many output windows as desired may be simultaneously open on screen (although only one may be selected). The selected window may be closed by *clicking* on  at the top right.

Except for CSD data, output from jobs which are currently executing is unavailable from the **Display** menu. The content of the normal output window (“**Output**”) can be viewed using the **Monitor** under the **Options** menu (see **Chapter 16**).

* Entries from the property archive may be brought into the spreadsheet using @prop (property name), where “property name” is the name of the property in the archive. See **Spreadsheet** in this chapter.

Properties

Spartan'04 provides specialized dialogs for reporting and (in some cases) changing the properties of molecules, atoms, bonds, graphical surfaces and geometrical constraints. They also allow for changing default plot styles and limits, as well as for altering the nature of “fitting functions”. Only one **Properties** dialog is permitted on screen, and this dialog refers either to the selected molecule (**Molecule Properties**), or to the selected component (atom, bond, etc.) or attribute (spectra, graphical surface, etc.) of the selected molecule (**Atom Properties**, **Bond Properties**, **Surface Properties**, etc.), or to a plot constructed from data in a spreadsheet (**Plot Properties**, **Curve Properties**, etc.), or to a fitting function (**Regression Properties**). Selection of a different molecule (with a **Properties** dialog on screen) leads to the **Molecule Properties** dialog for the newly selected molecule. Dialogs which refer to components or attributes of the (newly selected) molecule follow by *clicking* on the component or attribute.

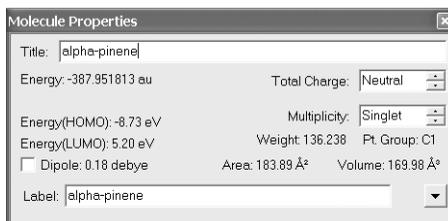
Dialog selection operates in “toggle” mode, with the **Molecule Properties** dialog being in the “neutral” or “off” position. In this position (with the **Molecule Properties** dialog on screen), *clicking* on a component or attribute (of the currently selected molecule) brings up the appropriate **Properties** dialog. For example, *clicking* on an atom brings up the **Atom Properties** dialog. *Clicking* on a different component or attribute brings up the **Properties** dialog for this component or attribute. However, *clicking* a second time on the same component reverts back to the **Molecule Properties** dialog.

Each of the **Properties** dialogs has an associated **Utilities** or **Style** dialog. For example, associated with the **Molecule Properties** dialog is a **Molecule Utilities** dialog. These access additional information about the molecule and its components or attributes, or provide style and color controls unique to the selected molecule, component or attribute. This is useful for highlighting (or dehighlighting) 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. *Clicking*

on a new molecule with a **Utilities/Style** dialog on screen leads to the **Molecule Properties** dialog for that new molecule.

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

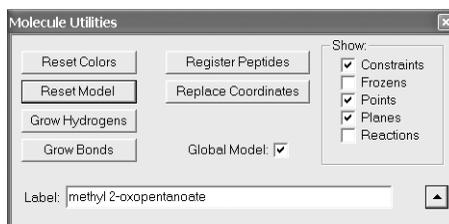
(i) **Molecule Properties**



The **Molecule Properties** dialog displays the total energy (in au), heat of formation in the case of a semi-empirical calculation (in kcal/mol), or strain energy in the case of a molecular mechanics calculation (in kcal/mol), HOMO and LUMO energies (in eV), dipole moment (in debyes), molecular weight (in amu), surface area and volume of a space-filling model* (in Å² and Å³, respectively) and symmetry point group. It also allows for changing total charge and multiplicity (replicating functions in the **Calculations** dialog; see **Chapter 13**) and for providing a title and a label for the molecule. The title is reproduced in the text output, while the label appears in the first column of the spreadsheet (see **Spreadsheet** in this chapter), and is the name given to the molecule as a database entry (see **Appendix H**). Finally, it permits turning “on” and “off” the dipole moment vector.

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

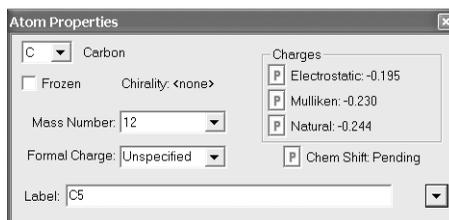
* Surface area and volume calculations for “large” molecules may require “significant” (more than 1-2 seconds) computation time and are not performed (and reported) automatically. In these cases, a button “Find Area and Volume” will appear. *Clicking* on this button will perform the required calculations and report surface area and volume.



This contains controls for resetting model color and style (see **Selected Properties** below), for adding missing hydrogens to the model, for adding “missing” bonds and for providing information about amino acids in polypeptides and for replacing coordinates by those based on atomic connectivities. The dialog also allows turning “on” and “off” display of constraint, frozen atom and reaction markers as well as user-defined points and planes. The dialog provides a second access point to **Global Model**, which, if “on”, forces a common model for all molecules in a list.

(ii) **Atom Properties**

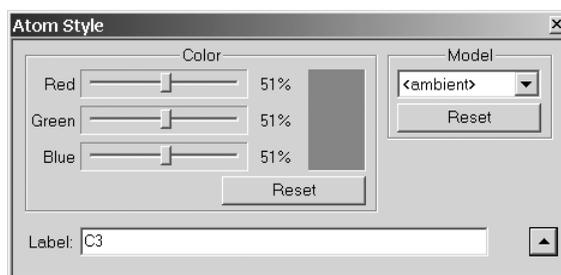
Selection of an atom with a **Properties** dialog on screen, or selection of **Properties** from the **Display** menu following selection of an atom, leads the **Atom Properties** dialog.



This displays the element name and allows for changing of element type, R/S chirality, Mulliken, electrostatic-fit and natural charges (in electrons) and chemical shifts (in ppm relative to the appropriate standards; see **Appendix E**) if the NMR spectrum has been requested. It also allows the atom to be **Frozen** (see **Freeze Center**

in **Chapter 11**), for changing its **Mass Number**, **Formal Charge** and for changing the default atomic **Label**.

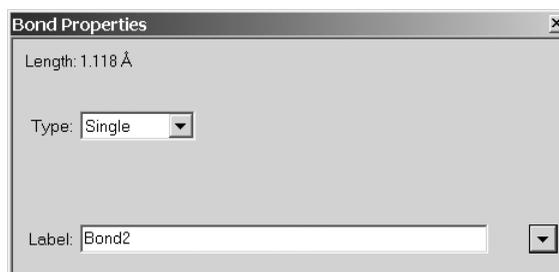
Clicking on  at the bottom right of the **Atom Properties** dialog brings up the **Atom Style** dialog (*clicking on*  at the bottom right of this dialog returns to the **Atom Properties** dialog).



This contains controls for selecting atom color.

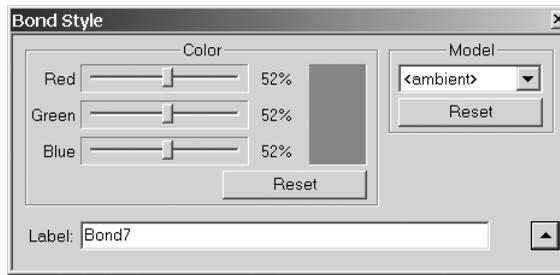
(iii) **Bond Properties**

Selection of a bond with a **Properties** dialog on screen, or selection of **Properties** from the **Display** menu following selection of a bond leads to the **Bond Properties** dialog.



This displays the bond length (in Å). It also provides for changing bond **Type** (also available in the expert model kit; see **Chapter 12**) and the default bond **Label**.

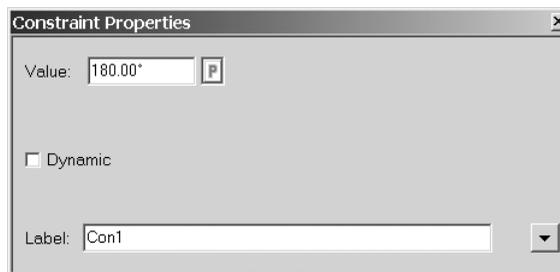
Clicking on  at the bottom right of the **Bond Properties** dialog brings up the **Bond Style** dialog (*clicking on*  at the bottom right of this dialog returns to the **Bond Properties** dialog).



This contains controls for selecting bond color.

(iv) **Constraint Properties**

Selection of a constraint marker with a **Properties** dialog on screen, or selection of **Properties** from the **Display** menu following selection of a constraint marker, leads to the **Constraint Properties** dialog.



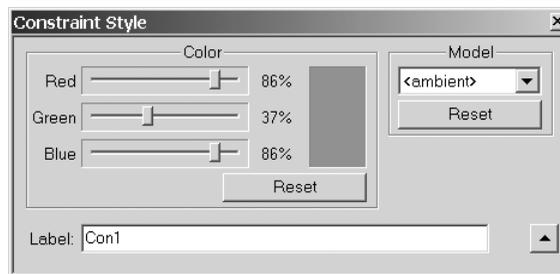
This allows setting the **Value** of the selected constraint, posting the constraint value to the spreadsheet, as well as for changing the default constraint **Label**. *Checking Dynamic* leads to an expanded dialog.



This allows specification of a series of constraints in order to generate an energy profile (see **Calculations...** in

Chapter 13). The value of the constraint for the first member of the series is given in the lefthand box to the right of **Value**, and the value of the constraint for the last member of the series is given in the righthand box to the right of **Value**. The number of members in the series is given in the box to the right of **Steps**. Upon initial entry, the numbers in both boxes to the right of **Value** will be the same, and **Steps** will be set to **1**. These may be altered as required by typing the desired numbers into the appropriate boxes and then *pressing* the **Enter** key. Note, that an energy profile may involve constraints on more than a single geometrical variable, that is, may involve several variables changed in “lock-step” with one another. In this case, the constraint ranges for the individual variables need to be selected. Note, however, that the number of steps must be the same for each variable.

Clicking on  at the bottom right of the **Constraint Properties** dialog brings up the **Constraint Style** dialog (*clicking* on  at the bottom right of this dialog returns to the **Constraint Properties** dialog).



This contains controls for selecting the color of the constraint marker.

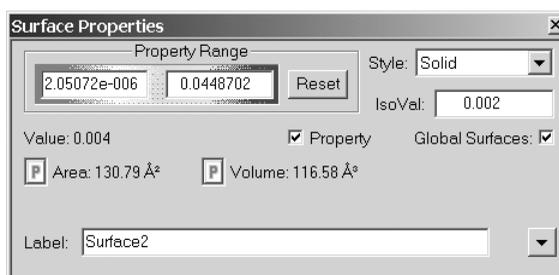
(v) **Point and Plane Properties**

Selection of a user-defined point or plane (see **Chapter 11** 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 changes to point or plane labels. *Clicking* on  at the bottom right of the **Point (Plane) Properties** dialog gives rise to the **Point (Plane) Style** dialogs (not shown), which contain controls for adjusting point and plane colors, respectively.

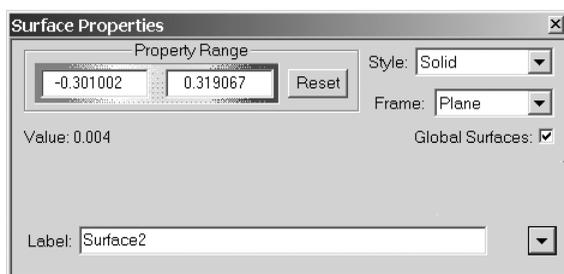
(vi) **Surface Properties**

Selection of graphical surfaces (isosurface, slice or property map) with a **Properties** dialog on screen, or selection of **Properties** from the **Display** menu following selection of a graphical surface, leads to the **Surface Properties** dialog.



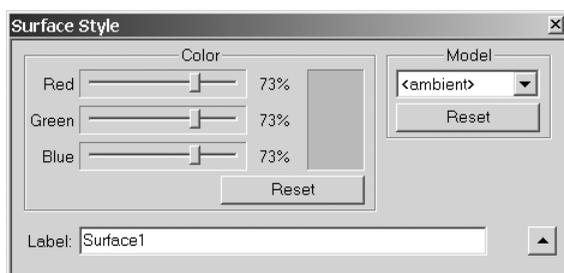
This displays the area (in Å^2) and volume (in Å^3) of the selected surface. It also allows for turning “on” and “off” and setting the range of a **Property** map (on top of an isosurface), for changing **IsoVal** the isovalue (except where a “fixed” isovalue has been requested) and for altering display **Style**. It also provides a second access point to **Global Surface** (also available in the **Surfaces** dialog under the **Setup** or **Display** menu, see **Chapter 13**) which, if “on”, forces common property ranges for property map displays for all molecules in a list. Finally, the dialog reports the “value” of the property at the cursor position on a property map. (To obtain the property value at another position, move the cursor and *click* twice.)

In the event that the selected graphical surface is a slice, a different **Surface Properties** dialog appears.



The **IsoVal** setting in the previous dialog has been replaced by a **Frame** menu which allows choosing the type of slice (plane, cylinder or sphere).

Clicking on  at the bottom right of the **Surface Properties** dialog brings up the **Surface Style** dialog (clicking on  at the bottom right of this dialog returns to the **Surface Properties** dialog).

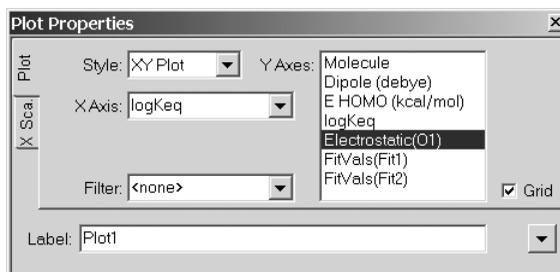


This contains controls for selecting surface color.

(vii) **Curve and Plot Properties**

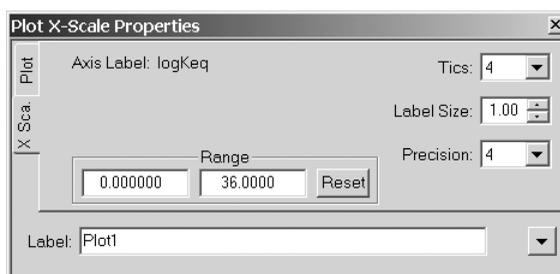
Plots created using data from the spreadsheet (see discussion under both **Spectra** and **Plots...** later in this chapter) may be edited using a set of closely-related dialogs. These refer to “curves”, meaning a single relationship between variables, and “plots” meaning a set of relationships which share one variable (or two variables in the case of a 3D plot).

Selection of a plot frame with a **Properties** dialog on screen, or selection of **Properties** from the **Display** menu following selection of a plot frame, leads to the **Plot Properties** dialog (2D XY plot case shown).



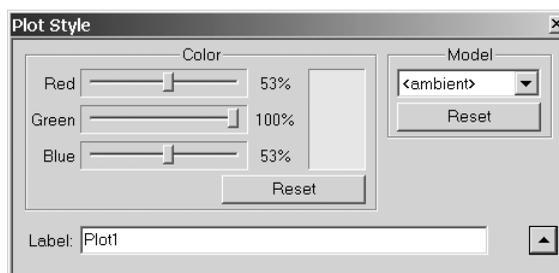
The **X Axis** menu and the **Y Axes** list duplicate functionality under the **Plots** dialog (see **Plots...** later in this chapter). They allow specification of a molecular property to serve as the X axis of the plot and one or more properties to serve as the Y axes. Initial selections may be altered as desired (by selecting a new property from the **X Axis** menu and/or adding or deleting properties from the **Y Axes** list). In addition, a **Grid** can be added to the plot, and the default **Label** can be changed.

The scale along the X axis (horizontal axis) may be altered from default settings (from the minimum to maximum value of the “X variable”) by *clicking* on the **X Sca.** tab at the left of the dialog. This brings up the **Plot X-Scale Properties** dialog (*clicking* on the **Plot** tab at the left of this dialog returns to the **Plot Properties** dialog).



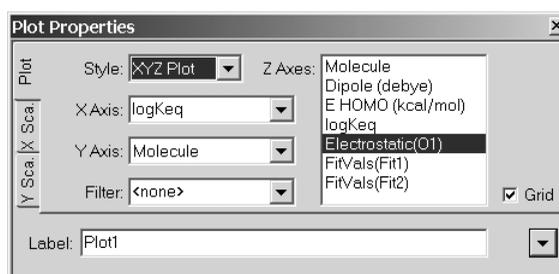
To alter the scale, type in new values inside the **Range** boxes. You need to *press* the **Enter** key following each entry. Controls are also available to alter characteristics of labels associated with the X axis, **Tics** (the number of “tic marks”), **Label Size** and **Precision**.

Clicking on  at the bottom right of either the **Plot Properties** or **Plot X-Scale Properties** dialog brings up the **Plot Style** dialog (clicking on  at the bottom right of this dialog returns to either the **Plot Properties** or **Plot X-Scale Properties** dialog).



This contains controls for selecting the color of the plot frame, as well as the **Label** associated with the X axis.

The **Style** menu in the **Plot Properties** dialog allows shifting between 2D (XY) and 3D (XYZ) plots. Selection of **XYZ Plot** leads to an extended **Plot Properties** dialog.



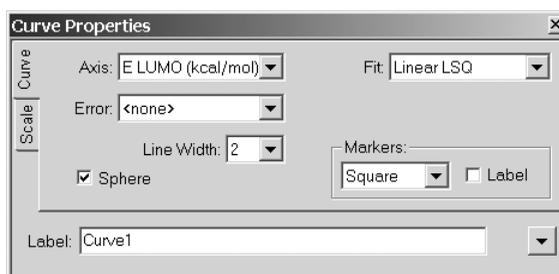
This is identical to the previous (“XY Plot”) **Plot Properties** dialog, except that it includes an additional menu (**Y Axis**) from which one property needs to be selected. In addition, the **Y Axes** list in the “XY Plot” dialog has been renamed to **Z Axes**.

Scales along X and Y axes may be independently adjusted by clicking on **X Sca.** and **Y Sca.** tabs to the left of the dialog. This leads to either the **Plot X-Scale** or **Plot Y-Scale Properties** dialog (clicking on the **Plot**

tab at the left of either of these dialogs returns to the **Plot Properties** dialog). These are analogous to the (**Plot X-Scale Properties**) dialog discussed for XY plots.

The same **Plot Style** dialog available for XY plots may be accessed here (by *clicking* on  at the bottom of the appropriate dialog).

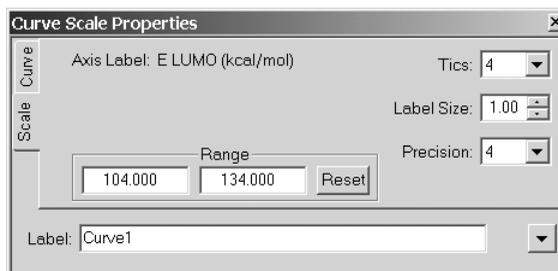
Selection of an individual curve in a plot with a **Properties** dialog on screen, or selection of **Properties** from the **Display** menu following selection of an individual curve, leads to the **Curve Properties** dialog.



This allows for change in the presentation format for the selected curve (or any other curve in the overall plot as specified from the **Axis** menu). This includes designation of the kind of **Markers** for the individual data points, request for **Marker Labels** (molecule names associated with the data points), designation of the kind of **Fit** to the data points and the **Line Width** of the fitting curve. Also optional is a **Sphere** showing the selected point (selected molecule in the list) on the curve. Provision is also made for including **Error** bars on the individual data points (drawn from a column on the spreadsheet).

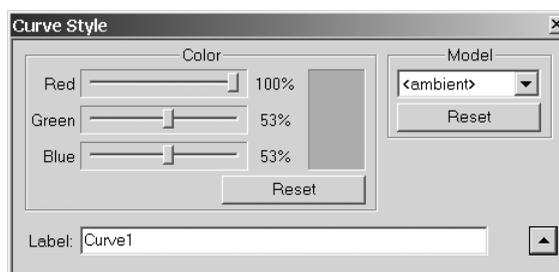
The scale along the Y axis (vertical axis) in the case of a 2D XY plot (or Z axis in the case of a 3D XYZ plot) may be altered from default settings (from the minimum to maximum value of the “Y or Z variable”) by *clicking* on the **Scale** tab at the left of the dialog. This brings up the **Curve Scale Properties** dialog (*clicking* on the

Curve tab at the left of this dialog returns to the **Curve Properties** dialog).



To alter the scale, type in new values inside the boxes underneath “Range”. You need to *press* the **Enter** key following each entry. Controls are also available to alter characteristics of labels associated with the Y or Z axis: **Tics** (the number of “tic marks”), **Label Size** and **Precision**.

Clicking on  at the bottom right of either the **Curve Properties** or **Curve Scale Properties** dialog brings up the **Curve Style** dialog (*clicking* on  at the bottom right of this dialog returns to either the **Curve Properties** or **Curve Scale Properties** dialog).



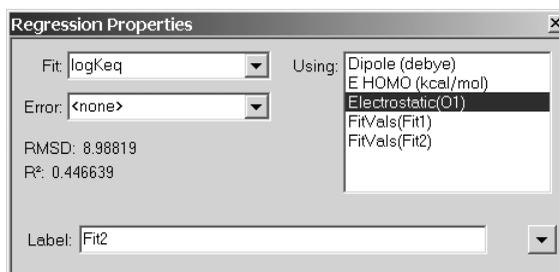
This contains controls for selecting the color of the curve (and the **Label** associated with the Y (or Z) axis).

(viii) **Regression Properties**

After performing a linear regression analysis on data in the spreadsheet (see discussion later in this chapter), a

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

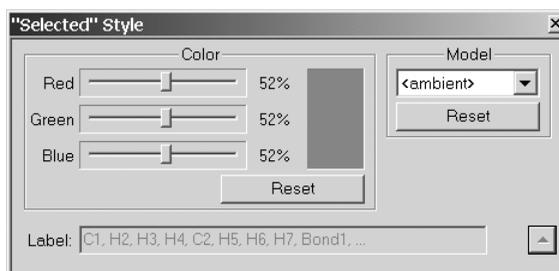
new row, labelled “Fit1”^{*}, appears at or near the bottom of the spreadsheet. This contains information about the fit. *Clicking* on this line with a **Properties** dialog on screen, or selecting **Properties** from the **Display** menu after *clicking* on the “fit line” in the spreadsheet, leads to the **Regression Properties** dialog.



This reports “RMSD” and “R²” error statistics related to the fit, as well as allows for changing “what is to be fit” (**Fit** menu) and “what it is to be fit to” (list to the right of **Using**). Following selection of either or both, the error statistics will update, allowing the user immediate feedback.

(ix) **“Selected” Style**

In addition to “**Style**” dialogs associated with each of the **Properties** dialogs, there is “**Selected**” **Style** dialog (for which there is no corresponding **Properties** dialog). This is accessed either by defining a selection box (see discussion in **Chapter 2**) with a **Properties** dialog on screen, or by selecting **Properties** from the **Display** menu after defining a selection box.



This dialog contains controls for changing the color and model type of whatever is included in the selection box.

Surfaces

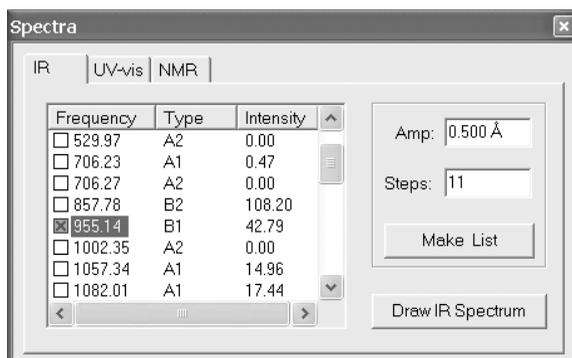
This accesses the same dialog already described in **Chapter 13**.

Spectra

Spartan'04 provides for display of infrared, UV/visible and NMR spectra. (All of these need to have been previously requested from the **Calculations** dialog under the **Setup** menu; see **Chapter 13**.) Access is via a series of tabbed dialogs under **Spectra**.

IR

Clicking on the **IR** tab leads to the **IR Spectra** dialog which not only provides for display of an infrared spectrum, but also allows for animated display of the vibrational modes as well as for generation of a sequence of structures along a vibrational coordinate.



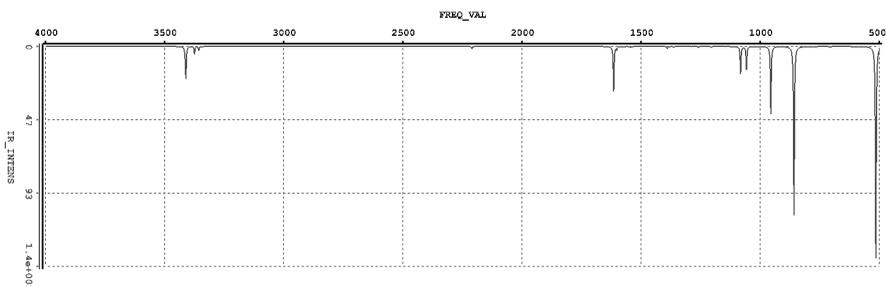
This contains an ascending list of frequencies (in cm^{-1}) together with (infrared) intensities and symmetry labels. Imaginary frequencies, e.g., corresponding to the reaction coordinate for a transition state, will appear first in the list, and will be designated by the letter “i” in front of the frequency value. A frequency is selected for display by *clicking* on it. *Clicking* again deselects it.

The amplitude of vibrational motion (the maximum displacement away from “equilibrium” of any pair of atoms) may be changed from

the default amplitude (0.5\AA which is much larger than appropriate for vibrational motion at room temperature) by altering the contents of the box to the right of **Amp**. The default number of steps which make up the display (11 frames) may be changed by altering the contents of the box to the right of **Steps***. The greater the number of frames, the slower will be the vibration.

Make List creates a list containing a sequence of “Steps” structures corresponding to motion along the selected normal mode. The original molecule is not closed, and several sequences (corresponding to different vibrations) can be created.

A spectrum may be drawn by *clicking* on **Draw IR Spectrum**.

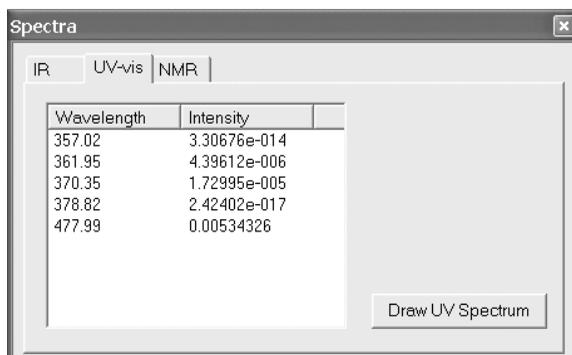


The default range, from 4000 cm^{-1} to 500 cm^{-1} , corresponds to that commonly obtained experimentally, and may be changed by bringing up the **Properties** dialog (**Display** menu), *clicking* on the horizontal axis to bring up the **Plot Properties** dialog, *clicking* on the **X Sca.** tab at the left of the dialog and editing the values under **Range**. The spectrum is treated like any other graphical object, and may be translated and scaled using the appropriate mouse operations. It may not be rotated. The spectrum may be removed from the screen by *clicking* on  (or alternatively by holding down the **Delete** key) and then *clicking* on the spectrum.

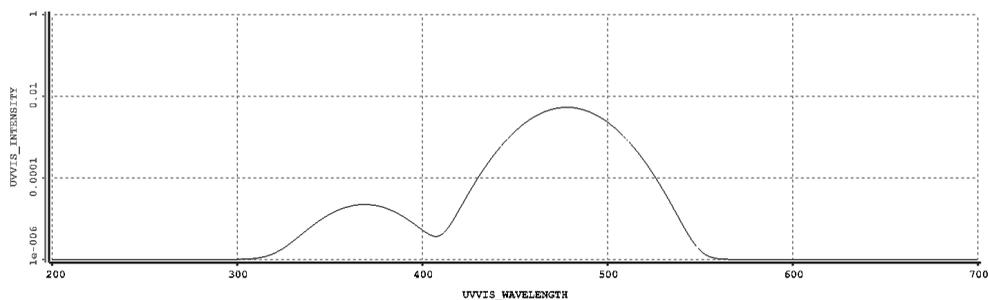
* It is recommended that the number of steps be odd ensuring that the center point corresponds to the actual equilibrium or transition-state structure.

UV/vis

Clicking on the **UV/vis** tab leads to the **UV/vis Spectra** dialog.



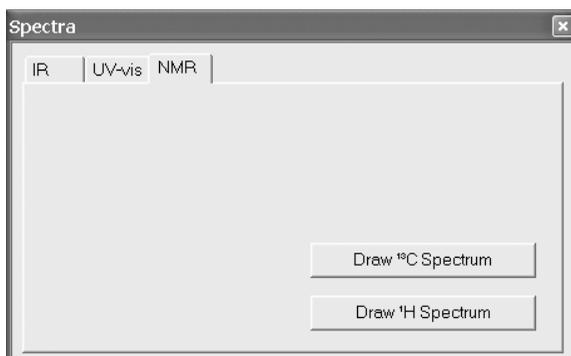
This lists excitation energies (from lowest to highest) together with intensities. A UV/visible spectrum may be drawn by *clicking* on **Draw UV Spectrum**.



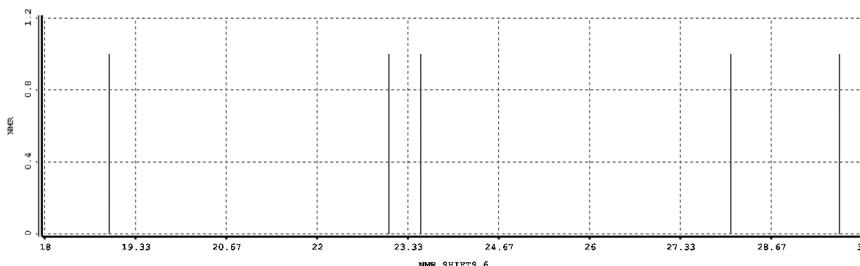
The default range, from 200 nm to 700 nm, corresponds to that commonly obtained experimentally, and may be changed by bringing up the **Properties** dialog (**Display** menu), *clicking* on the horizontal axis to bring up the **Plot Properties** dialog, *clicking* on the **X Sca.** tab at the left of the dialog and editing the values under **Range**. The spectrum is treated like any other graphical object, and may be translated and scaled using the appropriate mouse operations. It may not be rotated. The spectrum may be removed from the screen by *clicking* on  (or alternatively by holding down the **Delete** key) and then *clicking* on the spectrum.

NMR

Clicking on the **NMR** tab leads to the **NMR Spectra** dialog which provides for display of ^1H and ^{13}C NMR spectra.



These are drawn by *clicking* on **Draw ^1H Spectrum/Draw ^{13}C Spectrum** inside the dialog.

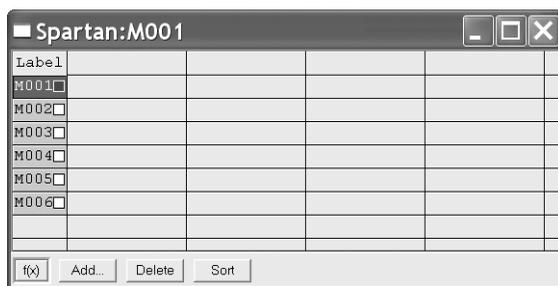


^1H and ^{13}C spectral plots are treated like any other graphical object, and may be translated and scaled using the appropriate mouse operations. They may not be rotated. Spectral plots may be removed from the screen by *clicking* on  (or alternatively by holding down the **Delete** key) and then *clicking* on the spectrum.

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

Spreadsheet

Associated with each list of molecules (including “lists” comprising only a single molecule) is a spreadsheet. This may be displayed by selecting **Spreadsheet**.



The spreadsheet comprises a series of rows (corresponding to the different molecules in the list) and columns (corresponding to different molecular properties). This gives rise to a series of “cells”, the number of which is given by the number of rows (molecules) times the number of columns (molecular properties). The spreadsheet can be expanded or contracted as required for display of all relevant information by positioning the cursor at any corner of the spreadsheet, *pressing* the left mouse button and *dragging* the mouse.

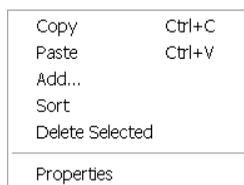
Only one molecule from one list may be selected. Molecule selection follows either by *clicking* on the spreadsheet cell containing the label, or by using the  and  buttons or the scroll bar at the bottom left of the screen. Molecules may be animated (stepped through in rapid succession) using the  button. Molecule selection (for members of a list) results in deselection of the previously selected molecule. However, it does not need to result in its removal from view. A molecule (in a list) may be designated for “permanent” display by *checking* the button to the right of its “Label” in the spreadsheet. This also selects the molecule, and deselects the previously selected molecule (but does not remove it from view if it were previously “checked”). The molecules in a list may either be translated and rotated in concert or manipulated independently. This is controlled by **Coupled** under the **Model** menu (see **Chapter 10**). The default is

that molecules move in concert. Select **Coupled** to designate independent motion.

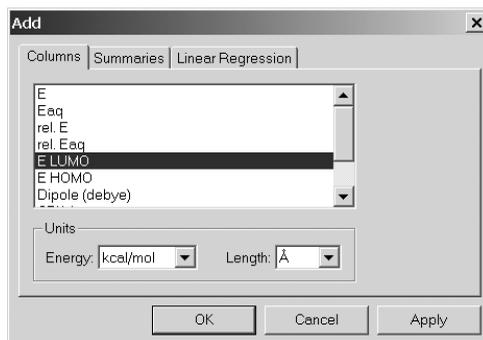
Upon initial entry into the spreadsheet, all columns except the leftmost column, are blank. The leftmost column (“Label”) contains a label of the molecule. It may be changed from the default (“M001”, “M002”, etc.) either by directly typing a new label into the spreadsheet or into the **Label** box in the **Molecule Properties** dialog. The label supplied will be used as the “molecule name” in a user-defined database (see **Appendix H**).

Information may be added to the spreadsheet in several different ways:

- (i) Molecular properties from the **Add** dialog: A variety of “important” molecular properties may be easily entered into the spreadsheet by first *clicking* on the header cell corresponding to an “empty” column, and then *clicking* on **Add...** at the bottom of the spreadsheet. An alternative is to hold down the right mouse button (following *clicking* on the header cell) and then to select **Add...** from the menu which results.

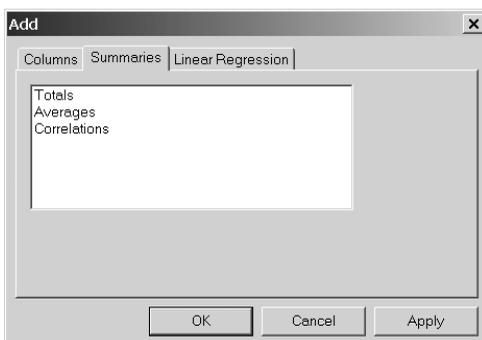


Either leads to the **Add Columns** dialog.



Columns (molecular properties) are added to the spreadsheet by *clicking* on one or more entries in the window at the top of the dialog, then specifying appropriate units from the **Energy** and **Length** menus, and finally *clicking* on **OK** or on **Apply**. In the former case, the dialog is dismissed and in the latter it is left on screen. *Clicking* on **Cancel** or on **✕** removes the dialog without affecting the contents of the spreadsheet.

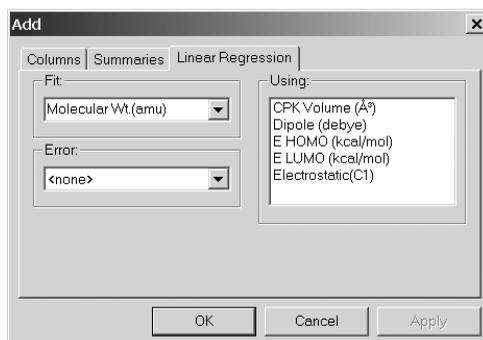
Column totals and averages, as well as information relating to the extent to which the data in the different columns are “correlated”, may be accessed by *clicking* on the **Summaries** tab. This leads to the **Add Summaries** dialog.



Clicking on “Totals”, “Averages” and/or “Correlations” (which have replaced molecular properties in the window at the top of the dialog) then *clicking* on **OK** or **Apply**, leads to the requested summaries as rows at the bottom of the spreadsheet, identified as “Totals”, “Averages” and “Correlations” (one row for each molecular property), respectively. Note, that the **Add Summaries** dialog can be brought up directly by *clicking* on an empty row header (instead of an empty column header) inside the spreadsheet prior to *clicking* on **Add...**

Finally, a linear regression analysis may be performed on the data in the spreadsheet. To access this functionality, *click*

on the **Linear Regression** tab to bring up the **Add Linear Regression** dialog.



Select one entry from the **Fit** menu and one or more entries from the list under **Using**. *Clicking* on **OK** or **Apply** performs the linear regression analysis and places the results in a row at the bottom of the spreadsheet identified by “Fit”. As many analyses as desired may be performed on the data in the spreadsheet. These will each 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).

- (ii) Direct entry of numerical data: Numerical data may be entered by typing directly into the spreadsheet. A column header first needs to be specified. *Click* on an empty column header cell, type in a name and *press* **Enter**. Then, type the data into individual cells of the new column (*press* **Enter** following each data entry).
- (iii) 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” is made up of arithmetic operations (**Table 14-1**), specialty functions (**Table 14-2**), quantities resulting from molecular mechanics

Table 14-1: Arithmetic and Boolean Operations and Mathematical Functions

<p>arithmetic operations</p> <p>+ addition</p> <p>– subtraction</p> <p>* multiplication</p> <p>/ division</p> <p>^ raise to a power</p>	<p>boolean operations</p> <p>> greater than</p> <p>>= greater than or equal to</p> <p>< less than</p> <p><= less than or equal to</p> <p>= equal to</p> <p>!= not equal to</p> <p> or</p> <p>& and</p>												
<p>mathematical functions</p> <table style="width: 100%; border: none;"> <tbody> <tr> <td style="width: 50%;">ABS(x) absolute value</td> <td style="width: 50%;">LN(x) natural logarithm</td> </tr> <tr> <td>ACOS(x) inverse cosine</td> <td>LOG(x) log (base 10)</td> </tr> <tr> <td>ASIN(x) inverse sine</td> <td>SIN(x) sine</td> </tr> <tr> <td>ATAN(x) inverse tangent</td> <td>SQRT(x) square root</td> </tr> <tr> <td>COS(x) cosine</td> <td>TAN(x) tangent</td> </tr> <tr> <td>EXP(x) exponential</td> <td></td> </tr> </tbody> </table>		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	
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													

Table 14-2: Specialty Functions

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

or quantum chemical calculations* (**Table 14-3**), conversion factors and constants (**Table 14-4**) in addition to numerical values. References to specialty functions, molecular mechanics and quantum chemical functions and conversion factors and constants need to be preceded by @. For example, “mu = @DIPOLE” typed into a header cell gives the dipole moment. Some quantities 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 Enter* following entry of the expression into a cell. The leading “name=” is optional for entries in an “individual” (non-header) cell. Examples of user-defined expressions are provided in **Table 14-5**.

- (iv) Molecular and atomic properties from “Post” () buttons: A number of properties which require user specification may be entered into the spreadsheet from “Post” buttons. These include individual bond distances, angles and dihedral angles (available from **Measure Distance**, **Measure Angle** and **Measure Dihedral** under the **Geometry** menu; see discussion in **Chapter 11**), bond distance, angle and dihedral angle constraints (available from **Constrain Distance**, **Constrain Angle** and **Constrain Dihedral** under the **Geometry** menu; see discussion in **Chapter 11**), and atomic charges and chemical shifts (available from the **Atom Properties** dialog; see discussion earlier in this chapter). “Post” generates an entire column of values based on atom labels for the selected molecule in the list. Only

* Additionally, any quantity available in the “property archive” (viewable from the **Output** window; see discussion earlier in this chapter) may be accessed in an expression using the “@prop(argument 1, argument 2, . . .)”. Among the different argument lists are the following: The name of the property (in the “property archive”), e.g., “SYM_STRING” for the symmetry label. The name of the property followed by the (serial) number of the atom in the list of atoms, e.g., “MM_CHARGE, 6” for the MMFF (molecular mechanics) charge on the sixth atom in the list of atoms. The name of the property followed by a number to indicate the desired member in the list of all members, e.g., “FREQ_VAL, 1” for the lowest vibrational frequency in the list of frequencies.

Table 14-3: Quantities from Molecular Mechanics or Quantum Chemical Calculations

ANGLE(i, j, k)	angle involving atoms i, j, k (degrees)
AREA	area of a user-defined plane
CPKAREA	surface area of a space-filling model (\AA^2)
CPKVOLUME	volume of a space-filling model (\AA^3)
PAREA (i, j, . . .)	partial surface area of a space-filling model due to all atoms of type i, j, ..., where i, j, ... are either atomic numbers or elemental symbols. i:, j:, ... signifies that attached hydrogens are also included. (the surface area due to nitrogen, oxygen and any bonded hydrogen is commonly referred to as the polar surface area) (\AA^2)
PVOLUME (i, j, . . .)	partial volume of a space-filling model due to all atoms of type i, j, ..., where i, j, ... are either atomic numbers or elemental symbols. i:, j:, ... signifies that attached hydrogens are also included (\AA^3)
DIHEDRAL(i, j, k, l)	dihedral angle involving atoms i, j, k, l (degrees)
DIPOLE	dipole moment (debyes)
DISTANCE(i, j)	distance involving atoms i, j (\AA)
ELECTROSTATIC (i)	electrostatic charge on atom i (electrons)
ENERGY	energy (hartrees)
ENERGYAQ	energy including SM5.4 aqueous solvent correction (hartrees)
ENTROPY	entropy (cal/mol degree)
FREEENERGY	free energy (kcal/mol)
HOMO(-n)	energy of n^{th} orbital below the HOMO (hartrees)
HOMOBETA(-n)	energy of the n^{th} orbital below the HOMO in the β spin manifold (hartrees)
ISOTOPE(i)	mass number of atom i
LENGTH (i)	length of bond i (\AA)
LOGPC	LogP from Crippen model
LOGPV	LogP from Villar model
LUMO(+n)	energy of the n^{th} orbital above the LUMO (hartrees)
LUMOBETA(+n)	energy of the n^{th} orbital above the LUMO in the β spin manifold (hartrees)
MULLIKEN(i)	Mulliken charge on atom i (electrons)
NATURAL(i)	natural charge on atom i (electrons)
ZEROPOINT	zero-point energy (kcal/mol)
WEIGHT	molecular weight (amu)

Table 14-4: Conversion Factors and Constants

ANGS2AU	Ångstroms to atomic units
AU2ANGS	atomic units to Ångstroms
EV2HART	eV to hartrees
EV2KCAL	eV to kcal/mol
EVTOKJ	eV to kJ/mol
HART2KCAL	hartrees to kcal/mol
HART2EV	hartrees to eV
HART2KJ	hartrees to kJ/mol
KCAL2EV	kcal/mol to eV
KCAL2HART	kcal/mol to hartrees
KCAL2KJ	kcal/mol to kJ/mol
KJ2EV	kJ/mol to eV
KJ2HART	kJ/mol to hartrees
KJ2KCAL	kJ/mol to kcal/mol
PI	π

Table 14-5: User Defined Expressions

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

where the molecules in the list are closely related, for example, molecules resulting from a conformational search or from “driving” a particular geometrical coordinate, or where labels have been explicitly reassigned*, is Post likely to lead to the desired result.

- (v) Molecular and atomic properties from the clipboard: Properties of individual molecules in a list may be copied into the clipboard and then pasted into individual spreadsheet cells. These include 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 Spectra** and **NMR Spectra** dialogs, respectively) and the value of a property on a property map (**Surface Properties** dialog). 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.

Each row in a spreadsheet corresponds to a molecule in a list, and new rows may be added by adding new molecules to the list. This may be accomplished either by building a new molecule (**New Molecule** from the **File** menu; **Chapter 8**), or by appending one or more existing molecules (see **Append Molecule(s)...** from the **File** menu; **Chapter 8**), or using the clipboard, or by *dragging* from an external window. Copy a molecule into the clipboard by first selecting (*clicking* on) it, and then selecting **Copy** from the **Edit** menu. Alternatively, *click* on its entry (“Label”) in its spreadsheet, and then select **Copy** from the **Edit** menu. The latter permits several molecules

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

to be selected (and copied) at once using the **Shift** and **Ctrl** keys in the usual manner. Move the contents of the clipboard to its destination by *clicking* on an empty row header in the spreadsheet (for the destination list), and then selecting **Paste** from the **Edit** menu. Copy a molecule from an external (to Spartan'04) window, by first selecting the molecule, and then *dragging* it from the external window onto the open spreadsheet (associated with the destination list) inside of Spartan'04. Several molecules can be selected (and *dragged*) at once using the **Shift** and **Ctrl** keys in the usual manner.

A row may be deleted from a spreadsheet (causing the corresponding molecule to be deleted from a list), either by first selecting the molecule and then selecting **Delete Molecule** from the **File** menu, or by first *clicking* on its "Label" in the spreadsheet (leftmost column) and then either *clicking* on the **Delete** button at the bottom of the spreadsheet, or by selecting **Delete Selected** from the menu which appears when the right mouse button is pressed (with the cursor over the spreadsheet). In all cases, a warning is provided prior to deletion. An entire column in the spreadsheet may be deleted by first *clicking* on the column header (the title) 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 by first *clicking* on the column header and then either *clicking* on the **Sort** button at the bottom of the spreadsheet or by selecting **Sort** from the menu which appears when the right mouse button is pressed (with the cursor over the spreadsheet). 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 you *click* on the **Sort** button.

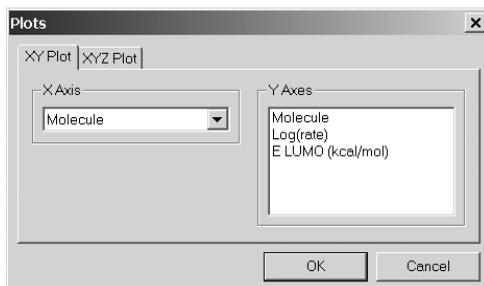
Totals and averages of column values may be obtained by first selecting new (blank) row header, then *clicking* on **Add...** and finally selecting "Totals" and/or "Averages" from the (**Add Summaries**) dialog which results.

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 selecting **Print Spreadsheet...** from the **File** menu (which has replaced **Print...** when a spreadsheet is selected). It may be removed by *clicking* on .

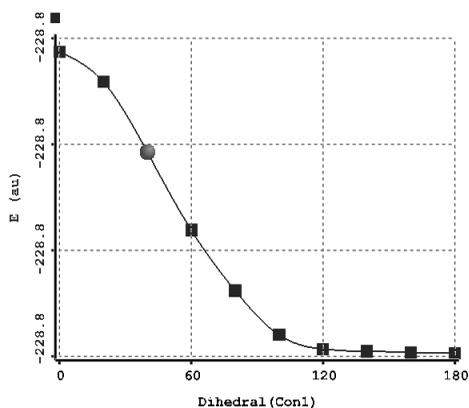
Plots...

Plots may be constructed from data in a spreadsheet and a variety of simple “curves” fit to these data. Selection of **Plots...** from the **Display** menu leads to the **Plots** dialog.



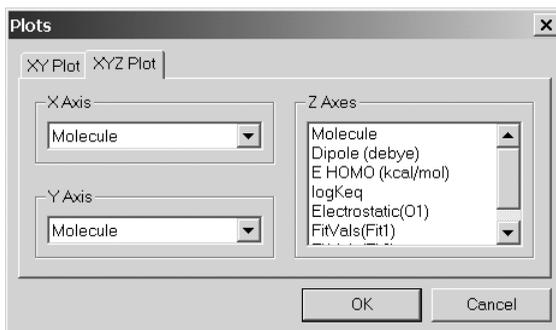
This has two variants depending on the tab at the top of the dialog “**XY Plot**” (two dimensions) or “**XYZ Plot**” (three dimensions). At the outset, XY Plot will be selected.

The “XY Plot” variant incorporates an **X Axis** menu designating the molecular property to be displayed among the X axis, and a list of properties to be displayed along the Y axis. These properties correspond one to one to the columns in the associated spreadsheet. To construct a 2D plot, select an item from the **X Axis** menu, then *click* on one or more items from the **Y Axes** list and finally *click* on **OK**. (Repeated *clicking* on a property in the **Y Axes** list turns it “on” and “off”.) The dialog is removed from the screen and a plot appears.

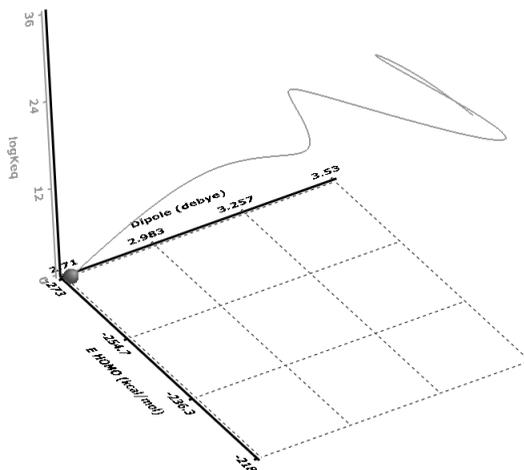


The plot can be moved about the screen. Select (*click* on) either the frame or on one of the curves (it will turn gold in response), then hold down the right mouse button and *drag* the mouse. The plot may also be scaled (expanded or shrunk) by first selecting either the frame or one of the curves and *dragging* the mouse while holding down both the right button and the **Shift** key. The plot may not be rotated.

The “XYZ Plot” variant is reached by clicking on the **XYZ Plot** tab at the top of the dialog. This leads to a new dialog.



This is very similar to the “XY Plot” variant, except that it incorporates **X Axis** and **Y Axes** menus to designate quantities to be displayed along the X and Y axes, respectively, as well as a list of properties to be displayed along the Z axis. To construct a 3D plot, select one item from each of the **X Axis** and **Y Axis** menus, then *click* on one or more items from the **Z Axes** list and finally *click* on **OK**. A plot appears.



The plot can be moved about the screen. Select (*click* on) either the frame or on one of the curves (it will turn gold in response), then hold down the right mouse button and *drag* the mouse. The plot may also be scaled (expanded or shrunk) by first selecting either the frame or one of the curves and *dragging* the mouse while holding down both the right button and the **Shift** key. Finally, 3D plots (unlike 2D plots discussed earlier) may be rotated, by first selecting either the frame or one of the curves and *dragging* the mouse while holding down the left button.

Plots initially presented to the user draw smooth curves (cubic splines) through the data points. Different types of “curve fits” as well as a variety of different presentation formats are available under the **Plot Properties** and associated dialogs (see **Properties** earlier in this chapter).

A plot may be deleted by first selecting (*clicking* on) **Delete** from the **Build** menu, or *clicking* on , or holding down the **Delete** key, and then *clicking* on either the plot frame or on an individual curve. *Clicking* on the frame removes it and all associated curves, while *clicking* on a curve removes only this curve. However, the last curve deleted also deletes the frame.

Chapter 15

The Search Menu

*This chapter describes functions available under the **Search** menu. These provide substructure searching of the Cambridge Structural Database of experimental X-ray crystal structures, both replacement from and substructure searching of the Spartan Molecular Database of calculated structures, energies and properties, a facility for guessing transition states for “new” reactions based on their similarity to transition states in an extensive reaction database, and a procedure for identifying tautomers.*

The **Search** menu provides access to the Cambridge Structural Database of experimental X-ray crystal structures, as well as the Spartan Molecular Database of calculated molecular structures, energies and properties, a facility for guessing transition state geometries and a procedure for identifying tautomers.



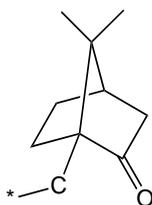
Databases ()

Access to two databases is provided under this heading; the Cambridge Structural Database (CSD) of experimental X-ray crystal structures and the Spartan Molecular Database (SMD) of calculated structures, energies and molecular properties. Both databases may be searched on the basis of a “substructure”. In addition, SMD is accessed automatically (and its results made available) whenever an entry is selected on screen.

Cambridge Structural Database (CSD)

The Cambridge Structural Database (CSD) is a collection of more than 300,000 experimental X-ray crystal structures for organic and organometallic molecules. It is maintained by the Cambridge Crystallographic Data Centre (CCDC) and grows approximately 10% per year.* CSD not only contains information about the molecular geometry, but also about crystal packing and, more generally, about intermolecular interactions. However, Spartan'04's interface to CSD permits access only to "molecular" information**. Even with this limitation, the CSD represents a "gold mine" of detailed experimental structural information (bond lengths and angles as well as conformations), and also serves to identify molecules which can be (and have been) synthesized and purified through crystallization.

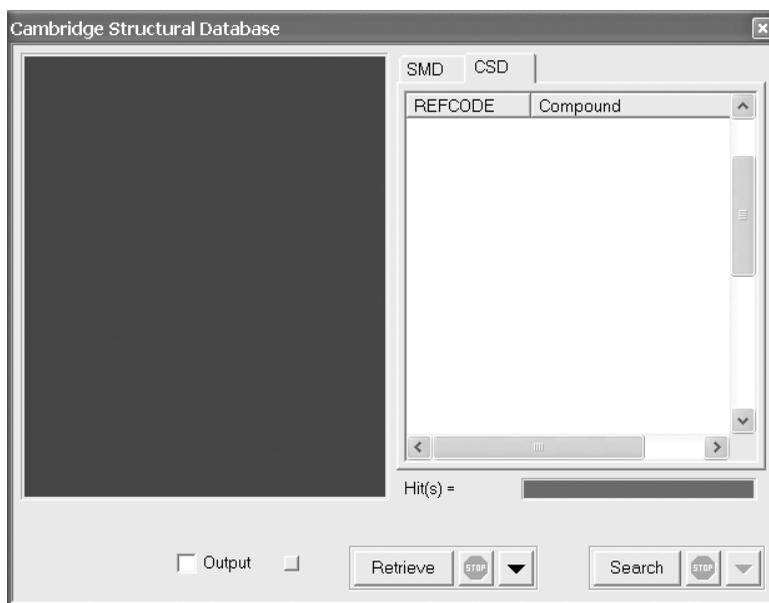
Access to the data in CSD is via a substructure searching procedure. A molecule is first constructed in the usual way, identifying one or more free valences in places where the structure is to be "grown". For example, to search for all molecules related to camphor, i.e., with different substituents on the sp^3 carbon occupying the bridgehead position adjacent to the carbonyl group, the following "substructure" would be constructed, and a growth point (a free valence on the *'ed carbon) designated.



Access to CSD is provided by *clicking* on the **CSD** tab at the top of the **Database** dialog. This gives rise to the **CSD** dialog.

* CSD is not included with Spartan'04 but is available by subscription from CCDC or one of its distributors. Contact Wavefunction for information. For installation instructions, see **Appendix G**.

** This additional information may be accessed using CCDC's Windows' program "ConQuest", which is supplied as part of the CSD subscription.



This contains a window at the left for previewing structures, a box at the right for listing “hits” on CSD as well as examining the text output from the search, and buttons at the bottom to control various aspects of the search and subsequent transfer of CSD data into Spartan’04’s file system. A substructure search is set up by specifying one or more of the following*:

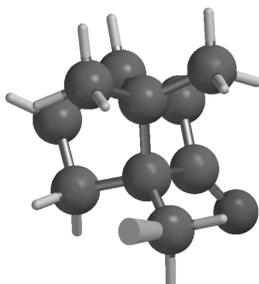
(i) **Attachment Points**

Free valences are designated as attachment points by *clicking* on them in the structure model. The “free valences” will be replaced by orange cones. *Clicking* again will remove the designation and return the free valences. As many attachment points as desired may be specified. Anything may be “grown” off an attachment point (including hydrogen). The coordination of the atom where attachment is made is maintained. Note, that free valences which are not identified as attachment points are assumed to be hydrogens.

In the case of a search for camphor derivatives resulting from substitution on the sp^3 carbon at the bridgehead position adjacent

* If nothing is specified, a search for an “exact” match is carried out (all free valenes are assumed to be hydrogens).

to the carbonyl group, it is necessary to *click* on the free valence at this position. The structure display will now appear as follows, with an “orange cone” replacing the free valence.

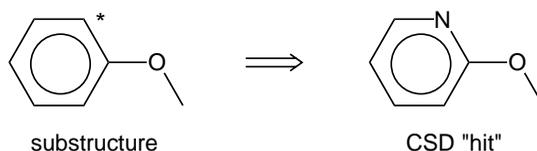


The camphor search requires no further specifications of substructure, although two other aspects of substructure designation may be required to carry out other searches.

(ii) Wild-Card Atoms

An atom may be designated as a “wild card” (no checking of atom type) by *clicking* on it. The ball in the model (designating a specific atom type) will turn orange (designating any atom type). *Clicking* on a wild-card atom removes the wild card designation. As many wild-card atoms as desired may be specified.

Use of wild card atoms will result in structures which incorporate variants of the original substructure with different atoms at designated positions. For example, use of a phenyl ether substructure with one of the ring atoms designated as a wild card (*) could result in “hits” with pyridyl ethers.



Note, that coordination around a wild-card atom is not maintained.

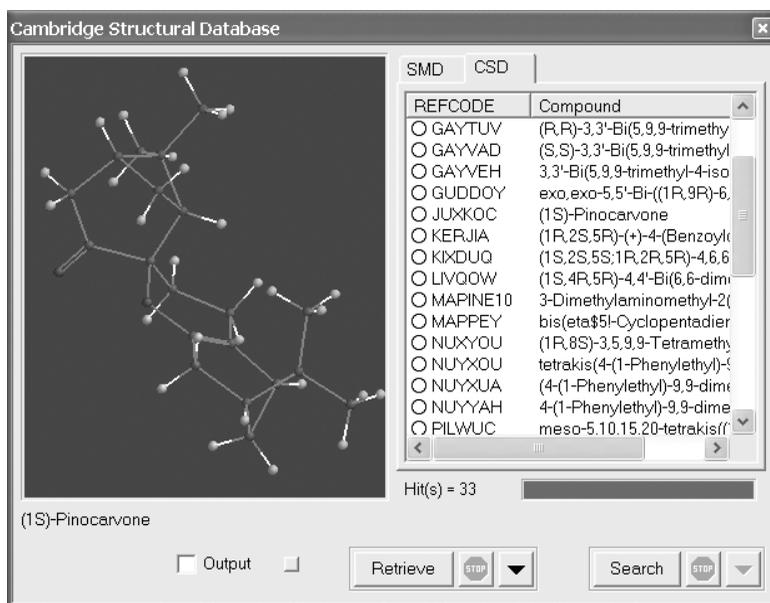
(iii) **Wild-Card Bonds**

A bond may be designated as a “wild card” by *clicking* on it. A orange cylinder will be drawn around it. *Clicking* on this cylinder removes it and reverts designation of bond type back to the original. As many wild-card bonds as desired may be specified.

Wild-card bonds are often essential in dealing with heteroatom-containing molecules, in particular, heterocycles.* Their use implies change in coordination.

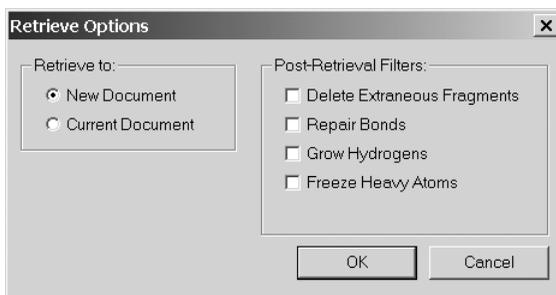
After a substructure has been fully specified, search of CSD is carried out by *clicking* on the **Search** button at the bottom right of the dialog. If there are “hits” to be found, these will begin to appear in the box at the right of the dialog after a few seconds. The entire search will require between a few seconds and one or two minutes, depending on the query (and on the speed of the computer). It can be terminated at any time by *clicking* on  to the right of the **Search** button at the bottom right of the dialog. Once completed (or stopped), the “CSD ref codes” and the names for the “hits” are displayed in the box and the number of “hits” is indicated immediately below. Actual structural data are available only for entries preceded by a filled yellow circle (the vast majority of entries). Other entries (designated by open circles) for which structure data are not available are provided for completeness only. A 3D structure for any entry for which it is available (yellow circle) may be seen by *clicking* on its name in the box. The ball-and-wire model is displayed in the window at the left of the dialog, and its name appears immediately below the window.

* This is closely related to identification of tautomers. See discussion later in this chapter.



The model can be manipulated (rotated, translated, scaled) inside the window with the usual mouse/keyboard commands (you need to position the cursor inside the window), but the model style cannot be changed, nor can geometrical measurements be made. These require that selected entries be transferred to the file system (see below).

Note, that the information available for preview is *exactly as it appears in CSD*. In particular, it may contain two or more different molecules, two or more different conformations of the same molecule and/or extraneous molecules (most commonly solvent molecules and counterions). Hydrogens will be shown only where they have been assigned in the experimental structure. Finally, the preview may contain errors in bonding due to uncertainties in the original data and/or crystal imperfections. “Filters” are available to address some of these issues prior to transfer of one or more hits to Spartan’04’s file system. In addition, the destination of the retrieved data may be specified. Available retrieval options are found in the **Retrieve Options** dialog accessed by *clicking* on to the right of the **Retrieve** button at the bottom of the **CSD** dialog.



- (i) **Retrieve to:**
Selection toggles between **New Document** and **Current Document**. Selection of the former results in request for a file name; selection of the latter results in the retrieved molecules being appended to the end of the current molecule list.
- (ii) **Delete Extraneous Fragments**
If *checked*, this deletes any “detached molecules” which do not contain the original substructure. These will most commonly be trapped solvent molecules or counterions.
- (iii) **Repair Bonds**
If *checked*, this attempts to “fix” obvious bond typing errors based on the actual geometry in the CSD entry, and on normal rules of valence.
- (iv) **Grow Hydrogens**
If *checked*, this “grows” hydrogens wherever they are (or appear to be) missing. “Growth” is based on the actual 3D structure and on normal valence rules. This is the same function that is available under **Grow Hydrogens** in the **Molecule Utilities** dialog (see **Chapter 14**).
- (v) **Freeze Heavy Atoms**
If *checked*, this “freezes” all atoms except for hydrogens. This allows experimental X-ray hydrogen positions, which are typically much too short, to later be refined using

molecular mechanics or quantum chemical methods, while maintaining the heavy atom skeleton.*

The **Retrieve Options** dialog is dismissed with all changes to existing settings maintained by *clicking* on **OK**. *Clicking* on **Cancel** or on  also dismissed the dialog but any changes to settings are lost.

Retrieval is accomplished by first selecting (*clicking* on) one or more “hits” in the box and then pressing the Retrieve button at the bottom of the **CSD** dialog. The **Shift** and **Ctrl** keys may be used to specify retrieval of multiple hits. A block of entries may be specified by *clicking* on the top (or bottom) entry, then holding down the **Shift** key and finally *clicking* on the bottom (or top) entry. Multiple entries may be specified by *clicking* on each in turn while holding down the **Ctrl** key. The retrieve process can be stopped at any time by *clicking* on  to the right of the **Retrieve** button at the bottom of the **CSD** dialog.

If **Implicit Search** in the **Miscellaneous Preferences** dialog (**Preferences...** under the **Options** menu; see **Chapter 16**) has been set, a search of CSD is performed in “build mode” each time a change is made to the molecular structure.** This search assumes that all free valences are attachment points, insuring the maximum number of hits. The **CSD** dialog does not need to be open on screen (but may be opened at any time to examine the resulting “hits”). However, running total of hits is provided at the bottom right of the screen whenever implicit search has been invoked.

* Hydrogen positions may be refined using the MMFF molecular mechanics model using **Minimize** from the **Build** menu ( button). Refinement using quantum chemical models is specified in the **Calculations** dialog (**Setup** menu) by way of **Frozen Atoms**. See discussion in **Chapter 13**.

** Use of implicit search may seriously degrade graphics performance during molecule building and should be switched off unless desired.

Spartan Molecular Database (SMD)

The Spartan Molecular Database (SMD) is a collection of more than 50,000 molecules, the structures, energies, and selected properties of which have been obtained from up to five different theoretical models: Hartree-Fock models with 3-21G and 6-31G* basis sets, EDF1/6-31G* and B3LYP/6-31G* density functional models and the MP2/6-31G* model. An entry is specified by a three-dimensional connectivity encoded as a one-dimensional (SMILES like) character string together with a theoretical model. Structural isomers, e.g., *cis-trans* isomers are distinguished as are diastereomers, but enantiomers are not distinguished.

SMD is open-ended and users may construct parallel databases with additional molecules and/or results from additional theoretical models on existing molecules (see **Appendix H**). Future extensions of SMD will include transition-metal inorganic and organometallic compounds and transition states as well as calculations using higher-level models.

While the majority of entries are represented in terms of a single “lowest-energy” conformer (see text box below), some entries are represented in terms of two or more conformers. In these cases, the available conformers will be ranked according to energy, and the user needs to choose among them.

The individual entries supplied in SMD have been obtained according to the following “recipe”.

1. Identify the lowest-energy conformer using molecular mechanics and the MMFF (Merck) force field. Systems with only a few degrees of conformational freedom are searched systematically “guaranteeing” location of the global minimum, while a Monte-Carlo search is applied to more complicated systems. The latter does not guarantee location of the global minimum.
2. Starting from the best conformer located, perform a geometry optimization using the appropriate quantum chemical model. This generally means that all quantum chemical calculations for a particular molecule will refer to the same conformer.

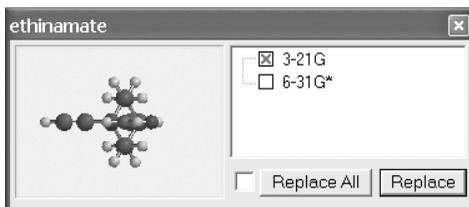
At the present time, SMD may be accessed in one of two ways: “exact” replacement of a structure with a database entry corresponding to a particular quantum chemical model, and location of entries in the database (corresponding to one or more quantum chemical models) which contain a particular substructure. The latter is strictly analogous to the way in which Spartan’04 accesses the Cambridge Structural Database (see previous discussion).

Replacement

The existence of one or more database entries (corresponding to different quantum chemical models) for the selected molecule is indicated by its name being displayed at the bottom of the screen.



Details are provided by *clicking* on  to the immediate left of the molecule name (it then changes to ). This brings up a dialog which comprises a viewing screen on the left and a list of quantum chemical models for which database entries exist on the left.

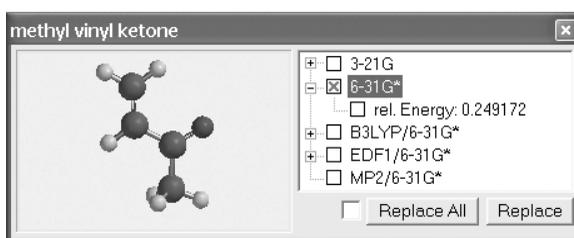


Upon initial entry, the topmost entry in the list is *checked* and a ball-and-spoke model corresponding to its structure appears in the viewing screen. This model can be rotated, translated and scaled using the usual mouse/keyboard commands (you need to position the cursor inside the viewing area). The model may be made to “tumble” automatically by *checking* the box to the left of **Replace All** at the bottom of the dialog. Model style may not be changed. A different database entry (corresponding in this case to a different quantum chemical model) may be selected by *checking* the box to the left of the name of the quantum chemical model in the dialog.

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; see **Chapter 9**). Note that replacement destroys any information associated with the molecule being replaced.

Some database entries also comprise information on higher-energy conformers (in addition to that on the “presumed” ground-state conformer). These entries are designated by a icon to the left of the check box. *Checking* this icon leads to an expanded entry which allows access to these higher-energy conformers, as well as provides their relative energies (in kcal/mol).



Entries are selected as before, at which time they may be examined in the viewing screen or used to replace the on-screen molecule.

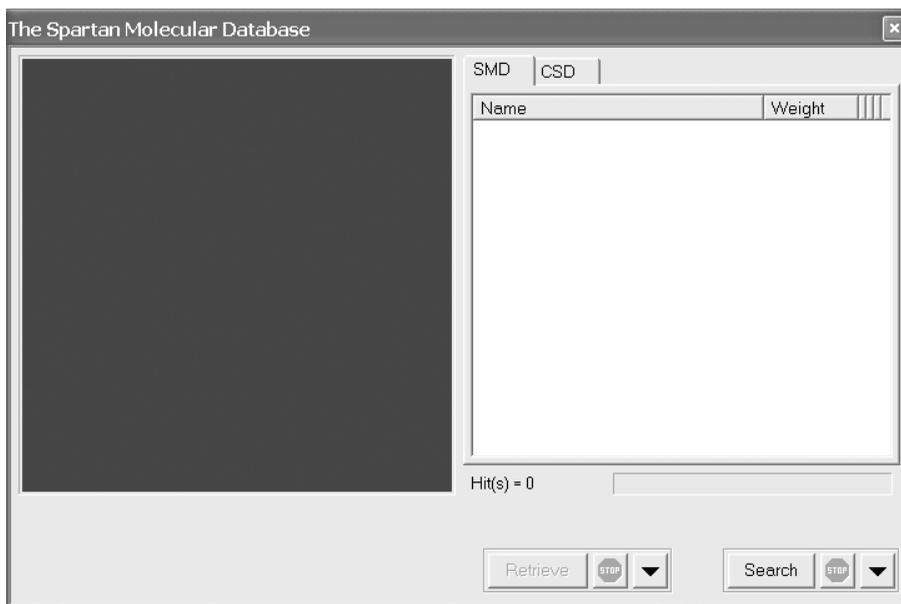
In the event that the selected (on-screen) molecule is a member of a list, it is possible to replace all members of the list for which database entries are available. This is accomplished as above except that **Replace All** instead of **Replace** is used. A warning message is provided prior to replacement. Note that the lowest-energy conformer for all other (non-selected) molecules in the list is used even though a higher-energy conformer may be indicated for the selected molecule. (Replacement of list entries with non lowest-energy conformations may be done one by one using **Replace** instead of **Replace All**.) Also note that molecules in the list for which there are no database entries are not affected.

Substructure Searching

Substructure searching from SMD is very similar to that from CSD described previously, in that all that is required is specification of one or more “growth points”. It differs in that SMD contains multiple sets of results (corresponding to different theoretical models), and it

is necessary to specify which model (or which set of models) is to be employed.

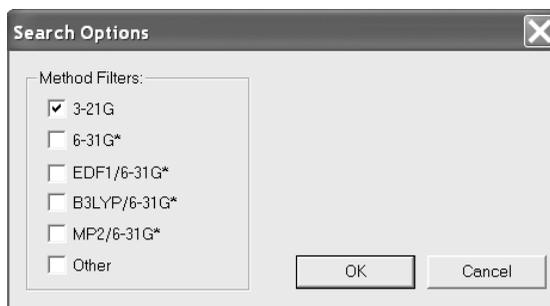
Access to SMD is provided by *clicking* on the **SMD** tab at the top of the **Database** dialog. This gives rise to the **SMD** dialog.



Like the **CSD** dialog, the **SMD** dialog contains a window on the left for previewing structures and a box on the right for listing “hits” on SMD, as well as buttons at the bottom to control various aspects of the search and subsequent transfer of data into Spartan’04’s file system.

A substructure search is set up by specifying one or more attachment points, in the same manner as for CSD (see previous discussion). “Wild-card” atoms and bonds are not available.

Prior to starting the actual search, it is necessary to specify which theoretical model or set of models is to be included. Model specification is accomplished by *clicking* on ▾ to the right of the **Search** button at the bottom right of the dialog. This brings up the **Search Options** dialog.



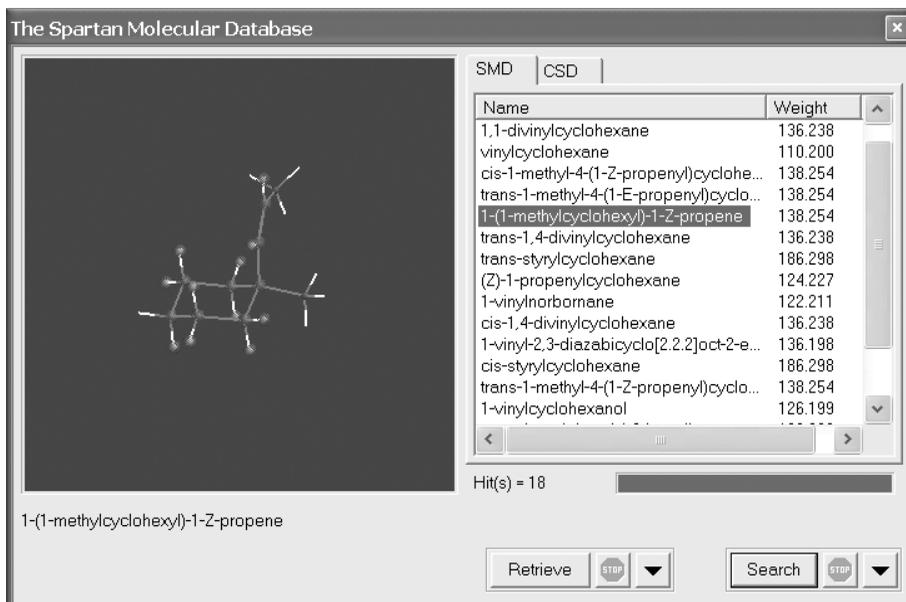
Checking the appropriate boxes specifies the appropriate model(s).

In general, SMD contains more data for the simpler models (3-21G and 6-31G*) than for the more complicated models (EDF1/6-31G*, B3LYP/6-31G* and MP2/6-31G*). In fact, only a few thousand entries are available with the MP2/6-31G* model in the initial release of the database.

Specification of **Other** provides access to data with theoretical models other than those explicitly mentioned in the dialog. *Clicking* on **OK** removes the dialog. (*Clicking* on **Cancel** or on  also removes the dialog, but selections are not made.)

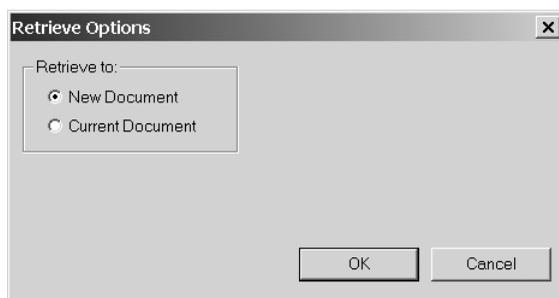
Following specification of attachment points and designation of theory level(s), a search on SMD is carried out by *clicking* on the **Search** button at the bottom right of the dialog. If there are hits to be found, these will begin to appear in the box at the right of the dialog after a few seconds. The entire search will require between a few seconds and one or two minutes, depending on the query (and on the speed of the computer). It can be terminated at any time by *clicking* on  to the right of the **Search** button at the bottom right of the dialog. Database hits are displayed in the box at the right of the dialog*. A 3D structure for a particular hit may be previewed by *clicking* on its name in the box. The ball-and-wire model is displayed in the window at the left of the dialog, and its name appears immediately below the window.

* Normally, only the name of the molecule is visible, but molecular weight and basis set may also be displayed by appropriately *sliding* the header cells at the top of the box.



The model can be manipulated (rotated, translated, scaled) inside the window in the usual way, but the model style cannot be changed, nor can geometrical measurements be made. These require that selected entries be transferred to the file system (see below).

Prior to retrieval of one or more database hits, it is necessary to specify a destination. This is accomplished with the **Retrieve Options** dialog, brought up by *clicking* on ▼ to the right of the **Retrieve** button at the bottom center of the dialog.



Selection of destination is accomplished by *toggling* between **New Document** and **Current Document**. Selection of the former results in request for a file name; selection of the latter results in the retrieved molecules being appended to the end of the current molecule list.

The **Retrieve Options** dialog is dismissed by *clicking* on **OK**. *Clicking* on **Cancel** or on  also dismissed the dialog but any changes to settings are lost.

Retrieval is accomplished by first selecting (*clicking* on) one or more hits in the box and then pressing the Retrieve button at the bottom of the **SMD** dialog. The **Shift** and **Ctrl** keys may be used to specify retrieval of multiple hits. A block of entries may be specified by *clicking* on the top (or bottom) entry, then holding down the **Shift** key and finally *clicking* on the bottom (or top) entry. Multiple entries may be specified by *clicking* on each in turn while holding down the **Ctrl** key. The retrieve process can be stopped at any time by *clicking* on  to the right of the **Retrieve** button at the bottom of the **SMD** dialog.

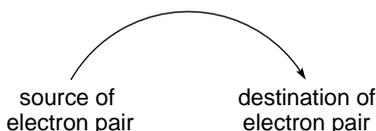
Transition States

Spartan'04 provides a facility for guessing transition state geometries based on the similarity of the reaction of interest with one or more entries in Spartan's reaction database. An exact hit is possible, in which case the guess will be the "exact transition state"* . More commonly, this will not be the case, and Spartan will attempt to provide as close a match as possible with a database entry. This will generally involve a less substituted system or one in which substituents differ. Here, Spartan will use those parts of the structure of the transition state in the database which are common, and will optimize the remaining parts (using molecular mechanics). No conformational searching is performed, and it is essential that the reactants be properly oriented to reflect the desired stereochemical outcome of the reaction. In this regard, whenever a reaction involves a change in the molecularity, i.e., $A + B \rightarrow C$, it will generally be easier to start from the "unimolecular side" (the product in the above).

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

* More precisely, the transition state supplied in this case will be exact for the particular theoretical model entered in the database. At the present time, the majority of database entries derive from very simple (semi-empirical and Hartree-Fock) quantum chemical models.

Input to Spartan'04's transition-state guessing procedure will be very familiar to (organic) chemists, in that it is based on "arrow pushing". 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 only two possible "sources" of an electron pair and only 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"	use lone pair to create new (single) bond
bond → lone pair	decrease bond order to make lone pair
bond → bond	decrease order of one bond to increase order of another bond
bond → "space"	decrease order of one bond to make a new (single) bond

Note that the first of these is a "null" operation, and its inclusion is optional.

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

Select atom or bond as tail.

The "tail" of the arrow corresponds to the source of the electron pair. If the source is a lone pair, then select the appropriate atom. If the source is a bond, then select the appropriate 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.

Select atom, bond, or two atoms as head. If two atoms hold SHIFT key.

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

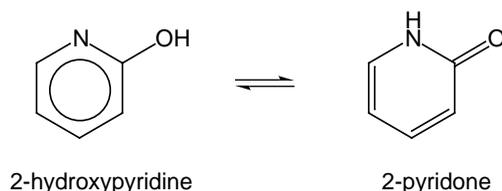
this atom. If the destination is an existing bond (leading to an increase in bond order from single \rightarrow double \rightarrow or double \rightarrow triple), then select the appropriate bond. If no bond presently exists at the destination, *press* the **Shift** key and select the two atoms that will become bonded. All of these operations lead to a curved arrow being drawn on the reactant structure, and to the original message at 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. In the latter case, you need to again select **Transition States** () in order to continue arrow selection. Alternatively, *click* on the arrow(s) to be deleted while holding down the **Delete** key

After all reaction arrows have been designated, *clicking* on  at the bottom right of the screen replaces the “reactant” with a “guess” at the transition state. In the event that the guess is “unreasonable”, this last operation may be “undone” by selecting **Undo** (**Edit** menu). This allows you to review your assignment of arrows and make changes as needed.

Tautomers ()

Spartan'04 provides a facility for automatically identifying isomers arising from (rapid) transfer of hydrogens among heteroatoms, that is, so-called tautomers. Tautomer identification is especially important in dealing with heterocyclic compounds where two or more different tautomers may exist in equilibrium and the identity of the dominant tautomer may not be apparent, e.g.



Having the “correct” tautomer may be essential in searches of the Cambridge Structural Database (CSD). For example, a search of the current CSD for derivatives of 2-hydroxypyridine yields no “hits” whatsoever, whereas a search for derivatives of 2-pyridone yields multiple hits.

The procedure incorporated into Spartan’04 is limited to tautomers involving nitrogen, oxygen, phosphorous and sulfur. Tautomers involving carbon, in particular, have been excluded. Within these limits, the procedure attempts to locate all possible tautomers, but makes no attempt either to remove duplicates or to remove tautomers which are likely to be highly unfavorable.*

The existence of tautomers is automatically sensed by Spartan’04 and is signaled by the word “Tautomer” being displayed at the bottom right of the screen. (No further action needs to be taken if tautomer identification is not of interest.) If tautomers exist, individual structures may be examined or a complete list of structures generated by selecting **Tautomers** from the **Search** menu (or *clicking* on the  icon from the **Search** toolbar). Following this, *clicking* on  and  buttons at the bottom right of the screen moves backwards and forwards through the list of tautomers. *Clicking* on  (at the bottom right of the screen) leads to an informative dialog.



Clicking on **OK** dismisses the dialog and leads to a new (unnamed) file containing the full list of tautomers. (The original file is unaffected.) *Clicking* on either **Cancel** or  dismisses the dialog without a tautomer list being generated.

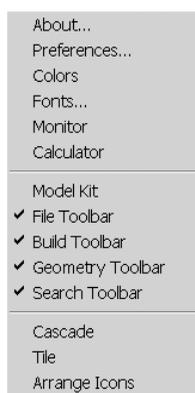
* Of course, once a complete list of tautomers has been generated it is straightforward to calculate their relative energies using any of Spartan’04’s quantum chemical models.

Chapter 16

The Options Menu

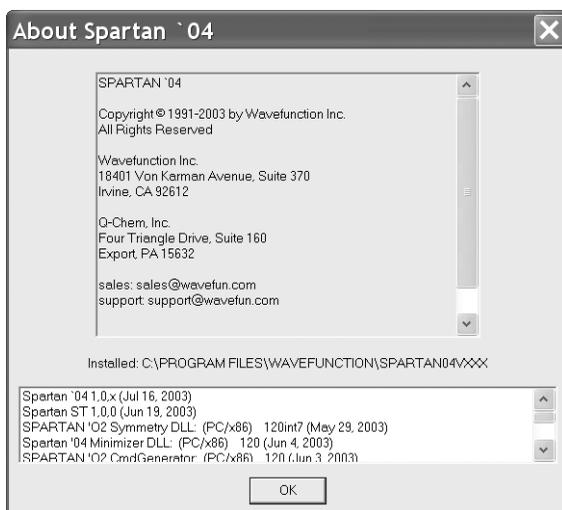
*This chapter describes functions under the **Options** menu. These set colors and user preferences and monitor jobs.*

Functions under the **Options** menu provide information and allow for setting user preferences.



About...

Provides information about the user's release of Spartan'04.



A menu at the bottom of the dialog provides version numbers and release dates for specific components of Spartan'04. The dialog is removed by *clicking* on **OK**.

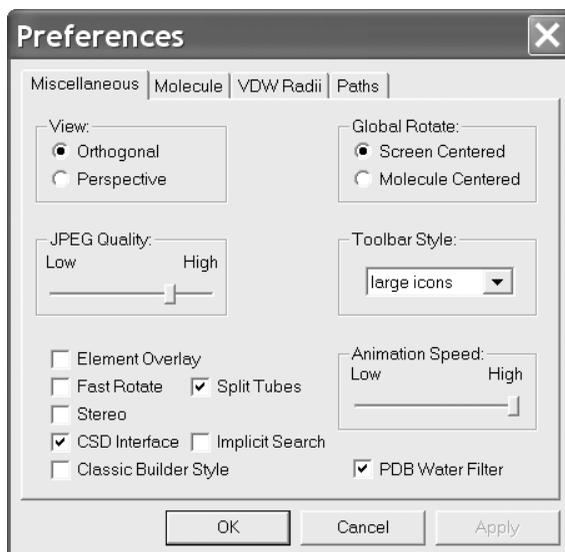
Preferences...

This sets up a number of preferences relating to the graphical user interface in general (**Miscellaneous**), to molecule displays (**Molecules**), and to the change of van der Waals radii (**VDW Radii**). It also specifies the locations of a user-defined molecule database (**Paths**).

Selection results in one of four dialogs, depending on whether the **Miscellaneous**, **Molecule**, **VDW Radii** or **Paths** tab (at the top of the dialog) has been selected in the previous entry.

Miscellaneous

Upon first entry, the **Miscellaneous** tab will be selected, and the **Miscellaneous Preferences** dialog displayed



- (i) **View: Orthogonal/Perspective**
Controls the view of structural models and graphics.
- (ii) **Global Rotate: Screen Centered/Molecule Centered**
Screen Centered provides a single center for rotation

of all molecules on screen, while **Molecule Centered** rotates each molecule about its individual center.

(iii) **JPEG Quality**

A slider bar controls the resolution of JPEG output.

(iv) **Toolbar Style**

Controls presentation (text vs. icons) and size of the icons.

(v) **Element Overlay**

If *checked*, this highlights elements in the expert model kit for which the model specified in the **Calculations** dialog are available.

(vi) **Fast Rotate**

If *checked*, this lowers the resolution of structure models (only) during rotation. This is used to improve graphics performance for displays of larger molecules.

(vii) **Split-Tubes**

If *checked*, the “tubes” in tube and ball-and-spoke models will be split to designate multiple bonds.

(viii) **Stereo**

If *checked*, this turns “on” stereo. The viewer must wear red/blue glasses. Also turned “on” with the “3” key (see **Keyboard Functions in Chapter 2**).

(ix) **CSD Interface**

If *checked*, this displays the **CSD** tab in the **Database** dialog (**Search** menu). Turn “off” if CSD is not installed.

(x) **Implicit Search**

If *checked*, this performs a search of **CSD** every time a change is made to the molecular structure, assuming that all free valences are attachment points.

(xi) **Classic Builder Style**

If *checked*, this reverts to the builder style used in earlier versions of Spartan.

(xii) **Animation Speed**

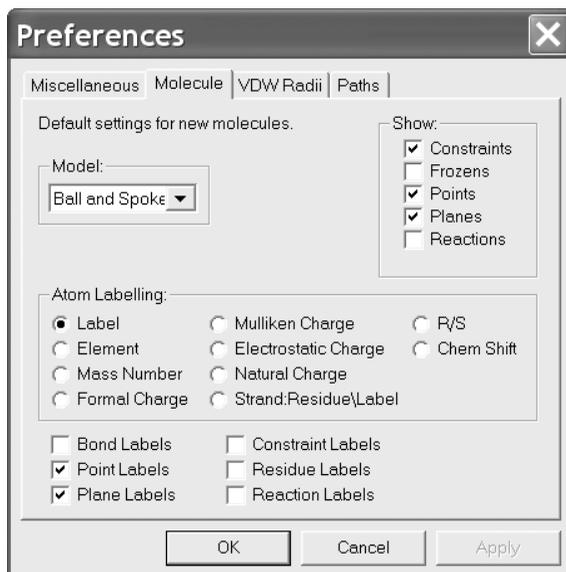
A slider bar controls the maximum speed for vibrations and animations.

(xiii) **PDB Water Filter**

If *checked*, removes water molecules from imported PDB files.

Molecule

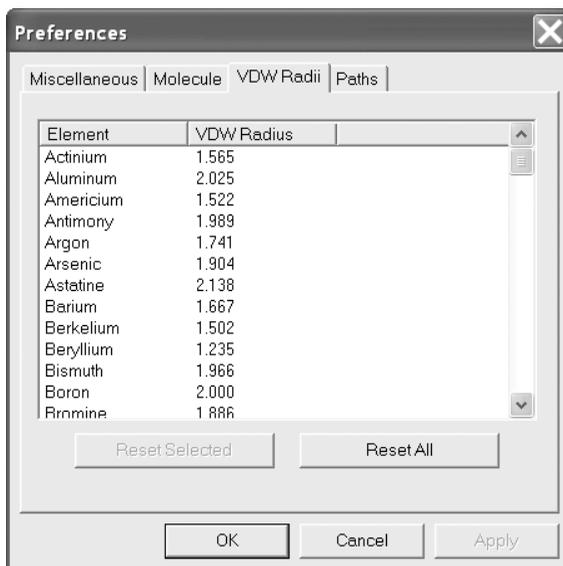
Clicking on the **Molecule** tab leads to the **Molecule Preferences** dialog.



This specifies global default settings for model and label types as well as specification of whether or not constraint and frozen atom markers are shown, whether or not points, planes and reaction arrows are shown and whether or not labels for bonds, points, planes, constraints, amino acid residues and reaction arrows are shown. These settings may be overridden for a specific molecule (or list of molecules) using entries under the **Model** menu and for specific portions of a molecule using entries associated with **Properties** under the **Display** menu.

VDW Radii

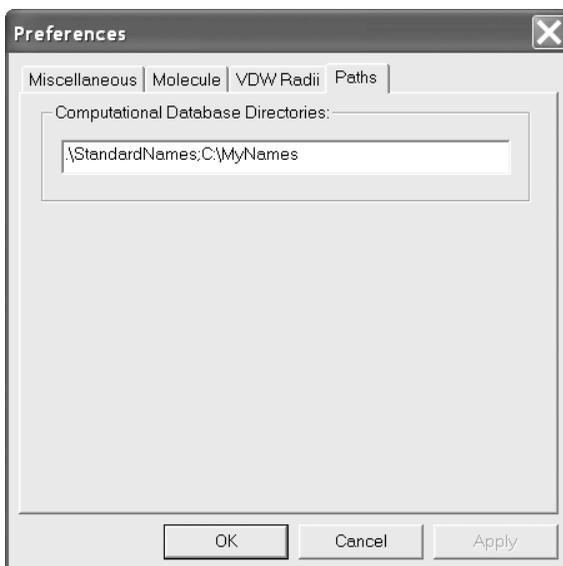
Clicking on the **VDW Radii** tab leads to the **VDW Radii Preferences** dialog.



This provides a list of van der Waals radii for elements ordered either by element name (*click* on “Element”) or by atomic radius (*click* on “VDW Radius”). Individual entries can be changed from default values by first *clicking* on the entry and then entering a new value. The currently selected entry can 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.

Paths

Clicking on the **Paths** tab leads to the **Paths Preferences** dialog.

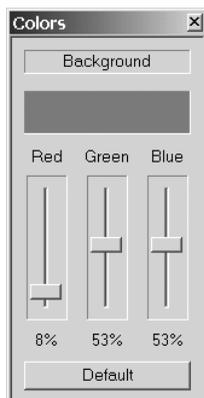


This allows the path to be set for a user-defined database (see **Appendix H**).

To exit the **Preferences** dialog *click* on **OK**; *clicking* on **Cancel** or on **X** exits the dialog without instituting any changes.

Colors

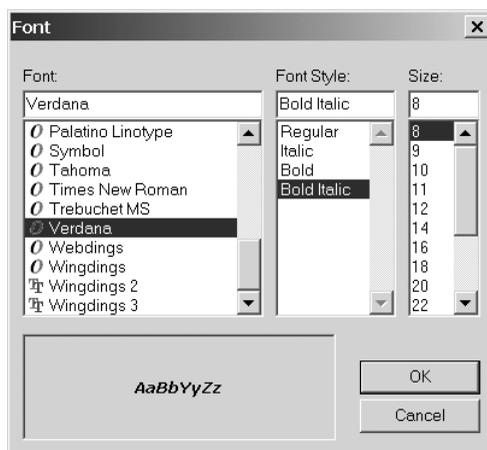
This is used to alter the default colors of most graphical objects. Selection leads to the **Colors** dialog.



An object first needs to be selected by *clicking* on it, after which its color may be set by adjusting the **Red**, **Green** and **Blue** slider bars. The default color (which depends on the object) may be selected by *clicking* on **Default**. Color selection may be performed for as many objects as desired, and applies to all objects of the same type, e.g., carbon atoms, and not just to the selected object. Further control of colors is available under **Properties** in the **Display** menu (see **Chapter 14**). *Clicking* on **✕** removes the dialog.

Fonts...

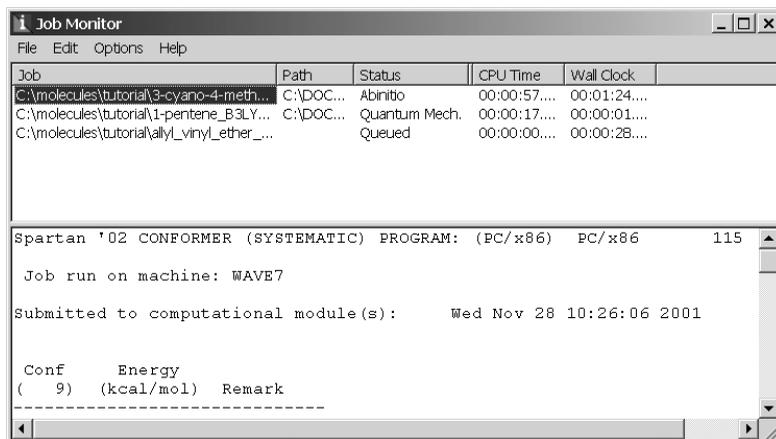
This allows user selection of fonts, style and size of labels attached to molecules (see **Labels** and **Configure...** under the **Model** menu; **Chapter 10**), and attached to plots (**Plots...** under the **Display** menu; **Chapter 14**). Selection leads to the **Fonts** dialog.



Selections need to be made from the **Font**, **Font Style** and **Size** menus. *Clicking* on **OK** dismisses the dialog with selections kept. *Clicking* on **Cancel** or on **✕** dismisses the dialog but selections are lost.

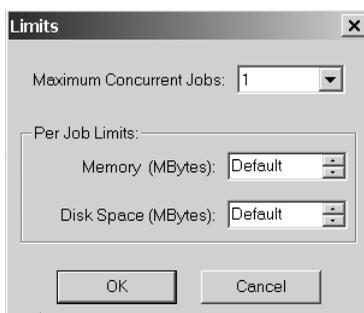
Monitor

Results in the **Monitor** dialog which lists all jobs which are presently executing or are queued for execution.



The box at the top gives the name of the job and the job status, i.e., either the name of the module presently executing or the word “queued”. To see accumulated output for an executing job, *click* on its name. To kill a job, *click* on its name, and then select **Kill Selected** from the **Edit** menu at the top of the **Monitor** dialog. To start a queued job (irrespective of the imposed queue limits; see below), *click* on its name and then select **Start Selected** from the **Edit** menu.

Queue limits as well as limits on memory and disk for an individual process may be set using **Limits** under the **Options** menu at the top of the **Monitor** dialog.



Maximum Concurrent Jobs sets the maximum number of jobs that can be run at one time and **Memory** and **Disk Space** set maximum

amounts of memory and disk for a single job. The dialog is dismissed with changes instituted by *clicking* on **OK**. *Clicking* on **Cancel** or on **X** dismisses the dialog but changes are lost.

Hartree-Fock calculations (only) will automatically make use of a fast “in memory” algorithm if sufficient memory is available. 100 basis functions can be accommodated with 110MB, 110 basis functions with 150MB, 120 basis functions with 200MB and 130 basis functions with 300MB. In this case, it may be advantageous to limit the number of maximum concurrent jobs to 1 in order to maximize available memory.

The **Monitor** may be removed either by selecting **Exit** from the **File** menu or by *clicking* on **X** 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 **X**.

Model Kit

If *checked*, this signifies that a model kit (entry, expert, peptide or nucleotide) is to remain on screen.

File Toolbar, Build Toolbar, Geometry Toolbar, Search Toolbar

If *checked*, this provides display of toolbars which access functions contained in the **File**, **Build**, **Geometry** and **Search** menus, respectively.

Cascade, Tile

Arranges open windows in a cascade or as tiles on top of Spartan'04's main window.

Arrange Icons

Arranges icons at bottom of Spartan'04's main window.

Chapter 17

The Help Menu

This chapter describes on-line help.

Spartan'04's on-line help facilities are available under the **Help** menu..

A rectangular button with a light gray background and a thin black border. The text "On-Line Help" is centered on the button in a small, black, sans-serif font.

On-Line Help

This provides information relating to application of computational methods in general, and to methods available in Spartan'04 in particular, as well as technical details regarding the program's operation.

The following topics make up on-line help:

Using the Mouse
Keyboard Functions
Calculation Options
Relative Computation Times
General Operating Features
Selecting a Model
Memory Usage

The Spartan'04 Tutorial and User's Guide (this document) is also available under **On-Line Help**. Help files are HTML documents and require that Internet Explorer be installed.

Finally, note that several of Spartan's dialogs incorporate imbedded help messages. These dialogs contain  at the upper right (to the immediate left of ). *Clicking* on , followed by *clicking* on a menu, button, etc. in the dialog gives rise to a brief informative message about the menu, button, etc.

Appendix A

Capabilities and Limitations

Essential Edition of Spartan'04 for Windows

Spartan'04 for Windows is available in two versions: a “full” version which is referred to as Spartan'04 and a lower-cost version, which is referred to as the “Essential Edition”. The latter shares the same graphical user interface as the full version, but lacks a number of the “more advanced” quantum chemical models as well as the ability to follow an intrinsic reaction coordinate, to calculate UV/visible and NMR Spectra and to perform molecular dynamics solvent calculations.

Molecular Mechanics Models¹

The molecular mechanics module provides for the calculation of equilibrium geometries, strain energies and vibrational frequencies, as well as for conformational searching. SYBYL (Tripos, Inc.) and MMFF94 (Merck Pharmaceuticals) force fields are available. There are no atom limits for molecular mechanics calculations.

Molecular mechanics parameters are read from a set of files: SYBYL.spp (SYBYL parameters) and MMFF94.spp (MMFF parameters). New parameters may be added or existing parameters modified by accessing these files.

Semi-Empirical Models¹

The semi-empirical module provides for calculation of heats of formation, wavefunctions, equilibrium and transition-state geometries and vibrational frequencies, as well as for conformational searching. MNDO, AM1 and PM3 models are supported. MNDO/d replaces MNDO for second-row (and heavier) main-group elements, and PM3 parameterizations for transition metals are available. MNDO has been parameterized for H, He, Li-F, Al-Cl, Ca, Zn, Ge, Br, Cd, Sn, I, Hg

and Pb; AM1 for H, B-F, Al-Cl, Zn, Ge, Br, Sn and I; PM3 for H-Ne, Mg-Ar, Ca, Ti-Br, Zr, Mo-Pd, Cd-I, Hf-Pt and Hg-Bi and Gd.

Preset limits for semi-empirical calculations are enumerated below.

maximum number of atoms (any type)	300
------------------------------------	-----

Semi-empirical parameters are read from a set of files: MNDO.spp (MNDO parameters), MNDOD.spp (MNDO/d parameters), AM1.spp (AM1 parameters), PM3.spp (PM3 parameters) and PM3D.spp (PM3 parameters for metals). New parameters may be added or existing parameters modified by accessing these files.

Hartree-Fock Models¹⁻³

The Hartree-Fock module provides for calculation of energies and wavefunctions, equilibrium and transition-state geometries and vibrational frequencies, as well as for conformational searching. Both closed-shell and open-shell (either ROHF or UHF) calculations are supported with minimal (STO-3G), split-valence (3-21G) and polarization (6-31G*, 6-311G*, cc-pVDZ⁴, cc-pVTZ⁴ and cc-pVQZ⁴) basis sets supplemented by additional polarization and/or diffuse functions. Also available are pseudopotentials for calculations on molecules incorporating heavy atoms.⁴

Preset limits for Hartree-Fock calculations are enumerated below.

maximum number of atoms	200
maximum number of basis functions	2000

Density Functional Models^{1,2,4}

The density functional module provides for calculation of energies and wavefunctions, equilibrium and transition-state geometries and vibrational frequencies, as well as for conformational searching. The module supports local density calculations and BP, BLYP, EDF1, B3LYP density functional calculations. The same basis sets and pseudopotentials supported for Hartree-Fock calculations are

available, although use of the minimal STO-3G and split-valence 3-21G basis sets is strongly discouraged.

Preset limits for density functional calculations are enumerated below.

maximum number of atoms	200
maximum number of basis functions	2000

Møller-Plesset Models^{1,2,4}

The Møller-Plesset module provides MP2, MP3 and MP4, as well as “local” MP2 (LMP2) energy calculations. In addition, the MP2 model (only) may be used for calculating equilibrium and transition-state geometries and vibrational frequencies, as well as for conformational searching. The same basis sets and pseudopotentials supported for Hartree-Fock calculations are available, although use of the minimal STO-3G and split-valence 3-21G basis sets is strongly discouraged.

Preset limits for MP2 calculations are enumerated below.

maximum number of atoms	200
maximum number of basis functions	2000

MP3 and MP4 calculations increase in cost very rapidly with increasing molecular size and are presently practical only for small molecules.

Advanced Correlated Models^{1,2,4}

The advanced correlated module provides for calculation of energies using the CCSD, CCSD(T), CCSD(2), OD, OD(T), QCISD, QCISD(T), QCCD and QCCD(2) correlated models. The same basis sets and pseudopotentials supported for Hartree-Fock calculations are also available, although use of the minimal STO-3G and split-valence 3-21G basis sets is strongly discouraged. Energy calculations are also supported with the G2, G3, and G3(MP2) models, which comprise a series of different models and are intended to provide accurate thermochemical data.

Advanced correlated calculations increase in cost very rapidly with increasing molecular size, and are presently practical only for very small molecules.

Excited-State Models

Two classes of models are available for calculations of excited states: configuration interaction (CI) models and time dependent density functional (TDDFT) models. The former comprises two models: CIS (configuration interaction singles) and CISD (configuration interaction singles with doubles correction), while the latter supports the local density model as well as BP, BLYP, EDF1 and B3LYP density functional models. At the present time, only the CIS model is available for geometry optimization and frequency calculations, all other models being restricted to single-point energy calculations.

Preset limits for excited-state calculations are enumerated below.

maximum number of atoms	200
maximum number of basis functions	2000

Properties and Spectra

The properties module (which is automatically called from the molecular mechanics module or one of the quantum chemical modules) provides for text output printing, population analyses (Mulliken, natural bond orbital and based on fits to electrostatic potentials), evaluation of thermodynamic quantities (enthalpy, entropy and free energy), and calculation of the dipole moment. Aqueous solvation energies, may be estimated using the SM5.4 model of Cramer and Truhlar⁵ (available for H, C-F, S-Cl, Br and I), and added to gas-phase total energies obtained at other levels of calculation. Additionally, solvent effects on energies as well as molecular properties and graphical surfaces, may be obtained from a molecular dynamics procedure in which the solvent-solute electrostatic interactions are incorporated into the Hamiltonian for the solute.⁴

The properties module is also responsible for providing data for later plotting of vibrational (infrared) spectra (all models except MP3, MP4 and advanced correlated models), UV/visible spectra⁴ (Hartree-Fock, local density and density functional models only) and NMR spectra⁴ (chemical shifts only and only for Hartree-Fock models).

Graphics

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.

-
1. For discussion and original references, see: W.J. Hehre, **A Guide to Molecular Mechanics and Quantum Chemical Calculations**, Wavefunction, Irvine, 2003
 2. For a review of the quantum chemical methods used in Spartan'04 (except for semi-empirical methods), see: J. Kong, C.A. White, A.I. Krylov, C.D. Sherrill, R.D. Adamson, T.R. Furlani, M.S. Lee, A.M. Lee, S.R. Gwaltney, T.R. Adams, C. Ochsenfeld, A.T.B. Gilbert, G.S. Kedziora, V.A. Rassolov, D.R. Maurice, N. Nair, Y. Shao, N.A. Besley, P.E. Maslen, J.P. Dombroski, H. Daschel, W. Zhang, P.P. Korambath, J. Baker, E.F.C. Byrd, T. Van Voorhis, M. Oumi, S. Hirata, C.-P. Hsu, N. Ishikawa, J. Florian, A. Warshel, B.G. Johnson, P.M.W. Gill, M. Head-Gordon, and J.A. Pople, *J. Computational Chem.*, **21**, 1532 (2000).
 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. Not available in Essential Edition.
 5. C.C. Chambers, G.D. Hawkins, C.J. Cramer and D.G. Truhlar, *J. Phys. Chem.*, **100**, 16385 (1996).

Appendix B

Menus

File

<u>N</u> ew	Brings up a model kit for molecule building
<u>O</u> pen...	Opens (imports) a molecule
<u>C</u> lose	Closes a molecule
<u>S</u> ave	Saves (exports) a molecule
Save <u>A</u> s...	Saves a molecule under a user-specified name
<u>N</u> ew Molecule	Adds a molecule to an existing list; brings up a model kit for molecule building
<u>D</u> elete Molecule	Deletes a molecule (or molecules) from a list
Append <u>M</u> olecule(s)...	Appends a molecule (or molecules) to an existing list
<u>P</u> rint...	Prints on-screen display
<u>P</u> rint Setup...	Setup for printing
<u>E</u> xit	Exits Spartan'04

Edit

<u>U</u> ndo	Undoes previous operations
<u>C</u> ut	Moves the current molecule or contents of the selection box to the clipboard
<u>C</u> opy	Copies the current molecule or contents of the selection box to the clipboard
<u>P</u> aste	Pastes contents of the clipboard to the screen
<u>F</u> ind...	Locates a text string in the output dialog or an on-screen molecular fragment
Find <u>N</u> ext	Locates next occurrence of a text string or molecular fragment
<u>C</u> enter	Centers the molecule on screen
<u>C</u> lear	Clears the screen (build mode only)

Model

<u>Wire</u>	Displays structure as wire-frame model
<u>Ball and Wire</u>	Displays structure as ball-and-wire model
<u>Tube</u>	Displays structure as tube model
<u>Ball and Spoke</u>	Displays structure as ball-and-spoke model
<u>Space Filling</u>	Displays structure as space-filling model
<u>Hide</u>	Hides structure model from view
<u>Global Model</u>	Applies model type and labels of current molecule to all molecules in the list
<u>Coupled</u>	Couples motions of all molecules in the list
<u>Hydrogens</u>	Toggles hydrogens “on” and “off”
<u>Labels</u>	Toggles labels “on” and “off”
<u>Ribbons</u>	Toggles ribbons “on” and “off”
<u>Hydrogen Bonds</u>	Toggles hydrogen bonds “on” and “off”
<u>Configure...</u>	Specifies labels for atoms, bonds, points, planes, etc., in addition to information about individual residues in polypeptides and polynucleotides and ribbon displays

Geometry

<u>Measure Distance</u>	Displays and/or sets bond distance
<u>Measure Angle</u>	Displays and/or sets bond angle
<u>Measure Dihedral</u>	Displays and/or sets dihedral angle
<u>Freeze Center</u>	Freezes selected atomic positions
<u>Set Torsions</u>	Selects bonds and rings for conformational searching
<u>Constrain Distance</u>	Constrains bond distance
<u>Constrain Angle</u>	Constrains bond angle
<u>Constrain Dihedral</u>	Constrains dihedral angle
<u>Define Point</u>	Defines a point as a geometric mean of a set of atoms
<u>Define Plane</u>	Defines a plane made by three atoms
<u>Align Molecules</u>	Aligns molecules in a list

Build

<u>V</u> iew	Removes the model kit
Add <u>E</u> ragment	Adds atomic fragment, functional group, ring, ligand or custom fragment
<u>D</u> elete	Deletes atoms, bonds, points, planes, etc.
<u>M</u> ake Bond	Makes a bond between two free valences, two atoms or a free valence and an atom
<u>B</u> reak Bond	Breaks a bond
<u>M</u> inimize	Performs molecular mechanics energy minimization

Setup

<u>C</u> alculations...	Sets up molecular mechanics and quantum chemical calculations
<u>S</u> urfaces	Sets up generation of and displays graphical surfaces
<u>S</u> ubmit	Submits job to the execution queue

Display

<u>O</u> utput	Displays text output
<u>P</u> roperties	Displays molecule, bond and atom properties as well as information about geometrical constraints, graphical surfaces, plots and statistical analyses
<u>S</u> urfaces	Sets up generation of and displays graphical surfaces (same as entry in Setup menu)
<u>S</u> pectra	Displays IR, NMR and/or UV/visible spectra and animates vibrational modes (associated with IR spectra).
<u>S</u> preadsheet	Displays spreadsheet
<u>P</u> lots...	Creates plots from the data in the spreadsheet

Search

<u>D</u> atabases	Performs substructure search on the Cambridge Structural Database (CSD) and/or the Spartan Molecular Database (SMD)
<u>T</u> ransition <u>S</u> tates	Provides guess at transition states based on reaction database or, in the absence of a suitable database entry, based on the linear synchronous transit method
<u>T</u> automers	Identifies tautomers

Options

<u>A</u> bout...	Provides information about Spartan'04, Wavefunction and Q-Chem
<u>P</u> references...	Sets various run-time preferences
<u>C</u> olors	Sets screen and model colors
<u>F</u> onts...	Sets fonts for molecule labels and plot displays
<u>M</u> onitor	Monitors and allows for “killing” executing jobs as well as control job queue
<u>C</u> alculator	“Pocket” calculator
<u>M</u> odel <u>K</u> it	Keeps a model kit on screen
<u>F</u> ile <u>T</u> oolbar	Toggles File toolbar “on” and “off”
<u>B</u> uild <u>T</u> oolbar	Toggles Build toolbar “on” and “off”
<u>G</u> eometry <u>T</u> oolbar	Toggles Geometry toolbar “on” and “off”
<u>S</u> earch <u>T</u> oolbar	Toggles Search toolbar “on” and “off”
<u>C</u> ascade	Arranges open windows in a cascade
<u>T</u> ile	Arranges open windows as tiles
<u>A</u> rrange <u>I</u> cons	Arranges icons at bottom of screen

Help

<u>O</u> n-Line <u>H</u> elp	Provides information about computational methods in Spartan'04 and details about program usage.
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Appendix C

Commonly-Used Program Options

This appendix describes a number of commonly-used program options. These are specified using keywords input into the **Options** box in the **Calculations** dialog (**Setup** menu). Keywords are case insensitive. An equals sign (“=”) separates a keyword from its integer, real or character string value. Keywords may either be single words or expressions. Keyword=N indicates an integer argument, keyword=C indicates a character argument, and keyword=F indicates a floating point argument. Real values can optionally include an “e” floating point power of ten. Default values for keywords are indicated in **bold**, and alternative values in *italics*.

Conformational Search

Keywords associated with conformational searching are as follows:

keyword	value	description
SearchMethod	C	conformational searching method employed; overrides default choice which depends on complexity of system may be overridden with one of the following: <i>Systematic</i> use systematic method <i>MonteCarlo</i> use Monte-Carlo method
MaxConfs	N	set maximum number of conformers to N; the program attempts to select the most diverse set representing the entire population; default is 100
Window	F	sets the maximum energy (in kcal/mol) at which a conformer will be kept to (minimum energy + F), where minimum energy is the

		energy of the lowest energy conformer encountered at that point in the search; default is 10 kcal/mol
MaxItr	N	sets the number of iterations allowed for a Monte Carlo search (only) to N; default is a function of the number of bonds and rings involved in the search
StartTemperature	F	sets initial “temperature” (in K) for a Monte Carlo search (only) to F; high temperatures will result in the molecule further “exploring” global space, while low temperatures will result in the molecule further “exploring” local space; default is 5000K

Geometry Optimization

Keywords associated with equilibrium geometry optimization (all methods) and transition-state geometry optimization (quantum chemical methods only) are as follows:

keyword	value	description
GeometryCycle	N	set maximum number of equilibrium and transition-state geometry optimization cycles to N; default is number of independent variables +20 for equilibrium geometry optimization and 3x number of independent variables for transition-state geometry optimization
GradientTolerance	F	set convergence criterion in equilibrium and transition-state) geometry optimization for the maximum gradient component (in hartrees/bohr) to F; default is 4.5×10^{-4}
DistanceTolerance	F	set convergence criterion in equilibrium and transition-state geometry optimization for the maximum change in a bond length (in Å) to F; default is 1.8×10^{-3}
Hess	C	Choose Hessian (matrix of second derivatives) for start of geometry (transition-state geometry) optimization (in the absence of a Hessian from a previous calculation, the default is MMFF)

molecular mechanics for geometry optimization and **PM3** semi-empirical for transition-state geometry optimization; may be overridden with one of the following:

<i>unit</i>	unit matrix
<i>MMFF</i>	MMFF molecular mechanics
<i>AMI</i>	AM1 semi-empirical
<i>STO-3G</i>	STO-3G Hartree-Fock
<i>3-21G</i>	3-21G Hartree-Fock
<i>6-31G*</i>	6-31G* Hartree-Fock

Quantum Chemical Calculations

Keywords associated with all quantum chemical calculations are as follows:

keyword	value	description
Diis	N	switch on diis all the time in SCF procedure. N is the size of the iterative subspace; it should be an integer between 2 and 10; default is 5
NoDiis		turn off diis SCF convergence accelerator
Energy	F	set SCF energy convergence criterion (in hartrees) to F; default is 1.0 x 10⁻⁶
ScfCycle	N	set maximum number of SCF iterations to N; default is 50
Guess	C	choose initial wavefunction guess; in the absence of a guess from a previous calculation, the default is either sad or PM3 depending on the calculation type, and may be overridden with one of the following: <i>core</i> diagonalize the core Hamiltonian <i>sad</i> superposition of atomic densities <i>PM3</i> PM3 semi-empirical
Scf	C	SCF procedure; default is restricted for closed-shell systems and unrestricted for open-shell systems, either of which may be specified for both closed and open-shell systems
Core	C	use of frozen core approximation in Møller-Plesset and advanced correlated calculations;

		default is frozen which may be changed to <i>thawed</i>
ScfTolerance	C	control of all tolerances in SCF procedure; default is normal which may be changed to <i>high</i> or <i>veryhigh</i>
	F	set SCF energy convergence criterion (in hartrees) to F; default is 1.0 x 10⁻⁶
BigGrid	–	uses very large grid in density functional calculations
Mix	–	specifies that α and β HOMO's in the guess wavefunction should be constructed according to:
		$\text{HOMO}_{\alpha} = \frac{\text{HOMO} + \text{LUMO}}{\sqrt{2}}$ $\text{HOMO}_{\beta} = \frac{\text{HOMO} - \text{LUMO}}{\sqrt{2}}$
		useful for generating a guess wavefunction for singlet diradical
SmallMemory, BigMolecule	–	forces use of direct methods in Hartree-Fock calculations
SmallMolecule	–	attempts to use in-core methods in Hartree-Fock calculations
PrintCoords	–	prints Cartesian coordinates
PrintLev	C	print level; default is normal which may be changed to <i>verbose</i> or <i>debug</i>

Semi-Empirical Calculations

Keywords unique to semi-empirical calculations are as follows:

keyword	value	description
NoPseudo	–	turns “off” pseudodiagonalization in response to convergence difficulties
NoAmideFix	–	turns “off” molecular mechanics amide correction in PM3 calculations
hhOff	–	turns “off” hydrogen-hydrogen repulsion term in PM3 calculations; default only where no

		transition metals are involved for compatibility with “standard” PM3
hhOn	–	turns “on” hydrogen-hydrogen repulsion term in PM3 calculations; default where transition metals are involved

Property and Spectra Calculations

Keywords associated with properties calculations are as follows:

keyword	value	description
NBO	C	specify details of NBO population analysis; default is normal which may be overridden for <i>ionic</i> and <i>3C</i> (three center) systems
NoElCharge	–	turns “off” calculation of electrostatic charges
NoMulCharge	–	turns “off” calculation of Mulliken charges
NoNatCharge	–	turns “off” calculation of NBO charges
ElCharge	N	adjusts size of grid used to calculate charge from electrostatic potential; default is 1 point/atomic unit
Temperature	F	temperature (in K) used in calculation of thermodynamic properties; default is 298°K
Pressure	F	pressure (in atm) used in calculation of thermodynamic properties; default is 1 atm
Moments	–	calculates and prints principal moments of inertia
NoSolvent	–	turns “off” calculation of aqueous solvation energy using SM5.4 model
FScale	F	scales calculated vibrational frequencies by F; default is 1
DynamicsTime	N	time (in fs) for molecular dynamics simulation for solvent calculations; default is 1500 fs
SampleTime	N	time (in fs) between sample points in molecular dynamics simulation for solvent calculations; default is 50 fs
MaxSamples	N	maximum number of sample configurations in molecular dynamics simulation for solvent calculations; default is 10

Cutoff	F	maximum solute-solute distance (in Å) for interactions to be explicitly treated in molecular dynamics simulations for solvent calculations; default is 14.0Å
IRCSteps	N	maximum number of steps allowed in constructing IRC; default is 40
IRCStepSize	N	maximum step size (in mass-weighted atomic units x 100) for IRC; default is 150

Appendix D

Units

Geometries

Cartesian coordinates are typically given in Ångstroms (Å), but are also available in atomic units (au).

Bond distances are typically given in Å but are also available in au. Bond angles and dihedral angles are given in degrees (°).

Surface areas are typically given in Å² and volumes in Å³, but are also available in au² (au³).

$$1 \text{ \AA} = 0.1 \text{ nm} = 1.889762 \text{ au}$$

Energies, Heats of Formation and Strain Energies

Total energies from Hartree-Fock, local density, density functional and correlated calculations are typically given in au, but are also available in kcal/mol, kJ/mol and electron volts (eV).

Heats of formation from semi-empirical calculations are typically given in kcal/mol, but are also available in au, kJ/mol and eV.

Strain energies from molecular mechanics calculations are typically given in kcal/mol, but are also available in au, kJ/mol and eV.

Orbital Energies

Orbital energies are typically given in eV, but are also available in 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 x 10⁻³

Electron Densities, Spin Densities, Dipole Moments, Charges, Electrostatic Potentials and Local Ionization Potentials

Electron densities and spin densities are given in electrons/au³.

Dipole moments are given in debyes.

Atomic charges are given in electrons.

Electrostatic potentials are given in kcal/mol.

Local ionization potentials are given in eV.

Vibrational Frequencies

Vibrational frequencies are given in wavenumbers (cm⁻¹).

Chemical Shifts

Chemical shifts are given in parts-per-million (ppm) relative to appropriate standards: proton, tetramethylsilane; carbon, tetramethylsilane. See **Appendix E** for numerical values.

UV/visible Spectra

λ_{\max} is given in wavenumbers (cm⁻¹).

Appendix E

NMR Chemical Shift Standards

Listed below are calculated absolute chemical shifts for ^1H , ^{13}C , ^{15}N , ^{19}F , ^{29}Si and ^{31}P from Hartree-Fock models with the following basis sets for the usual “reference” compounds.

nuclei	reference compound	3-21G	6-31G*	6-31G**
^1H	tetramethylsilane	33.61	32.89	32.33
^{13}C	tetramethylsilane	213.15	201.67	203.10
^{15}N	nitromethane	251.02	169.28	160.43
^{19}F	fluorotrichloromethane	279.76	269.48	269.48
^{29}Si	tetramethylsilane	508.94	450.14	448.39
^{31}P	phosphoric acid	504.17	423.64	423.16

nuclei	reference compound	6-31+G*	6-311G*	6-311+G**
^1H	tetramethylsilane	32.82	32.83	32.78
^{13}C	tetramethylsilane	201.85	195.92	195.87
^{15}N	nitromethane	159.64	177.41	184.80
^{19}F	fluorotrichloromethane	260.87	247.02	246.38
^{29}Si	tetramethylsilane	446.69	395.43	396.84
^{31}P	phosphoric acid	415.38	368.32	363.65

Chemical shift values reported by Spartan'04 for these nuclei with these Hartree-Fock models are in ppm relative to these standards. Chemical shift values for Hartree-Fock models with other basis sets are reported as absolute values.

Appendix F

Citation

The proper citation for Spartan'04 is as follows:

Spartan'04
Wavefunction, Inc.
Irvine, CA

Except for molecular mechanics and semi-empirical models, the calculation methods used in Spartan'04 have been documented in: J. Kong, C.A. White, A.I. Krylov, C.D. Sherrill, R.D. Adamson, T.R. Furlani, M.S. Lee, A.M. Lee, S.R. Gwaltney, T.R. Adams, C. Ochsenfeld, A.T.B. Gilbert, G.S. Kedziora, V.A. Rassolov, D.R. Maurice, N. Nair, Y. Shao, N.A. Besley, P.E. Maslen, J.P. Dombroski, H. Daschel, W. Zhang, P.P. Korambath, J. Baker, E.F.C. Byrd, T. Van Voorhis, M. Oumi, S. Hirata, C.-P. Hsu, N. Ishikawa, J. Florian, A. Warshel, B.G. Johnson, P.M.W. Gill, M. Head-Gordon, and J.A. Pople, *J. Computational Chem.*, **21**, 1532 (2000).

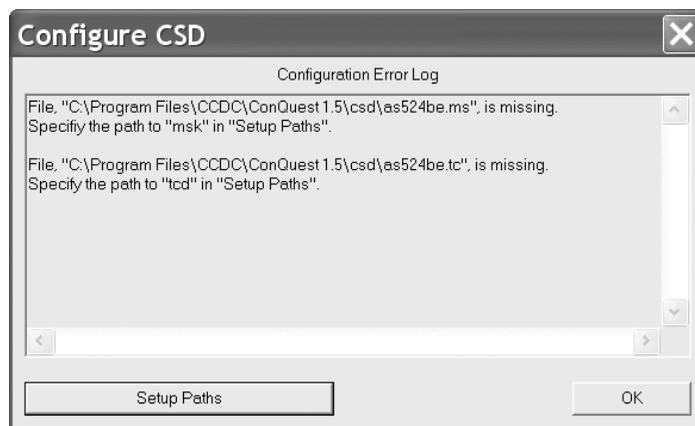
A discussion and assessment of commonly-used calculation methods is found in: W.J. Hehre, **A Guide to Molecular Mechanics and Quantum Chemical Calculations**, Wavefunction, Irvine, 2003.

Appendix G

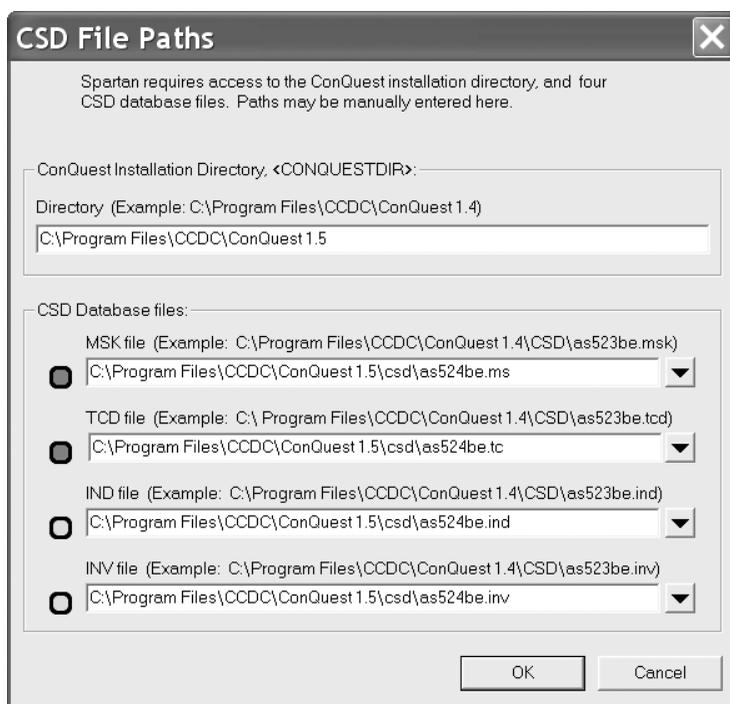
Installing the Cambridge Structural Database

Access to the Cambridge Structural Database (CSD) from Spartan'04 should be “automatic”, following successful installation of the ConQuest program (supplied with CSD) according to the detailed instructions provided. If access is denied, the following steps need to be taken:

- (i) *Click* on the square box immediately to the left of the **Retrieve** button at the bottom of the **CSD** dialog. This brings up the **Configure CSD** dialog,



This will list any files which are “missing”. *Click* on **Setup Paths** at the bottom of the dialog to bring up the **CSD File Paths** dialog,



This dialog should show one or more “red lights”.

- (ii) Make certain that the path to ConQuest is correctly specified. The most common error will be that the version number is not current. (At the time of writing, the current version is 1.5.) You can get the current version number from your installation of ConQuest.
- (iii) Given the proper version number for ConQuest, update the file names in the boxes below “MSK file”, “TCD file”, “IND file” and “INV file”. You can get the current file names from your installation of ConQuest. As you enter the current file names, the “red lights” should turn to “green lights”. When all lights are “green”, *click* on **OK** to dismiss the **CSD File Paths** dialog and then *click* on **OK** to dismiss the **Configure CSD** dialog.

Appendix H

Constructing Custom Databases

The user is free to add molecules to the Spartan Molecular Database, or to add different calculation levels for molecules which already exist. These new entries will not actually supplement (or replace) existing SMD entries, but rather will go into one or more (user defined) directories which will be accessed in addition to the existing SMD directory. At the present time, database information (abstracted from the original calculations) is limited to geometry, total energy, HOMO and LUMO energies, dipole moment, Mulliken, NBO and electrostatic-fit atomic charges, chemical shifts and vibrational frequencies. Future versions of the database may extend this list.

Creation of new database entries follows by saving a molecule (or list of molecules) as a Spartan Entry (.spentry) file (**Save As** under the **File** menu with **Save as type** set to **Spartan Entry**). The file name is not important, but the path to the directory must be entered into the **Paths Preferences** dialog (under **Preferences...** in the **Options** menu; see **Chapter 16**). This will typically follow the name of the default (SMD) directory “.\Standard Names” and be preceded by a semicolon “;”. As many user-defined directories as desired may be defined (separated by semicolons).

Note that a “name” for each molecule needs to be specified. This is done as a **Label** either in the **Molecule Properties** dialog (see **Properties** under the **Display** menu in **Chapter 14**) or in the spreadsheet (see **Spreadsheet** under the **Display** menu in **Chapter 14**).

IT IS IMPORTANT THAT ALL ORIGINAL DATA BE SAVED. ACCESS INFORMATION (SMILES-LIKE STRINGS) WILL BE EXTENDED AND/OR CHANGED TO INCLUDE NEW DATA TYPES (IN PARTICULAR, TRANSITION METAL

**SYSTEMS AND TRANSITION STATES). PROCEDURES
WILL BE SUPPLIED WITH FUTURE RELEASES TO
CREATE UPDATED ACCESS INFORMATION BASED ON
YOUR DATA.**

Appendix I

Installing a Network HASP

Spartan'04 requires a hardware license key which is normally installed on each machine. However, a network hardware key can be obtained from Wavefunction and installed on a server. This allows Spartan'04 to be run on a specified number of "client" machines on the network. A one-time installation is required.

On the Server:

1. Install Spartan and **HASP device driver** on the server. The server must be running Windows 98 or higher (Wavefunction strongly recommends Windows NT/2000 or higher).
2. Copy **Lmsetup.exe** from the Spartan CD ROM onto the server's hard drive and install the program by *double-clicking* on the icon.
3. When the program is finished installing, restart the server and verify that the **NetHASP license manager** has loaded the necessary protocols for your network.

On Each Client Computer:

4. Install software on the network clients that will access the NetHASP through the network. The **HASP device driver** is not required for installing the program on client computer. **DO NOT** install the **NetHASP license manager**. This is typically an auto-install.
5. Verify that the license manager is functioning correctly by trying to access Spartan from a network client computer (computer without the NetHASP hardware).

Additional:

6. If you want to run Spartan locally on the server, you must also install Spartan on the server. If client computers are on a different subnet from the license server, a **Nethasp.ini** file must be created and included in the directory with the Wavefunction program files.

Need additional help? Please visit our “Network Installation Frequently Asked Questions” (FAQ) page:

<http://www.wavefun.com/support/pc/faqpcnetwork1.html>

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