



Spartan *'04 Macintosh*

Tutorial and User's Guide



Wavefunction, Inc.

18401 Von Karman Avenue, Suite 370
Irvine, CA 92612 U.S.A.
www.wavefun.com

Wavefunction, Inc., Japan Branch Office

Level 14 Hibiya Central Building, 1-2-9 Nishi-Shinbashi
Minato-ku, Tokyo, Japan 105-0003
japan@wavefun.com • www.wavefun.com/japan



Copyright © 2001-2005 by Wavefunction, Inc.

All rights reserved in all countries. No part of this book may be reproduced in any form or by any electronic or mechanical means including information storage and retrieval systems without permission in writing from the publisher, except by a reviewer who may quote brief passages in a review.

ISBN 1-890661-28-7

Printed in the United States of America



Acknowledgments

This book derives from materials and experience accumulated at Wavefunction and Q-Chem over the past several years. It owes much to members of both companies, both past and present. Special thanks goes to Pamela Ohsan for turning a “sloppy manuscript” into a finished book.





Scope of this Guide

This guide provides a general reference for both Spartan'04 and the Essential Edition of Spartan'04 for Macintosh. 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 Macintosh, 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 of Spartan'04 for Macintosh. 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 Macintosh.

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**) and directions for installing a network HASP (**G**). 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, for Macintosh 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.
- **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 in the future 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.
- **Solvation Model for Molecular Mechanics.** The SM50R model of Cramer and Truhlar for aqueous solvation has been implemented.



It is intended to be used in conjunction with molecular mechanics, in particular, for conformational searching.

- **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.
- **Support for Sharp[®] Stereographic Monitor.** Spartan'04 for Macintosh fully supports Sharp monitors that allow unassisted (no glasses) stereographic displays.

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

- 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.

Spartan'04 for Macintosh 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.



Table of Contents

Section I	INTRODUCTION	1
Chapter 1	Spartan'04 for Macintosh	3
Section II	GETTING STARTED	9
Chapter 2	Operating Spartan'04	11
	Starting and Quitting	11
	Menus	11
	Keystroke Equivalents	12
	Tool Palette	12
	Using the Mouse	13
	Contextual Menus	15
	Keyboard Functions	16
	Selecting Molecules, etc	16
	List-to-List Operations	17
	3-Dimensional Displays	18
	Dialogs	18
	Changing Colors and Setting Preferences	18
	Monitoring and Killing Jobs	18
Chapter 3	Organic Molecules	19
	Acrylonitrile	21
	Cyclohexanone	32
	Camphor	35
	Ethinamate	36
	3-Cyano-4-methylcyclohexenyl radical	38
	Infrared Spectrum of Benzyne	41
	¹³ C NMR of <i>cis</i> -1,2-Dimethylcyclohexane	44
Chapter 4	Groups of Organic Molecules	47
	Dienophiles in Diels-Alder Cycloadditions	49
	Allyl Vinyl Ether	54
	Internal Rotation in Dimethylperoxide	57



	Hydration of Carbonyl Compounds.....	61
	Acidities of Carboxylic Acids	64
	Stereochemical Assignments from ^{13}C NMR	67
	Favoring One Tautomer Over Another	69
Chapter 5	Organic Reactions	73
	Ene Reaction of 1-Pentene	75
	Thermodynamic vs. Kinetic Control	79
	Stereospecific Diels-Alder Reactions	82
	Carbene Additions to Alkenes	85
	$\text{S}_{\text{N}}2$ Reaction of Bromide and Methyl Chloride....	89
Chapter 6	Biologically Interesting Molecules	93
	Vitamin E	95
	Androsterone.....	97
	Tautomers of Nucleotide Bases	100
	Polyglycine	102
	Propamidine DNA Complex	106
	Hydrogen Bonding in Biopolymers	108
Chapter 7	Inorganic and Organometallic Molecules	109
	Sulfur Tetrafluoride.....	111
	Benzene Chromium Tricarbonyl.....	114
	Ziegler-Natta Polymerization of Ethylene	116
Section III.	FEATURES AND FUNCTIONS	119
Chapter 8	The Spartan Menu	121
	About Spartan	121
	Spartan Monitor	122
	Preferences	123
	Services	125
	Hide Spartan	125
	Hide Others	125
	Show All	125
	Quit Spartan	125



Chapter 9	The File Menu	127
	New	127
	Open	127
	Retrieve	128
	Close	129
	Save	129
	Save As	129
	New Molecule	130
	Delete Molecule	130
	Append Molecule(s)	131
	Export	131
	Page Setup	132
	Print	132
Chapter 10	The Edit Menu	133
	Undo/Redo	133
	Cut	133
	Copy	134
	Paste	134
	Clear	134
	Select All	134
	Center	135
	Colors	135
Chapter 11	The Model Menu	137
	Wire	138
	Ball and Wire	138
	Tube	140
	Ball and Spoke	140
	Space Filling	141
	Hide	141
	Global Model	142
	Coupled	142
	Hydrogens	142
	Labels	142
	Ribbons	142



Hydrogen Bonds	143
Configure	143
Chapter 12 The Geometry Menu	145
Measure Distance	146
Measure Angle	147
Measure Dihedral	147
Define Point/Define Ligand Point	148
Define Plane	149
Freeze Center	149
Set Torsions	150
Align Molecules	151
Chapter 13 The Build Menu	153
Organic Model Kit	154
Inorganic Model Kit	158
Peptide Model Kit	162
Nucleotide Model Kit	165
General Molecule Building Functionality	168
Bond Rotation/Bond Sketching	168
Atom/Fragment Replacement	168
Chirality Inversion	168
View	169
Add Fragment	169
Delete	169
Make Bond	170
Break Bond	171
Minimize	171
Chapter 14 The Setup Menu	173
Calculations	174
Calculate	175
Start From	180
Subject to	181
Compute	182
UV/vis	182
IR	182
NMR	183



Total Charge	183
Multiplicity	184
Print	184
Options	185
Converge	185
Apply Globally	185
Surfaces	186
Surface	188
Property	189
Static Isovalue	190
Apply Globally	191
Submit	193
Chapter 15 The Display Menu	195
Output	195
Properties	196
Molecule Properties	196
Atom Properties	197
Bond Properties	197
Surface Properties	198
Constraint Properties	198
Plot Properties and Curve Properties	199
Surfaces	201
Spectra	201
IR	201
UV/vis	203
NMR	204
Spreadsheet	205
Plots	212
Regression	214
Chapter 16 The Search Menu	215
Database	215
Replacement	216
Substructure Searching	218
Transition States	222
Tautomers	224



Chapter 17 The Help Menu	225
Spartan Help	225
Appendix A Capabilities and Limitations	227
Essential Edition of Spartan'04 for Macintosh	227
Molecular Mechanics Models	227
Semi-Empirical Models	227
Hartree-Fock Models	228
Density Functional Models	228
Møller-Plesset Models	229
Advanced Correlated Models	229
Excited-State Models	230
Properties and Spectra	230
Graphics	231
Appendix B Menus	233
Appendix C Commonly-Used Program Options	239
Conformational Search	239
Geometry Optimization	240
Quantum Chemical Calculations	241
Molecular Mechanics and Semi-Empirical Calculations	242
Property and Spectra Calculations	243
Appendix D Units	245
Appendix E NMR Chemical Shift Standards	247
Appendix F Citation	245
Appendix G Installing a Network HASP	251
Index	253



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 that 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 that 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 Macintosh 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.

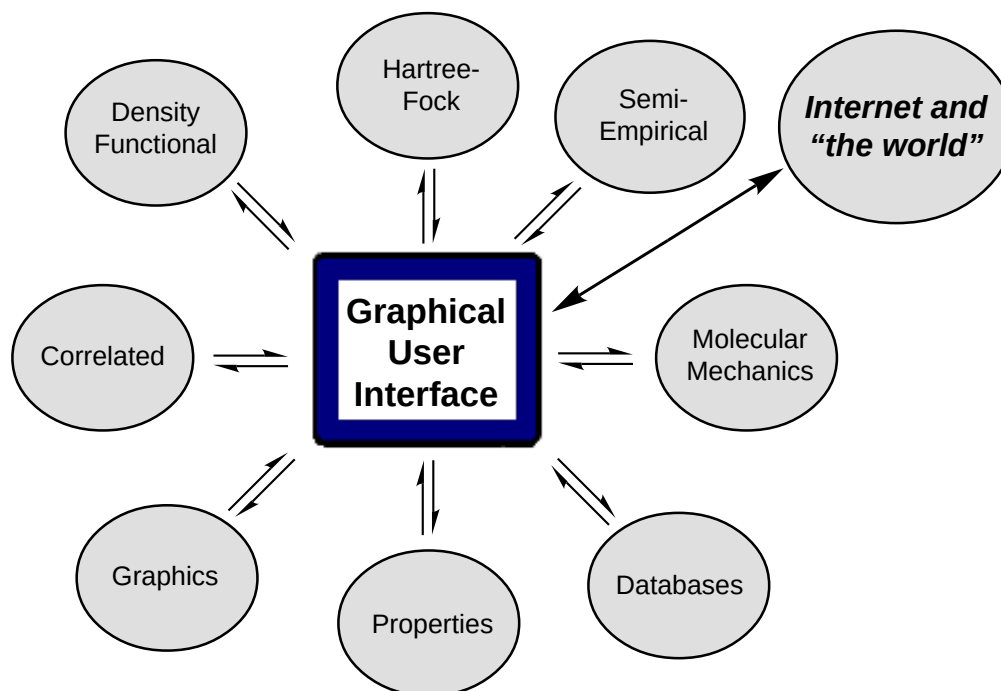
Spartan'04 for Macintosh *is intended to be utilized by chemists*, not only computational chemists who are already familiar with the capabilities of molecular mechanics and quantum chemical methods, but also experimental chemists who may have little or no prior experience, but who want to use calculations 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 Macintosh

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

Spartan'04 for Macintosh comprises a series of independent modules tightly connected via a graphical user interface, that 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. 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 provides the gateway into a range of modern computational methods, “theoretical models”, 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 available 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 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

* Full discussion and assessment of the specific molecular mechanics and quantum chemical models available in Spartan’04 for Macintosh 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).



atoms. Molecular mechanics models are at present the only computational techniques that are applicable to biopolymers including proteins. Calculation on very large molecule 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 roles for molecular mechanics models.

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, that can be routinely applied to systems with one to two hundred atoms. Supported in Spartan’04 for Macintosh are the MNDO model (with “d” extensions for second-row and heavier main-group elements), the AM1 model, and the PM3. The PM3 model has been parameterized for most transition metals, and is perhaps the least costly procedure available with which to explore the structures, properties and reactivities of inorganic and organometallic compounds.

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 for Macintosh 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 for Macintosh*: 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

* Not available in the Essential Edition.



approximate “local 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 for Macintosh.* 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 for Macintosh 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'04 for Macintosh 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 for Macintosh 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 Macintosh 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 that 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 to calculate equilibrium and transition-state geometries, to search conformation space and to evaluate reaction thermochemistry and activation energetics. 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.* Thorough assessment of all models available in Spartan'04 for Macintosh is provided in “***A Guide to Molecular Mechanics and Quantum Chemical Calculations***”.

Graphical models are illustrated in several of the tutorials that 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 is provided in the accompanying guide. Spartan'04 for Macintosh provides greatly enhanced capabilities over previous versions for display and

* This is deliberate, 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 for Macintosh (which lacks density functional, MP2 and other correlated calculations). Sections of tutorials which cannot be completed with the Essential Edition are indicated as such.

manipulation of structure models for biopolymers, and these too are illustrated.

Operating Spartan'04 outlines the basic workings of Spartan's graphical user interface. It should be perused before starting the tutorials and referred back to as needed. The tutorials, that make up the bulk of this section, are spread across five chapters: *Organic Molecules*, *Groups of Organic Molecules*, *Organic Reactions*, *Biologically Interesting Molecules* and *Inorganic and 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 and may be completed in any order.

The tutorials have been written to describe use of a two-button mouse in lieu of the Macintosh standard one-button mouse. Users wishing to employ a one-button mouse need to consult **Chapter 2** for the appropriate mouse/keyboards commands.

Estimates for required computer time (assuming a 700 MHz G4) are indicated at the top of the first page of each tutorial.

5 mins

Where two numbers are provided, the second corresponds to the total time including the optional part.

Chapter 2

Operating Spartan'04

This section describes general operating features of Spartan'04 for Macintosh. Some of these are common to all Macintosh applications and will be familiar to the “Mac” community, while others are specific to Spartan.

Starting and Quitting

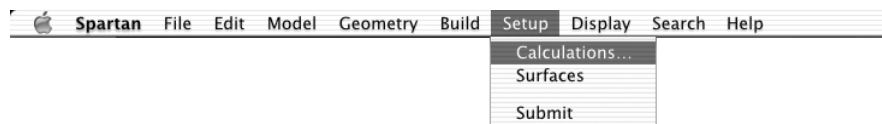
To start Spartan, *double click* on the appropriate icon. A window will appear, with its menu bar at the top of the screen.



To quit Spartan, select **Quit** from the **Spartan** menu.

Menus

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



A complete listing of functions available under the menus is provided in **Appendix B**.

“...” following the menu entry indicates that user action will be required before other operations can take place.

Keystroke Equivalents

Keystroke equivalents for some menu functions appear to the right of their menu entries, e.g., for the **File** menu.

New	⌘N
Open...	⌘O
Retrieve...	
Close	⌘W
Save	⌘S
Save As...	
New Molecule	⇧⌘N
Delete Molecule	
Append Molecule(s)...	
Export	▶
Page Setup...	
Print...	⌘P

A complete listing of keystroke equivalents for functions under the menus is provided in **Appendix B**.

Additionally, the **return** key may be used in place of *clicking* on highlighted buttons in most dialogs.

Tool Palette

A tool palette “floats” above the main window and contains icons for performing a number of commonly used functions.

	New		Save As
	Open		Close
	View		Make Bond
	Add Fragment		Break Bond
	Delete		Minimize
	Measure Distance		Measure Angle
	Measure Dihedral		Transition State
	Align		Database



Using the Mouse

Spartan'04 for Macintosh operates with either a one (Apple® standard) or a two-button mouse.

One-button mouse:

keyboard		keyboard	
–	picking, x/y rotate, chirality invert	option	x/y translate
⌘	z rotate	option, ⌘	scaling
ctrl	global x/y rotate ^a	option, ctrl	global x/y translate
⌘, ctrl	global z rotate ^a	shift	area selection
spacebar	bond rotation	option, spacebar	bond stretching
a) Global rotations can be either molecule or screen centered, set using Global Rotate in the Preferences dialog (Spartan menu; see Chapter 8).			

Selection: Molecule selection follows by *picking*, i.e., positioning the cursor and *clicking*. Area selection occurs by positioning the cursor above and to the left of the area to be selected, *pressing* both the button and the **shift** key, moving the mouse below and to the right of the area to be selected, and releasing both the button and the **shift** key.

Manipulation: Molecule rotation is accomplished by holding down on the button while moving the mouse, while rotation in the plane of the screen (Z axis) is accomplished by holding down on both the button and the ⌘ key while moving the mouse “up and down”. Molecule translation in the plane of the screen is accomplished by holding down on both the button and the **option** key while moving the mouse, while translation perpendicular to the screen (“scaling”) is accomplished by holding down the button in addition to both the **option** and ⌘ keys while moving the mouse “up and down”. Except for scaling, all operations apply only to the selected molecule, but can be made to apply to all molecules on screen by holding down on the **ctrl** key in addition to the button and other keys. In build mode only, rotation about a selected bond is accomplished by moving the mouse “up and down” while holding down on both the button and



the **spacebar**, bond stretching is accomplished by moving the mouse “up and down” while holding down on the button in addition to both the **option** key and the **spacebar**, and inversion of a chiral center ($R \leftrightarrow S$) is accomplished by *double clicking* on the center while holding down the **ctrl** key.

Two-button mouse:

keyboard	button	
	left	right
–	picking, X/Y rotate, chirality invert	X/Y translate
⌘	Z rotate	scaling ^b
ctrl	global X/Y rotate ^a	global X/Y translate
ctrl + ⌘	global Z rotate ^a	scaling ^b
shift	area selection	area selection
spacebar	bond rotation	bond stretching
a) Global rotations can be either molecule or screen centered, set using Global Rotate in the Preferences dialog (Spartan menu; see Chapter 8).		
b) If the mouse is equipped with a scroll wheel, this may also be used for scaling.		

Selection: Molecule selection follows by *picking*, i.e., positioning the cursor and *clicking* with the left button. Area selection occurs by positioning the cursor above and to the left of the area to be selected, *pressing* either the left or right button in addition to the **shift** key, moving the mouse below and to the right of the area to be selected, and releasing both the button and the **shift** key.

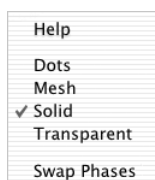
Manipulation: Molecule rotation is accomplished by holding down on the left button while moving the mouse, while rotation in the plane of the screen (Z axis) is accomplished by holding down on both the left button and the ⌘ key while moving the mouse “up and down”. Molecule translation is accomplished by holding down on the right button while moving the mouse, while translation perpendicular to the screen (“scaling”) is accomplished by holding down on both the right button and the ⌘ key while moving the mouse “up and down”. Scaling may also be accomplished using the scroll wheel if one is available. Except for scaling, all operations apply only to the selected



molecule, but can be made to apply to all molecules on screen by holding down on the **ctrl** key in addition to the appropriate mouse button and keys. In “build mode” only, rotation about a selected bond is accomplished by moving the mouse “up and down” while holding down on both the left button and **spacebar**, bond stretching is accomplished by moving the mouse “up and down” while holding down on both the right button and **spacebar**, and inversion of a chiral center ($R \leftrightarrow S$) is accomplished by *double clicking* on the center while holding down the **ctrl** key.

Contextual Menus

Atoms and bonds as well as isosurfaces, property maps and slices have attributes which can be queried and/or altered via contextual menus. Contextual menus may be accessed by positioning the cursor on an atom or bond, or on an isosurface or property map, or on the frame of a slice, e.g. for a property map, and then holding down on the mouse button (either button in the case of a two-button mouse).



The contents of the menu depend on context. Contextual menus act as a shortcut to functions normally accessible from dialogs under Spartan’s menus.

Keyboard Functions

Additional keys control various functions. These are enumerated below.

3	Shifts into 3D (stereo) mode. Pressing 3 again returns to normal mode.
Page Up, Page Down Home, End	Moves “up” (Page Up), “down” (Page Down), to the “top” (Home) and to the “bottom” (End) of a list of molecules. These keys also function in the Output window.
↑, ↓, →, ←	Moves “up and down” and “right and left” through the cells in the spreadsheet.

Selecting Molecules, etc.

Two or more molecules may be simultaneously displayed. 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. Note that scaling applies to all molecules on screen, and that the **control (ctrl)** key may be used for simultaneous manipulations of all molecules on screen.

Selection of a molecule occurs by *clicking* (left button for a two-button mouse) on its structure model or on any of its associated graphical displays. This results in deselection of the previously selected molecule. Molecular properties for the selected molecule are available under **Properties (Display menu)**. Atom, bond and graphical 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 “empty space” resets the display to molecular properties. *Clicking* on an atom, bond, constraint marker or graphical display for another molecule results in display of



atom, bond, etc. properties for that molecule. Information about plots 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 the  and  buttons or the scroll bar at the bottom left of the screen or the “up” and “down” arrow keys, or by *clicking* on the button to the left of 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. Selection of columns inside the spreadsheet may either be made by *clicking* inside individual cells or using the “right” and “left” arrow keys.

Two or more molecules from the same list may be displayed at once (although only one may be selected). Multiple molecule display is designated by *clicking* on  at the bottom left of the screen (it will then become ). In this mode, molecules are marked for display by *checking* the box immediately to the left of the molecule name in the spreadsheet. Note that molecule motions are “coupled” by default. To uncouple the motions, remove the checkmark beside **Coupled** in the **Model** menu, i.e., select **Coupled** from the **Model** menu.

List-to-List Operations

Individual molecules (or sets of molecules) may be directly transferred from one list to another. This requires that spreadsheets corresponding to both (originating and destination) lists be open on screen. Select the molecule(s) to be copied by *clicking* inside the left hand (“Name”) column in the appropriate row(s) of the spreadsheet corresponding to the originating list, and *drag* the mouse anywhere onto the spreadsheet corresponding to the destination list. This operation corresponds to a “copy”; the originating list is unchanged.

Molecule transfer from one list to another moves not only structure data, but also any calculated properties and graphical information.



3-Dimensional Displays

Any graphical object displayed on screen may be rendered in 3D (stereo) using color filtration techniques. “Red/blue” glasses (supplied with the programs) must be worn. While there is obvious loss of color in the resulting image, this simple technique works relatively well. 3D is turned “on” and “off” by toggling the “3” key.

In addition, Spartan’04 for Macintosh supports Sharp® monitors that allow unassisted (no glasses) stereographic displays. (For information about Sharp stereographic monitors, contact Wavefunction.) Stereographic monitor support is turned “on” and “off” by toggling the “4” key.

Dialogs

Dialogs are either “modal” (as indicated by “...” following their reference in a menu) or “non-modal”. Modal dialogs need to be dismissed before program operation can continue, while non-modal dialogs may be kept open on screen.

Changing Colors and Setting Preferences

Colors under the **Edit** menu (**Chapter 10**) allows for changing default background and graphical object colors. **Preferences** under the **Spartan** menu (**Chapter 8**) allows for setting program defaults.

Monitoring and Killing Jobs

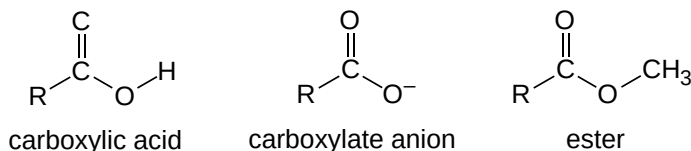
Spartan Monitor under the **Spartan** menu (**Chapter 8**) allows for monitoring of executing jobs as well as for killing jobs.

Chapter 3

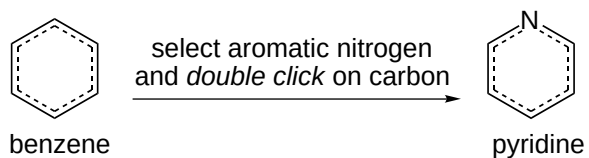
Organic Molecules

This chapter shows how to construct organic molecules from atomic fragments, functional groups and rings, how to carry out simple quantum chemical calculations and how to interpret graphical models.

The simplest building blocks incorporated into Spartan's organic 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 organic 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 organic model kit incorporates a library of commonly-encountered hydrocarbon rings, that 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.



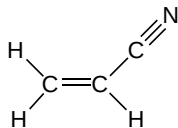
Functional groups may also be modified in this manner.

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 and their results examined and interpreted. A variety of graphical models are introduced and illustrated.



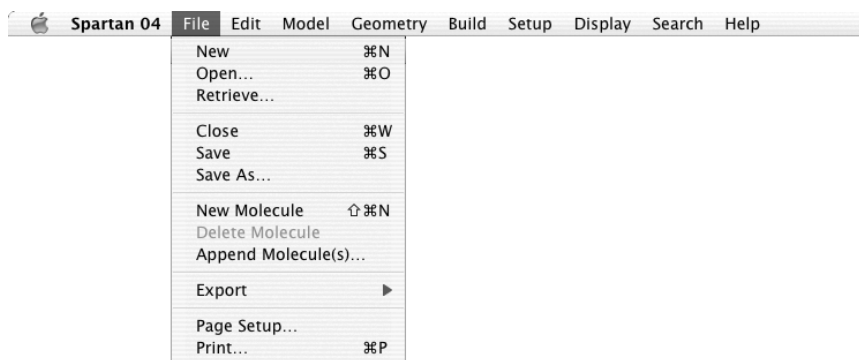
1 min

Acrylonitrile

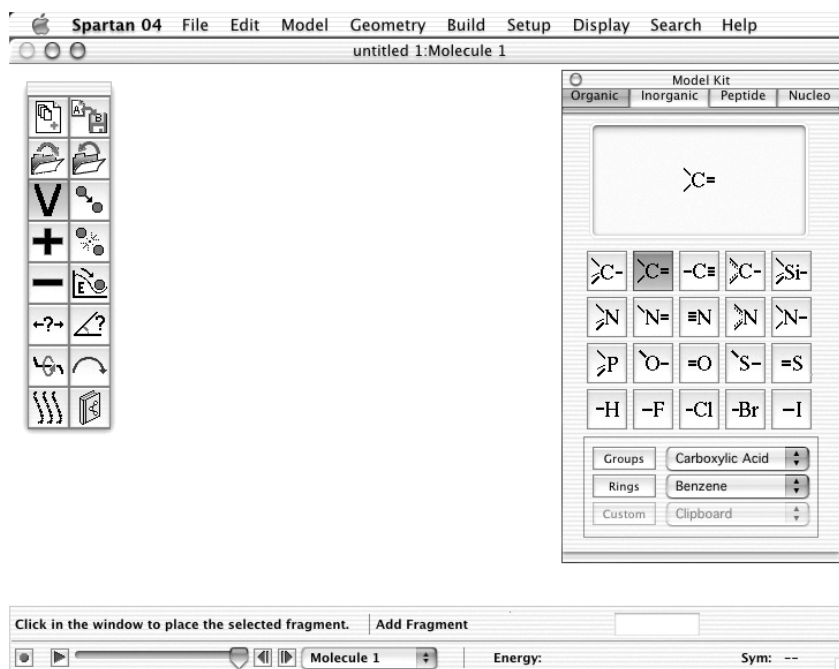


Acrylonitrile provides a good opportunity to illustrate the basics of molecule building in Spartan, as well as the steps involved in carrying out and analyzing a simple quantum chemical calculation.

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 **Tool Palette**). The “organic” model kit appears.





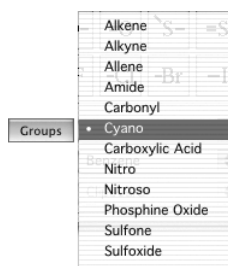
Among other things, it contains a library of atomic fragments. *Click* on trigonal planar sp^2 hybridized carbon  from the fragment library. The atom icon is highlighted to indicate that it is “active”. In addition, a model of the fragment appears at the top of the model kit. Bring the cursor anywhere on screen and *click*. Rotate the carbon fragment (move 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’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.

2. sp^2 carbon is still selected. *Click* on the tip of the double free valence. The two fragments are connected by a double bond, leaving you with ethylene.*

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

3. Select **Cyano** from among the functional groups available from the **Groups** menu.

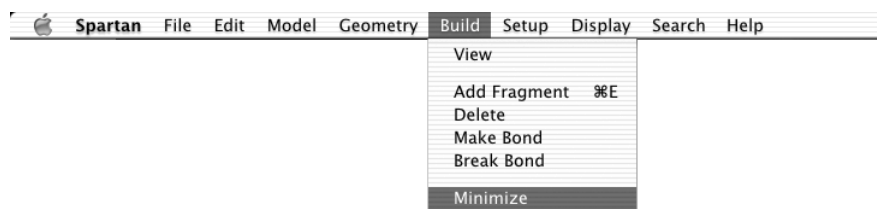


* If you make a mistake, for example, if you *click* on a single valence rather than the double valence, you can either select **Undo** or **Clear** from the **Edit** menu.

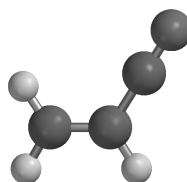


Click on any of the four single free valences on ethylene (they are all the same). This bonds the cyano group to ethylene, leaving you with acrylonitrile.*

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



5. Select **View** from the **Build** menu (or click on the  icon in the **Tool Palette**). The model kit disappears and a ball-and-spoke model of acrylonitrile appears on screen.



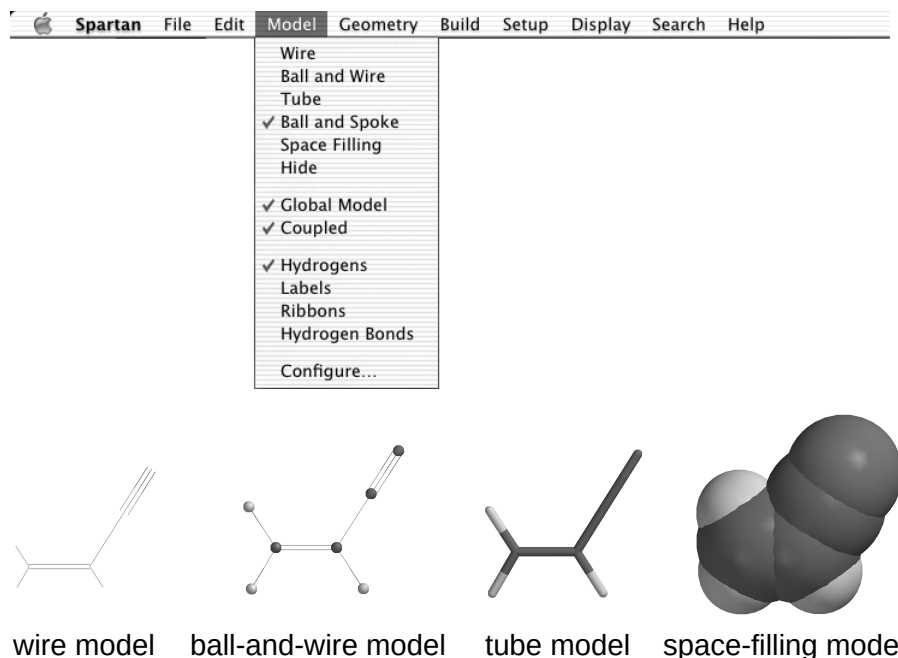
ball-and-spoke model

This model can be manipulated (rotated, translated and zoomed) by using the mouse (if necessary, in conjunction with keyboard functions). To rotate the model, move the mouse while holding down the left button; to rotate in the plane of the screen, hold down both the left button and the  key and move the mouse “up and down”. To translate the model, hold down the right button and move the mouse. To zoom the model (translation perpendicular to the screen), hold down the  key in addition

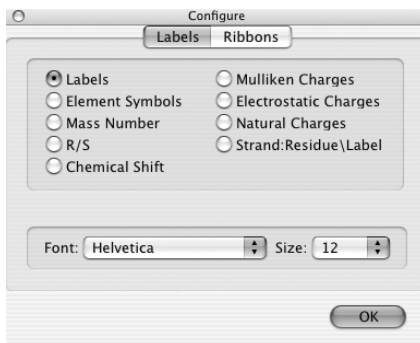
* You could also have built acrylonitrile without using the **Groups** menu. Starting from ethylene, select sp hybridized carbon  from the model kit and then click on the tip of one of the free valences on ethylene. Next, select sp hybridized nitrogen  from the model kit and click on the tip of the triple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

to the right button while moving the mouse “up and down”. Alternatively, use the scroll wheel if available.

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 Labels* in the **Configure** dialog which appears.

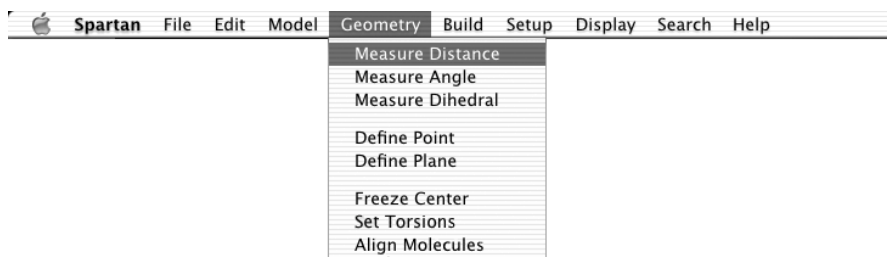


Numbers will appear next to the individual atoms together with atomic symbols. (**Labels** under the **Model** menu will



automatically be selected in response to your entry into the **Configure** dialog.) *Click* on **OK** to remove the dialog. To remove the labels, select **Labels** from the **Model** menu.

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



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

Select two atoms, a bond, ...

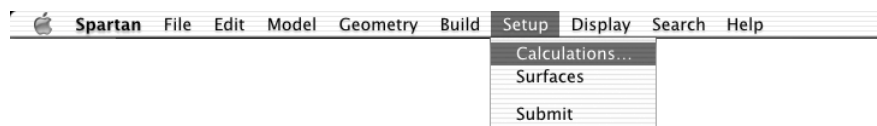
Click on two atoms, e.g., the two carbons involved in the double bond. Each atom will be colored gold, and the distance between the two will be displayed at the bottom right of the screen.

Distance C1 - C2 1.339 Angstroms 

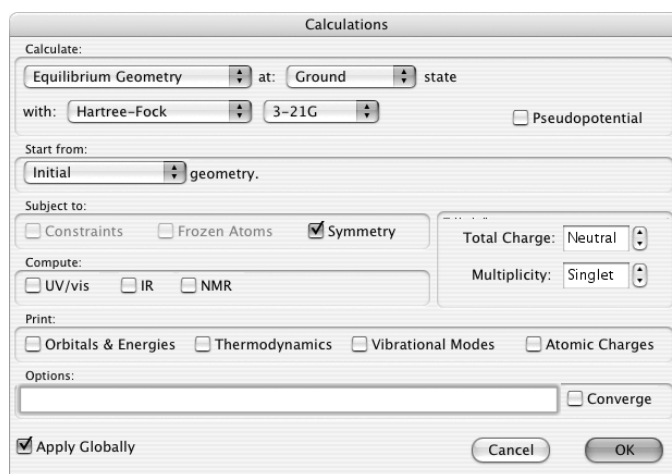
Where the two atoms are bonded, an alternative is to *click* on the bond. Another distance may be obtained by selecting another pair of atoms (or another bond), and so forth.

Measure Angle and **Measure Dihedral** from the **Geometry** menu ( and  icons from the **Tool Palette**) 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 **V**.

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



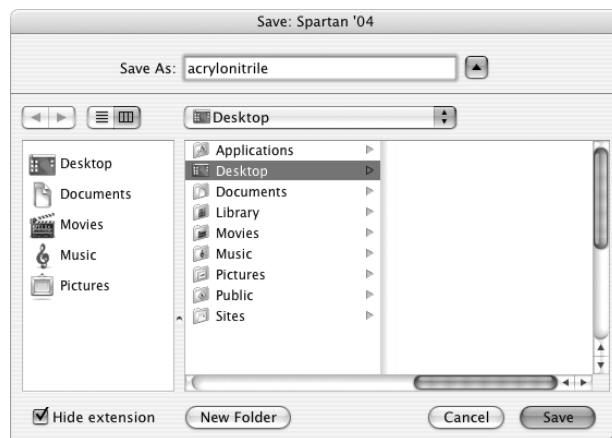
Perform the following operations in the dialog that appears.



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

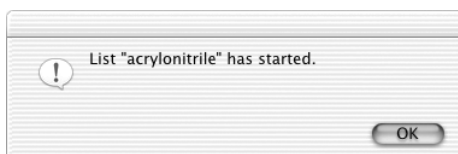
When you finish, *click* on **OK** to remove the dialog.

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



Provide a name “acrylonitrile”^{*} in the box to the right of “Save As”, and then *click* on **Save**. You will be notified that the calculation has started.

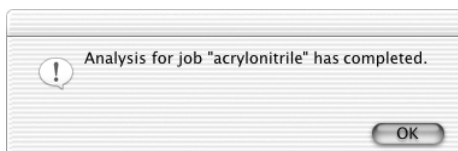
^{*} A name will appear if the molecule is in Spartan’s database. This name may be changed.



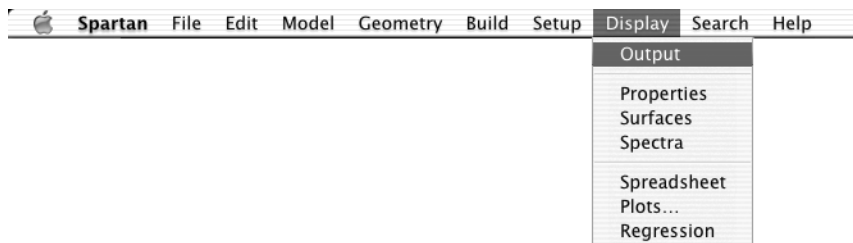
Click on **OK** to remove the message from the screen.

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.

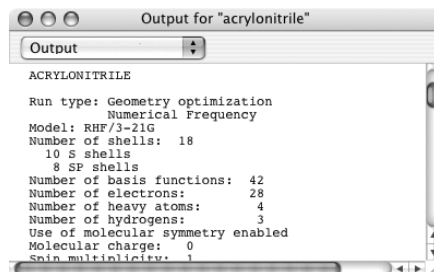
11. You will be notified when the calculation has completed.



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



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 point group of the molecule.

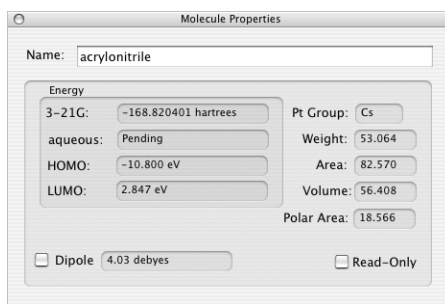
A series of lines, each beginning with “Cycle no:”, tell the history of the optimization. Each provides results for a particular geometry; “Energy” gives the energy in atomic units (1 atomic unit = 627.51 kcal/mol = 2625 kJ/mol), “Max Grad.” gives the maximum Cartesian gradient, and “Max Dist.” gives the maximum displacement of atoms between cycles. “Neg. Eigen.” reports the number of negative eigenvalues uncovered in the optimization. This should be blank at the end of an 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. At the end of this section is the final total energy (-168.82040 atomic units) and the computation time.

Information about atomic charges, as well as charges broken down by individual basis functions, follows. In addition, an “approximate” dipole moment based on these charges is provided. This should be similar to the experimental dipole moment (4.03 debyes).

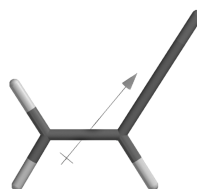
Click on  in the top left-hand corner of the dialog (the “red lozenge”) to remove the dialog from the screen.*

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

* The red, yellow and green lozenges are standard Mac OS 10 functionality for closing, iconizing and expanding a window/dialog. They will not be referred to again. Rather we shall use such wording as “close the dialog” or “dismiss the dialog”.

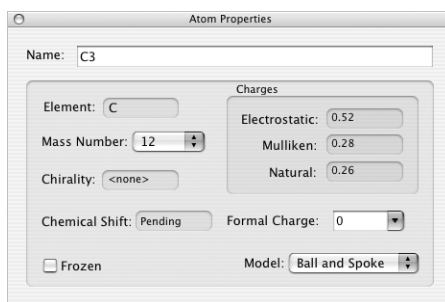


To see the dipole moment vector (indicating the sign and direction of the dipole moment), *check* the box to the left of “Dipole”. Switch to a tube model (**Tube** from the **Model** menu).



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

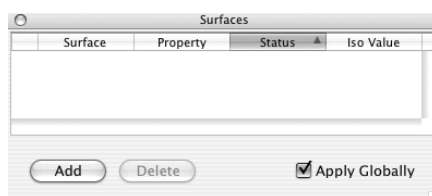
Click on an atom. The (**Molecule Properties**) dialog will be replaced by the **Atom Properties** dialog.*



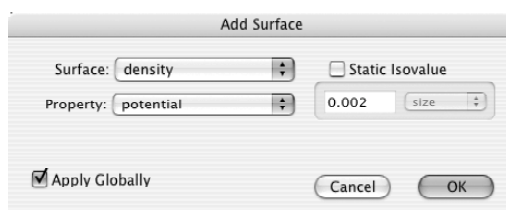
Among other things, this provides three different sets of atomic charges “Electrostatic”, “Mulliken” and “Natural”. To obtain the charge on another atom, simply *click* on it. Inspect all the atomic charges on acrylonitrile (by *clicking* on the appropriate atoms). When you are done, dismiss the **Atom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

* To return to the **Molecule Properties** dialog, *click* on the background.

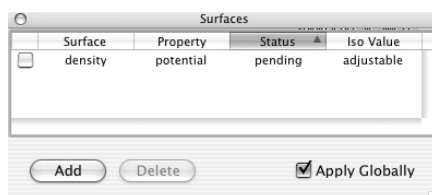
12. Select **Surfaces** from either the **Setup** or **Display** menu.



Click on **Add** (at the bottom of the 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 **Surfaces** dialog.

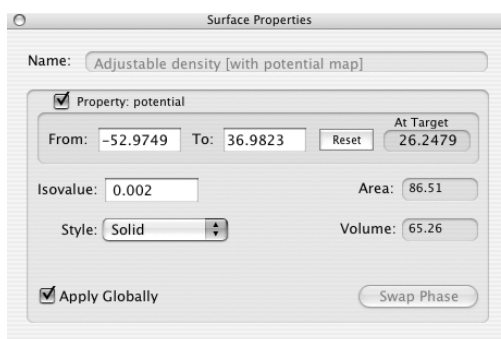


If you make a mistake, *click* on this line and then *click* on **Delete** at the bottom of the dialog. Leave the **Surfaces** dialog on screen.

13. Submit the job (**Submit** from the **Setup** menu). When complete, *double 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 the density surface; colors toward red correspond to negative potential (stabilizing interaction with 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.

You can change the style of the graphics display from “solid” to “dots”, “mesh” or “transparent”. Bring up the **Surface Properties** dialog by first selecting **Properties** from the **Display** menu and then *clicking* on the surface. Select **Dots**, **Mesh** or **Transparent** from the **Style** menu.



Alternatively, hold down on either mouse button with the cursor positioned on the surface, and select a style from the menu which appears.



14. Select **Close** from the **File** menu (or *click* on the  icon from the **Tool Palette**) to remove acrylonitrile from the screen. You will be asked whether or not you want to save your model.

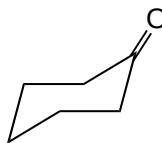


*Click on **Save**.*



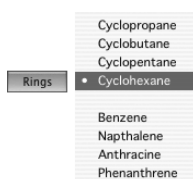
5 mins

Cyclohexanone



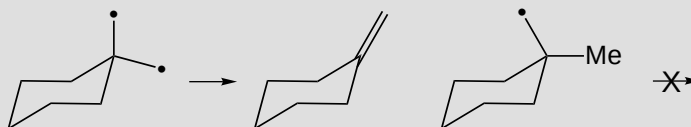
Cyclohexanone provides the opportunity to illustrate additional building features as well as graphical models for investigation of stereoselectivity.

1. Click on . Select **Cyclohexane** from the menu of rings in the model kit.



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

Spartan's organic 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 tip of the double free valence on the sp^2 carbon. You have made cyclohexanone. Click on  to produce a final structure with C_s symmetry, then click on **V**.



2. Select **Calculations...** from the **Setup** menu. Specify **Equilibrium Geometry** from the top menu below “Calculate”, and **Hartree Fock** and **3-21G** from the two bottom menus below “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, bring up the **Surfaces** dialog (**Surfaces** under either the **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 and *click* on **OK**. Leave the **Surfaces** dialog on screen. Submit the job (**Submit** from the **Setup** menu) with the name “cyclohexanone”.

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 keeps track of what has been done and will not perform unnecessary calculations.

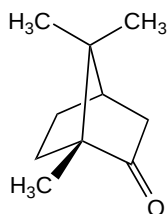
4. After the calculations have completed, reenter the **Surfaces** dialog and *double click* on the line “LUMO . . .”. The LUMO of cyclohexanone appears. As expected, this is a π^* orbital primarily localized on the carbonyl group.
5. Turn “off” the display of the LUMO by *double clicking* on the line “LUMO . . .” inside the **Surfaces** dialog. Next, *double 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 **Surface Properties** dialog by first selecting **Properties** from the **Display** menu and then *clicking* anywhere on the surface. Turn the map such that you can clearly see the *axial* face of the carbonyl carbon, and *click* on the area of maximum blue. The (absolute) value of the LUMO at the surface point you have selected is provided in the dialog (below “At Target”). 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” from the screen (*click* on ).

Camphor



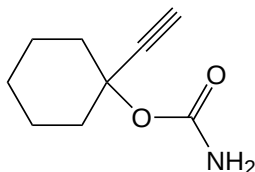
Camphor illustrates how one molecule may be used as the starting point for another. No calculations are involved in this example.

1. Bring “cyclohexanone” (previous example) back onto the screen. Select **Open** from the **File** menu (or *click* on the  icon in the **Tool Palette**) and *double click* on “cyclohexanone” in the dialog which results. Next select **Save As** from the **File** menu (or *click* on the  icon in the **Tool Palette**), supply the name “camphor” and *click* on **Save**.
2. Select **Add Fragment** from the **Build** menu (or *click* on the  icon from the **Tool Palette**) to bring up the organic 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* 2-methylcyclohexanone.
3. Select **Make Bond** from the **Build** menu (or *click* on the  icon from the **Tool Palette**). *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 . 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; see figure above). Finally, *click* on  to give a minimized camphor geometry with C₁ symmetry. *Click* on .
4. Select **Configure...** (**Model** menu), *check* **R/S** under “Atom” in the dialog which results, and *click* on **OK**. R/S labels appear on the two bridgehead carbons (both R or both S).
5. Close “camphor” (.



1 min

Ethinamate



Acrylonitrile, cyclohexanone and camphor are examples of molecules that can adopt only a single conformation. Much more common are molecules that can adopt more than one conformation, usually due to rotation about single bonds or to 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 organic model kit () . Select **Cyclohexane** from the **Rings** 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 the 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.

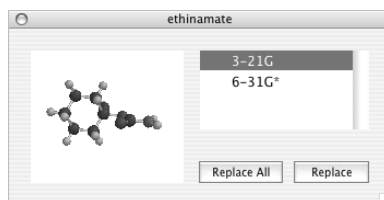


You can move the bonding position by repeatedly *clicking* on the icon. When you are satisfied, add the amide to oxygen to make the carbamate functionality. Finally, select **Alkyne** from the **Groups** menu and add to the same carbon on the cyclohexane ring as occupied by the carbamate group (using



the remaining *axial* or *equatorial* free valence). Click on , to produce a refined structure and finally click on .

2. Bring up the **Calculations** dialog (**Setup** menu). Select **Equilibrium Conformer** from the top menu below “Calculate” and **Molecular Mechanics** and **MMFF** from the two bottom menus. In this mode, Spartan will examine “all possible” conformers*, but then select only the most stable conformer (according to the MMFF model). Exit the dialog (click on **OK**) and submit for calculation (**Submit** from the **Setup** menu). Name the molecule “ethinamate”.
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?

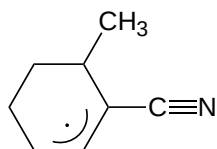
5. Close “ethanimat” as well as any open dialogs.

* 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.



10 mins

3-Cyano-4-methylcyclohexenyl Radical



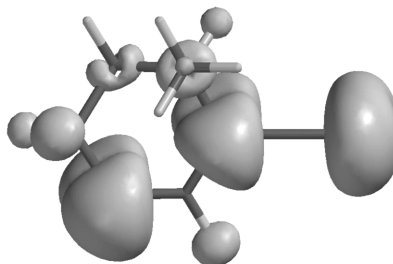
This tutorial illustrates how different models may be combined to achieve a desired result with minimum computation. MMFF molecular mechanics will be employed to establish equilibrium conformation, the semi-empirical AM1 model to establish equilibrium geometry and the Hartree-Fock 3-21G model to provide 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. *Click* on . Add **Cyano** from the **Groups** menu to an *equatorial* free valence on one of the carbons adjacent to the double bond you have just made. Finally, add a “methyl group” ( from the model kit) to the appropriate ring position (see figure above) using either the *equatorial* or *axial* free valence.
2. Select **Delete** from the **Build** menu (or *click* on the  icon from the **Tool Palette**), 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 .
3. Select **Calculations...** (**Setup** menu). Specify **Energy** from the top menu below “Calculate” and **Hartree-Fock** and **3-21G** from the two bottom menus. Next, specify **MMFF Conformer** from the menu below “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 a “radical”). It is necessary to change **Multiplicity** from **Singlet** to **Doublet**. *Click* on **OK** to remove the **Calculations** dialog.



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 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**. Leave the **Surfaces** dialog on screen.
5. Submit the job. Name it “3-cyano-4-methylcyclohexenyl radical” When completed, examine the conformation. Is the methyl group *equatorial* or *axial*? Next, enter the **Surfaces** dialog. Display the spin density surface by *double 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. Remove the spin density surface by *double clicking* on the line “spin . . .”. Then, display the spin density map. *Double 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. The range of spin density values is provided in the dialog (“From” to “To”). Note, in particular, that negative values of the spin density are possible.



7. Dismiss the **Surface Properties** dialog and turn “off” display of the spin density map (*double click* on the line “density spin . . .” inside the **Surfaces** dialog). Then turn “on” display of the SOMO (*double click* on the line “SOMO . . .”). Note that the singly-occupied molecular orbital is qualitatively similar to the previously-displayed image of the spin density.
8. Turn “off” display of the SOMO by *double 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. It is designated as “completed”, meaning that no further calculations are required. *Double click* on this line.
9. A plane (a “slice”) of spin density surrounded by a gold frame appears in the middle of the model on screen. (If it is white instead of gold, *click* on the frame (or inside of the frame) and it will turn gold.) Position the cursor outside the frame, then *press* both the  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” from the screen.

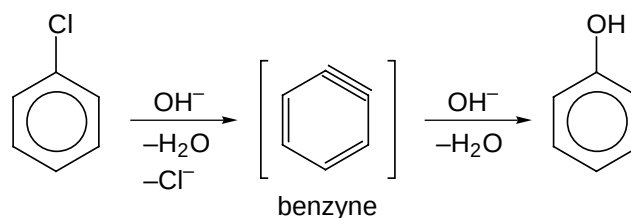
* Other slice styles are available. Position the cursor on the plot frame, and hold down on either button to get a menu of choices.



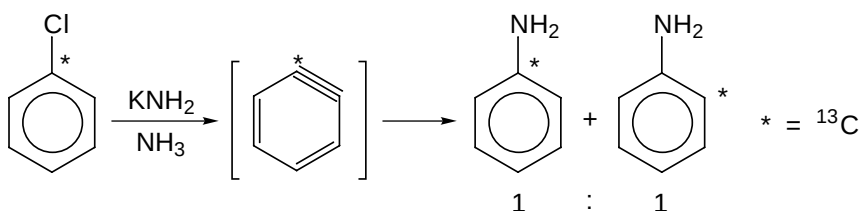
5 mins

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.

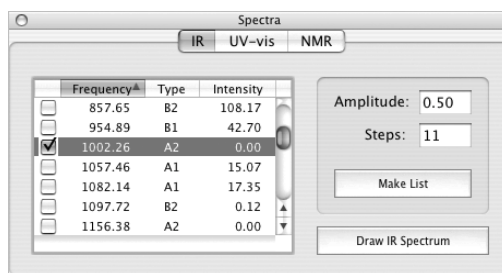
1. Bring up the organic model kit, select **Benzene** from the **Rings** menu and *click* anywhere on screen. *Click* on and *click* on two adjacent free valences on benzene. *Click* on and then on .
2. Enter the **Calculations** dialog (**Setup** menu). Select **Equilibrium Geometry** from the top menu to the right of "Calculate" and **Hartree-Fock** and **3-21G** from the

two bottom menus. *Check IR* below “Compute” in the center of the dialog. You have requested that an infrared spectrum be computed following optimization of geometry. *Click* on **OK** and then select **Submit** from the **Setup** menu. Provide the name “benzyne”.

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”. 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.

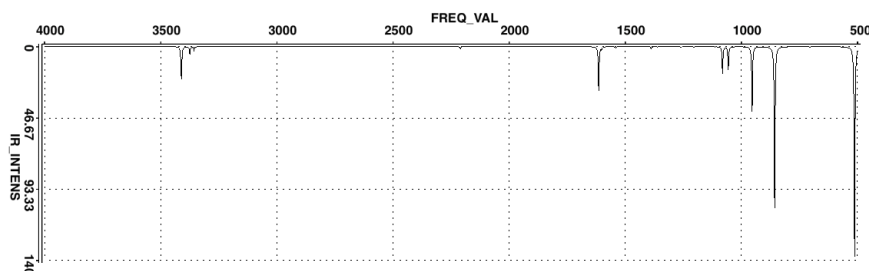
5. Select (*click* on) benzyne and then select **Spectra** from the **Display** menu. *Click* on the **IR** tab in the dialog which results to bring up the **IR Spectra** dialog.



One after the other, *check* the boxes to the left of the frequencies in the dialog (or *double click* on the frequencies). In response, the vibrational motion associated with this frequency will be animated. Find the frequency that best fits the description of a C≡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 approximately 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 the (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.

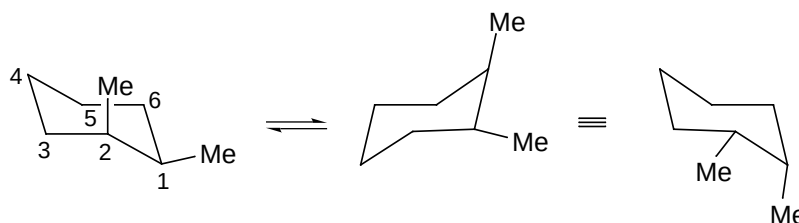
* Rationalization of this behavior together with frequency performance statistics for a number of the commonly used theoretical models available in Spartan'04 for Macintosh may be found in “***A Guide to Molecular Mechanics and Quantum Chemical Calculations***”.



15 mins/45 mins

¹³C 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 ¹³C 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 C₁ and C₂, C₃ and C₆, and C₄ and C₅ 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) ¹³C NMR spectrum of *cis*-1,2-dimethylcyclohexane, and then average chemical shifts for the three pairs of “equivalent” ring carbons to yield a spectrum that can be directly compared with the observed (room temperature) spectrum. You will use the carbon shifts in cyclohexane as a “standard” (instead of TMS). Optionally, you will obtain a ¹³C 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.

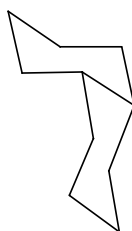
1. Build and minimize *cis*-1,2-dimethylcyclohexane. Inside the **Calculations** dialog, specify calculation of equilibrium geometry using the Hartree-Fock 6-31G* model. *Check NMR* below “Compute”. Click on **OK** to exit the dialog and then select **Submit** from the **Setup** menu and submit the job. Name it “cis-1,2-dimethylcyclohexane”.



2. Perform the same calculation (6-31G* equilibrium geometry and NMR spectrum) on cyclohexane (name it “cyclohexane”). This will be used (in place of TMS) as the reference compound for the ring carbons in dimethylcyclohexane.
3. After the calculations have completed, 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 that results). In the latter case, you may want to remove the hydrogens to simplify the display (select **Hydrogens** from the **Model** menu; select again to restore the hydrogens). 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?

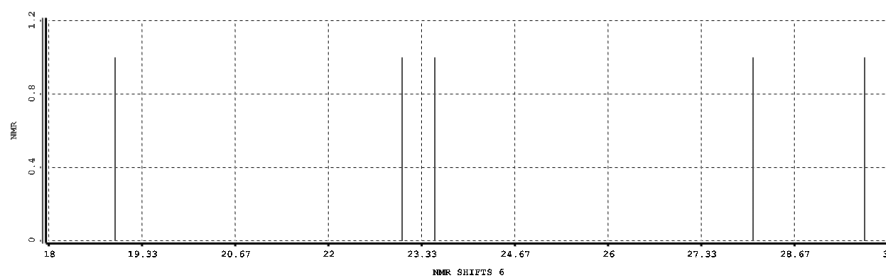
4 to 6 optional

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, retrieve 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. *Click* on “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 an energy calculation using the Hartree-Fock 6-31G* model. *Check NMR* under “Compute”. (Make certain that **IR** is not *checked*.) *Click* on **OK**. Submit for calculation with the name “cis-decalin”.
6. When the calculation has completed, select **Spectra** from the **Display** menu and *click* on the **NMR** tab. *Click* on **Draw ^{13}C Spectrum**.



Because of the (C_2) symmetry of *cis*-decalin, the 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 facilitates these tasks. 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 easily, 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 plots constructed.

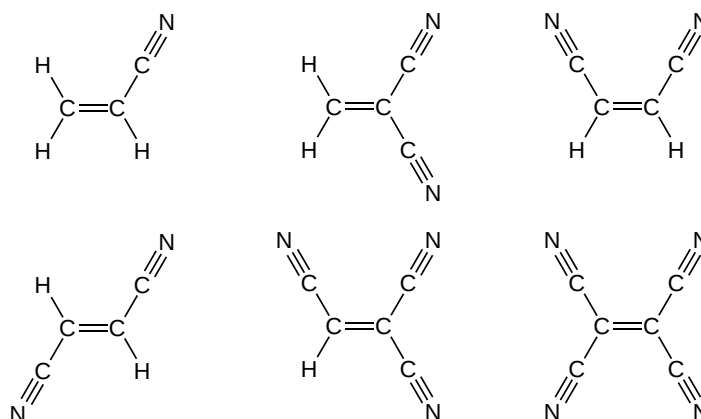
The tutorials in this chapter introduce a number of the basic group operations available in Spartan’04 for Macintosh. These include building a group “from scratch”, and processing groups resulting from a conformational search and from varying a torsion angle. Also provided is a simple example of fitting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



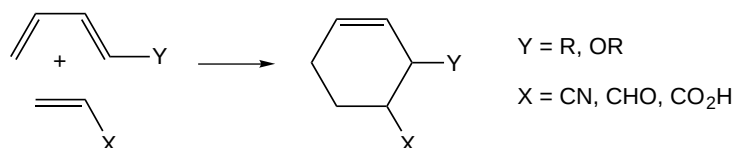


10 mins

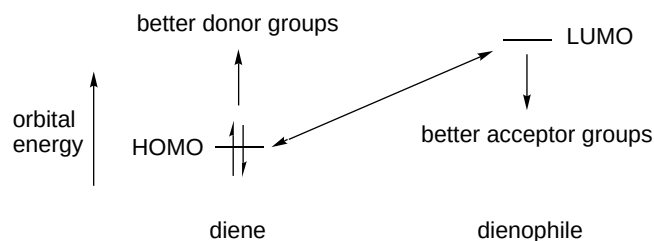
Dienophiles in Diels-Alder Cycloadditions



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

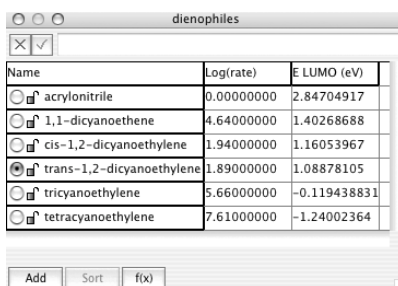


The rate of Diels-Alder reactions generally increases with increasing π -donor ability of the diene substituent, and with increasing π -acceptor ability of the substituent on the dienophile. This can be rationalized by recognizing that donor groups raise the energy of the highest-occupied molecular orbital (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.



Here, you will attempt to correlate experimental relative rates of Diels-Alder cycloadditions involving cyclopentadiene and a variety of cyanoethylenes with dienophile LUMO energies.

1. Build and minimize acrylonitrile. When you are done, do not *click* on **V**. Select **New Molecule** (not **New**) from the **File** menu. This insures that the next molecule (1,1-dicyanoethylene) will be put into the same list as the first (acrylonitrile). When you have built and minimized 1,1-dicyanoethylene, again select **New Molecule** and build and minimize *cis*-1,2-dicyanoethylene. Repeat the procedure (**New Molecule**, build and minimize) for *trans*-1,2-dicyanoethylene, tricyanoethylene and tetracyanoethylene. After you have completed the last molecule, *click* on **V** to remove the model kit from the screen. Bring up the associated spreadsheet (**Spreadsheet** under the **Display** menu).



Name	Log(rate)	E LUMO (eV)
acrylonitrile	0.00000000	2.84704917
1,1-dicyanoethylene	4.64000000	1.40268688
cis-1,2-dicyanoethylene	1.94000000	1.16053967
trans-1,2-dicyanoethylene	1.89000000	1.08878105
tricyanoethylene	5.66000000	-0.119438831
tetracyanoethylene	7.61000000	-1.24002364

Proper names should appear in the lefthand column of the spreadsheet.*

2. Enter the **Calculations** dialog, and specify calculation of an equilibrium geometry using the Hartree-Fock 3-21G model. Make certain that **Apply Globally** is *checked* to ensure that calculations are to be applied to all members in the list.
3. Submit the job. Name it: “dienophiles”. While you are waiting for it to complete, enter the experimental relative rates from the table below into the spreadsheet.

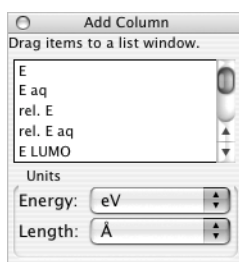
* If a name is missing, or if you wish to change a name, *click* inside the lefthand column in the spreadsheet, type in the molecule name and *press* the **return** key.



Experimental relative rates for Diels-Alder cycloadditions of cyclopentadiene*	
dienophile	log ₁₀ (relative rate)
acrylonitrile	0
trans-1,2-dicyanoethylene	1.89
cis-1,2-dicyanoethylene	1.94
1,1-dicyanoethylene	4.64
tricyanoethylene	5.66
tetracyanoethylene	7.61
* J. Sauer, H. Weist and A. Mielert, <i>Chem. Ber.</i> , 97 , 3183 (1964).	

Click inside the cell at the top of a “blank” column and type “Log(rate)” into the text box at the top of the spreadsheet. Press the **return** key. Then enter the rate data in the appropriate cells. For each, click inside the blank cell, enter the appropriate relative rate into the text box at the top of the spreadsheet and press the **return** key after each entry. Sort the list according to relative rate. Click on the column header “Log(rate)”, and then click on **Sort** at the bottom of the spreadsheet.

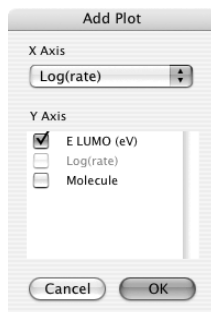
- After all calculations have completed, click on **Add** at the bottom of the spreadsheet, select **eV** from the **Energy** menu in the **Add Column** dialog which appears,



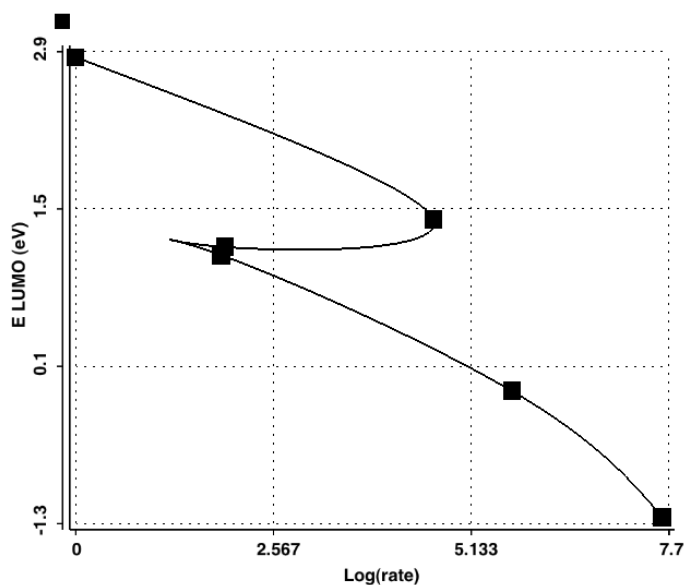
and drag **E LUMO** from the box at the top of the dialog into the spreadsheet. Dismiss the **Add Column** dialog. If you want, you may also remove the spreadsheet from the screen. You can move among the molecules using the  and  buttons at the bottom left of the screen. Align the molecules. Select acrylonitrile from the list, and then select **Align Molecules**

from the **Geometry** menu (or *click* on the  icon in the **Tool Palette**). *Click* on the three carbons and the nitrogen and then *press* the **Align** button (at the bottom right of the screen).

5. Select **Plots...** from the **Display** menu to bring up the **Add Plot** dialog.

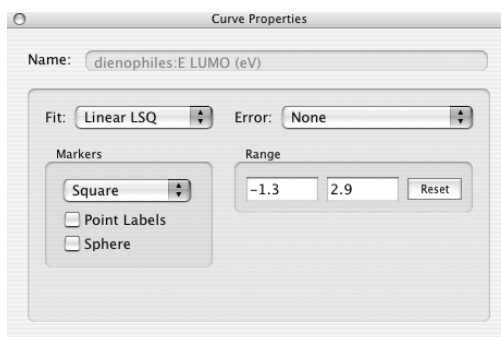


Select **Log(rate)** from the **X Axis** menu, and *check* **E LUMO (eV)** from the list beneath “Y Axis”. A so-called cubic spline connects the data points.

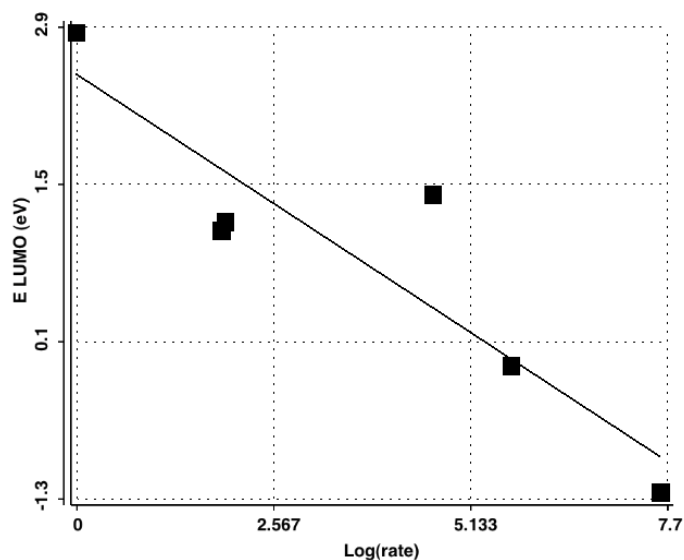


Click on **OK** to remove the **Add Plot** dialog.

More appropriate is a simple linear least-squares fit. Select **Properties** from the **Display** menu and *click* anywhere on the curve (not the plot axes) which you have just drawn. The **Curve Properties** dialog appears.



Select **Linear LSQ** from the **Fit** menu. A new plot appears, and underneath the plot the fitting expression.



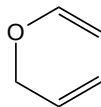
Do you see the expected correlation between relative rate and LUMO energy?

- Remove all molecules from the screen.

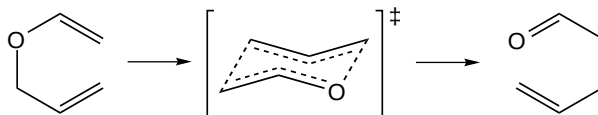


1 min/5 mins

Allyl Vinyl Ether



Allyl vinyl ether undergoes Claisen rearrangement, the mechanism for which demands that the reactant adopt a “chair” conformation.



Is this the lowest-energy conformer of allyl vinyl ether (the global minimum)? If not, how much energy is required to properly orient the molecule for reaction? To find out, it is necessary 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. A combination of molecular mechanics and quantum chemical models will be used to accomplish this.

1. Bring up the organic 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 and then click on **V**.
2. Inside the **Calculations** dialog, select **Conformer Distribution**, **Molecular Mechanics** and **MMFF** from the three menus below “Calculate”. Click on **OK**.
3. Submit the job. Name it: “allyl vinyl ether”. When completed, it will give rise to a list of low-energy conformers placed in a new file: “allyl vinyl ether_conf”, that will be opened automatically when the calculation has completed. It is probably a good idea to close “allyl vinyl ether” () to avoid confusing it with this list. Select **Spreadsheet** from the **Display** menu. Size the spreadsheet such that all rows (corresponding to different conformers) are visible at one time. Drag at the bottom right of the spreadsheet. Click on **Add** at the bottom of the spreadsheet. Select **kJ/mol** from the **Energy** menu, and



drag **E** from the **Add Column** dialog which appears into the spreadsheet. A column of MMFF energies will be added to the spreadsheet. Click on **OK**. Sort the conformers by energy (in ascending order). Click on the column header “E (kJ/mol)”, and then click on **Sort** at the bottom of the spreadsheet.* Examine the lowest-energy conformer (the top entry). Is it in a conformation suitable for Claisen rearrangement? If not, identify the lowest-energy conformer which is properly disposed, i.e., in a chair geometry. It might help to align the conformers. Select **Align Molecules** from the **Geometry** menu. Click on three (or more) atoms to designate them as alignment centers. (If you make a mistake, click again two times on the atom.) When you are done, click on the **Align** button at the bottom right of the screen.

4 to 6 optional

To get a more accurate estimate of conformational energy differences, perform single-point 3-21G calculations using AM1 geometries on the lowest-energy conformer assigned using MMFF molecular mechanics and the lowest-energy conformer which is properly disposed for rearrangement.

4. Make a copy of “allyl vinyl ether_conf”; name it: “allyl vinyl ether lowest” (⌘-C). Using the copy, delete all conformers except the global minimum and the lowest-energy conformer that is properly disposed for Claisen rearrangement. In turn, 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 title for the molecule to be deleted, and select **Clear** from the **Edit** menu. When you are done, the spreadsheet should contain only two entries.
5. Inside the **Calculations** dialog, specify calculation of a single-point energy using the Hartree-Fock 3-21G model. Also, specify **AM1** from the menu below “Start from”.

* To sort in descending order, hold down the **option** key and click on **Sort**.

** The **⌘** key may be used for multiple selection and **shift** key for selection over a range.

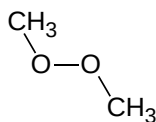


6. Submit the job. When completed, examine the energies of the two conformers. Is the lower-energy conformer the one that is properly disposed for the Claisen rearrangement? If not, how much energy is required to get a conformer poised for Claisen rearrangement?
7. Remove all molecules from the screen.



20 mins/40 mins

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 energies, for these are the most difficult to obtain experimentally. Here, the empirical energy function needs to reflect the inherent periodicity. For example, the energy of rotation about the oxygen-oxygen bond in a molecule such as dimethylperoxide may be described by a truncated Fourier series:

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

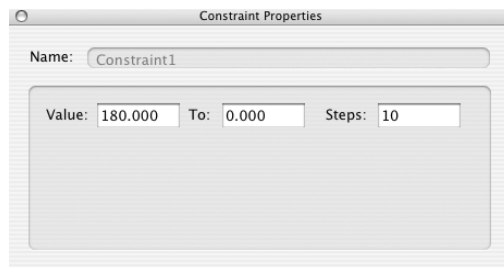
Here, ω^{eq} is the ideal dihedral angle and k^{torsion1} , k^{torsion2} and k^{torsion3} are parameters. The first (one-fold) term accounts for the difference in energy between *syn* and *anti* conformers, the second (two-fold) term for the difference in energy between planar and perpendicular conformers, 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 organic 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°). You need to *press* the **return** key. **Do not minimize**.
2. If you have not already done so in the previous step, *click* on , and select the COOC dihedral angle. *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**



from the **Display** menu and *click* on the constraint marker. This leads to the **Constraint Properties** dialog.



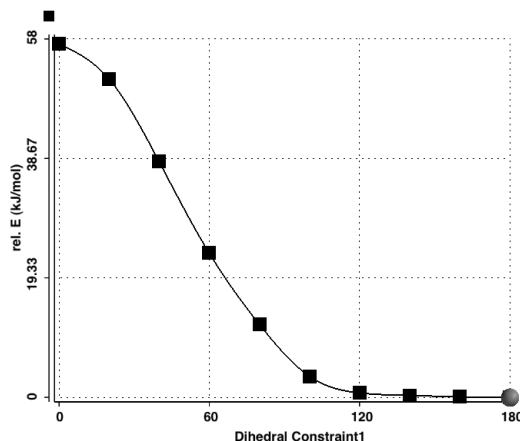
3. Replace the single (dihedral angle) constraint value by a “range” of constraint values. Leave the value of **180** (180°) in the box to the right of “Value” as it is, but change the contents of the box to the right of “To” to **0** (0°). Also, change the contents of the box to the right of “Steps” to **10**. What you have specified is that the dihedral angle will be constrained first to 180° , then to 160° *, etc. and finally to 0° . Dismiss the dialog.
4. Bring up the **Calculations** dialog and select **Energy Profile** from the top menu below “Calculate”, and **Hartree-Fock** and **6-31G*** from the two bottom menus. *Click* on **OK** to remove the dialog, and submit the job (**Submit** from the **Setup** menu). Name it “dimethylperoxide”.
5. When all ten geometry optimizations have completed (several minutes), they will be placed in a new file already opened on screen: “dimethylperoxide_prof”. First, align the conformers using both oxygens and one of the carbons (*click* on ). Next, bring up the **Spreadsheet**, and enter the energies relative to the 180° conformer and the COOC dihedral angles. First select the 180° conformer to make it the “reference”. Then, *click* on **Add** at the bottom of the spreadsheet. Select **kJ/mol** from the **Energy** menu in the **Add Column** dialog and *drag rel. E* into the spreadsheet. Dismiss the dialog. To enter the dihedral angles, *click* on , *click* on the constraint marker and *drag* the

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

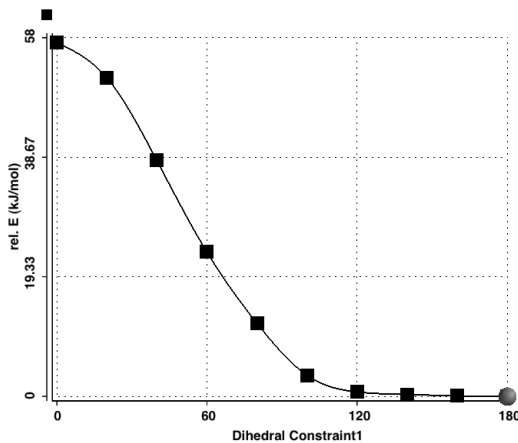


text string “Constraint1” at the bottom on the screen into the spreadsheet.

Select **Plots** from the **Display** menu to bring up the **Add Plot** dialog. Select **Dihedral(Constraint1)** from among the items in the **X Axis** menu and **rel. E(kJ/mol)** from the list of items beneath “Y Axis”. Click on **OK**.



The curve (a so-called cubic spline) smoothly connects the data points. To fit the points to a Fourier series, select **Properties** from the **Display** menu and *click* anywhere on the plot. Select **Fourier LSQ** from the **Fit** menu in the **Curve Properties** dialog which appears. A new plot appears.



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



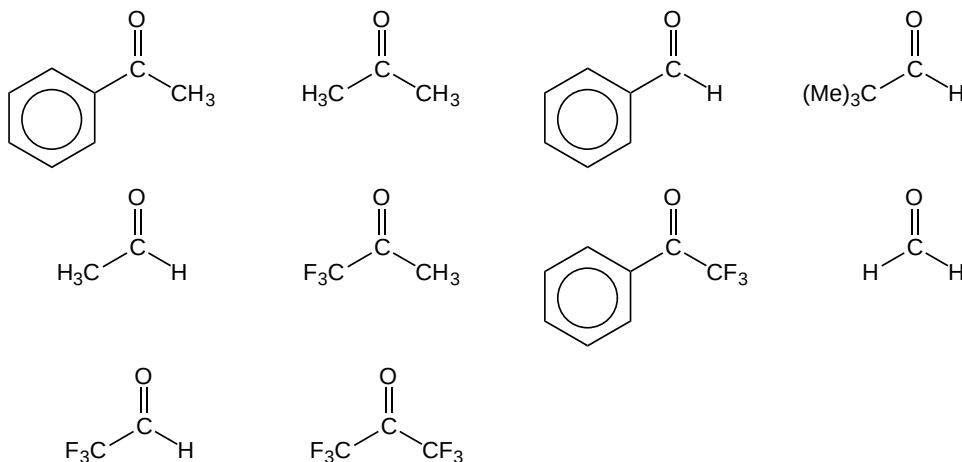
7 and 8 optional (*cannot be completed with the Essential Edition*)

7. Repeat the function fit using energies from B3LYP/6-31G* density functional calculations, using the Hartree-Fock geometries. First, make a copy of “dimethylperoxide_prof” (). Name it “dimethylperoxide_B3LYP”. Next, enter the **Calculations** dialog and specify calculation of single-point energies using the B3LYP/6-31G* density functional model. Make certain that **Apply Globally** (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, fit it to a Fourier series and compare it to the energy plot produced earlier.
9. Remove all molecules from the screen.

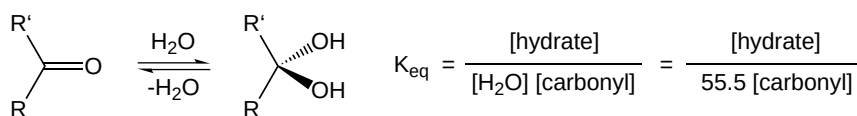


30 mins

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*			
$\log(k_{eq}/55.5)$		$\log(k_{eq}/55.5)$	
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).

Here, you will attempt to correlate “properties” obtained from quantum chemical calculations with measured equilibrium constants for carbonyl hydration. The primary purpose of this tutorial is to illustrate the use of Spartan’s linear regression analysis tool.

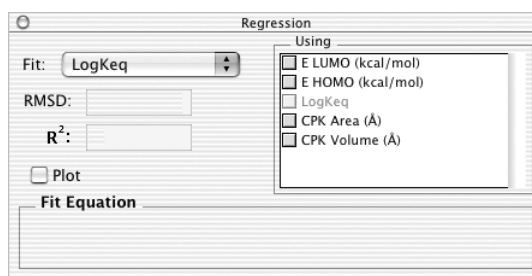


1. Build the carbonyl compounds* listed above. Use **Carbonyl** from the **Groups** menu as a starting point for each to ensure consistent atom numbering. Put all in the same list by selecting **New Molecule** following construction of each molecule (except the last), i.e., build and minimize acetophenone, select, **New Molecule**, build and minimize acetone, select **New Molecule**, etc. When you are done (10 molecules in total), *click* on **V**.
2. Enter the **Calculations** dialog and specify calculation of energy using the Hartree-Fock 3-21G model. Select AM1 from the menu below “Start from”. This indicates that AM1 equilibrium geometries will be used in place of 3-21G geometries, and will lead to considerable savings of computer time. Make certain that **Apply Globally** is *checked*. *Click* on **OK** to remove the dialog and then select **Submit** from the **Setup** menu. Name the job “carbonyl compounds”.
3. While you are waiting for the calculations to complete, bring up the spreadsheet. *Click* inside the header cell of an empty column, type in a title “Log(Keq)” and *press* the **return** key. Then enter the experimental equilibrium constants (see box on the previous page) into the appropriate cells. You need to *press* the **return** key following each data entry. Replace the “names” in the spreadsheet by correct names (“acetophenone”, ...). 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.
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**, and then *drag* them as a set into the spreadsheet.
5. Select **Properties (Display menu)** and *click* on the oxygen atom

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

for whatever compound is displayed. Drag **Electrostatic** (under “Charges”) in the **Atom Properties** dialog (which has replaced the **Molecular Properties** dialog), into the spreadsheet.

6. Select **Regression** from the **Display** menu to bring up the **Regression** dialog.



Select **Log(Keq)** from the **Fit** menu and **Electrostatic (O2)*** from the list below “Using”. Information about the fit of $\text{Log}(K_{\text{eq}})$ to the charge on oxygen, in particular RMSD and R^2 values, will appear in the dialog. The former will tend toward zero and the latter toward unity as the quality of the fit improves.

7. Try fitting to a 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 .
8. Check **Plot** inside the **Regression** dialog. A plot of the “best fit” to LogKeq vs. the actual data will appear. This same plot can also be generated using the **Plots** dialog (**Display** menu) by selecting **Log(Keq)** from the **X Axis** menu, and **BestFit** from the list of items beneath “Y Axis”, and *clicking* on **OK**. You also need to bring up the **Curve Properties** dialog and select **Linear LSQ** (to replace **Cubic Spline** from the **Fit** menu).
9. Remove “carbonyl compounds” from the screen along with any remaining dialogs.

* The actual numbering may differ.



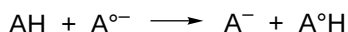
10 mins

Acidities of Carboxylic Acids

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



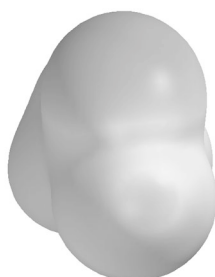
or, more commonly, as the deprotonation energy relative to that of some “standard” acid (A°H).



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.



ethanol



acetic acid



nitric acid

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 use the Spartan Molecular Database of calculated structures, energies and properties 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. *Click* on “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 Hartree-Fock 3-21G energy calculation has been requested. Also make certain **IR** below “Compute” is unchecked and that **Apply Globally** 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 **Apply Globally** 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 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”.
4. While you are waiting for the calculations to complete, bring up the spreadsheet (**Spreadsheet** from the **Display** menu). Expand it so that you can see all seven molecules, and that two data columns are available. *Click* inside the header cell for a blank column. First, *click* inside the header cell of the next available data column, *type* “pKa” and *press* the **return** key. Enter the individual (experimental) pK_a’s into the appropriate cells under this column. You need to *press* the **return** 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, <i>Ionization Constants of Organic Acids in Aqueous Solution</i> , IUPAC no. 23, Pergamon Press, 1979.			

Then, *click* inside the header cell of the next available data column and *type* “potential”. Press the **return** 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, first *click* on  at the bottom left of the screen (it will become ) , then *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.
- Double 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 **return** 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” and remove any remaining dialogs from the screen.



30 mins

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

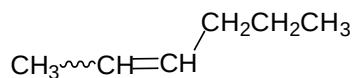
NMR spectroscopy, in particular ^{13}C spectroscopy, is often the method of choice to establish the three-dimensional structure of organic molecules. Only X-ray diffraction provides more definitive results, although the requirement of a crystalline sample severely limits its application. It is now practical 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), click on “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 Hartree-Fock energy calculation using the 6-31G* basis set. Check **NMR** below “Compute”. Also make certain that **IR** in this section is unchecked. Submit the job with the name “2-hexene”.
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



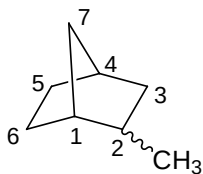
with particular attention to the difference in shifts between *cis* and *trans* stereoisomers.



	<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”.
- 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 **V**.
- Inside the **Calculations** dialog, specify a Hartree-Fock 6-31G* energy calculation, and *check* **NMR** (below “Compute”). Make certain that **IR** in this section is unchecked. Submit the job with the name “2-methyl norbornane”.
- When completed, compare the ¹³C chemical shifts with experimental values with particular attention to differences between *endo* and *exo* stereoisomers.



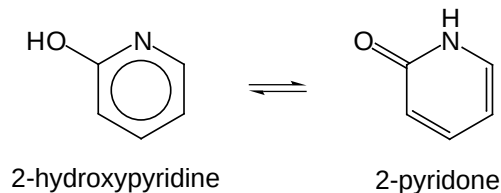
	<i>endo</i>	<i>exo</i>	Δ
C ₁	43.5	42.2	-1.3
C ₂	36.8	34.6	-2.2
C ₃	40.2	40.7	0.5
C ₄	37.3	38.2	0.9
C ₅	30.3	30.6	0.3
C ₆	29.0	22.4	-6.6
C ₇	35.0	38.9	3.9
CH ₃	22.3	17.4	-4.9

Do the calculations distinguish between the two isomers?

- Close “2-methylnorbornane”.

Favoring One Tautomer Over Another

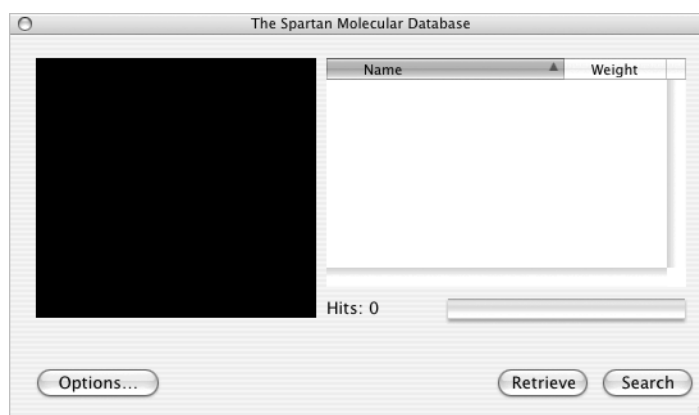
2-hydroxypyridine is in equilibrium with its tautomer, 2-pyridone.



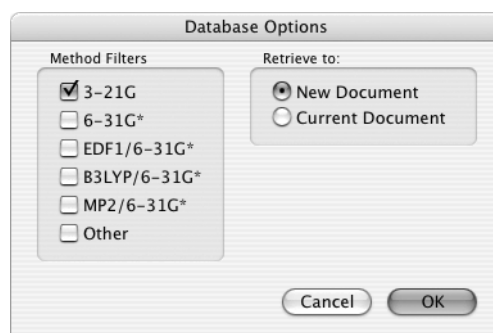
The relative abundance of the two is given by the Boltzmann equation and depends both on their relative energies and on the temperature.

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, *click* on “3-21G” and *click* on **Replace**. Select **New Molecule** from the **File** menu, build 2-pyridone (start with **Amide** from the **Groups** menu), *click* on “3-21G” in the preview dialog and *click* on **Replace**. Dismiss the preview dialog (*click* on  at the bottom of the screen) 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 **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?
3. Select (*click* on) 2-hydroxypyridine, and then select **Database** from the **Search** menu (or *click* on ). The **SMD** dialog appears.



Click on the **Options** button at the left of the **SMD** dialog to bring up the **Database Options** dialog.



Check “3-21G” (only) under “Method Filters”, select **New Document** under “Retrieve to:” and click on **OK**. Next, click on the free valence on the 4 position (across the ring from nitrogen) on 2-hydroxypyridine. 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, 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 to be 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 **Add...** at the bottom of the spreadsheet, select **au** from the **Energy** menu and *drag E* onto the spreadsheet.

4. 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.
5. 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 much more 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 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 also provides a procedure for “driving” user-defined coordinates. Aside from conformational analysis (see ***Internal Rotation in Dimethylperoxide*** 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.

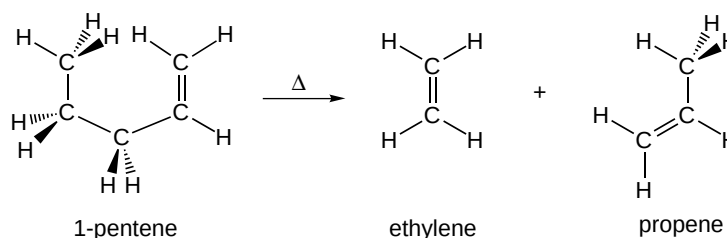
* Where a reaction is unknown to Spartan’s library, a fallback technique which “averages” reactant and product geometries (similar to the so-called linear synchronous transit method) is invoked.





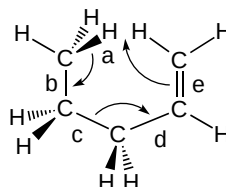
10 mins/20 mins

Ene Reaction of 1-Pentene



The 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 reactant and transition-state structures, to obtain an estimate of the activation energy for the ene reaction.

1. Bring up the organic model kit and build 1-pentene in a conformation in which one of the terminal hydrogens on the ethyl group is “poised” to transfer to the terminal methylene group. Click on .
2. First, save 1-pentene as “1-pentene_B3LYP” for later use (). Also make a copy for immediate use; name it “ene reaction 1-pentene”. Proceed with this copy.
3. Select **Transition States** from the **Search** menu (or click on the  icon in the **Tool Palette**). Click on bond “a” (a CH bond) in the figure below and then click on bond “b”.

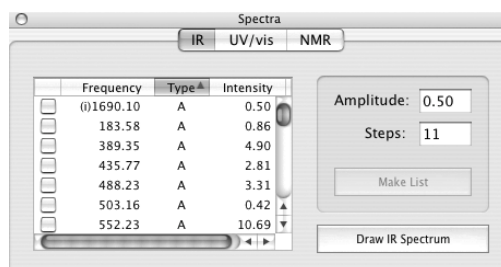


A curved arrow from bond “a” to bond “b” will be drawn (as shown in the figure). Next, click on bond “c” and then on bond



“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.) 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.

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 below “Calculate” and **Hartree-Fock** and **3-21G** from the two bottom menus. Also, *check* **IR** below “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 in the dialog that results.



Double click on the top entry in the list in the **IR Spectra** dialog. It corresponds to an imaginary frequency, and will be noted under “Type” to the right of the frequency. Is the

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



- vibrational motion consistent with the reaction of interest and not with some other process?
- Controls at the bottom of the **IR Spectra** dialog allow for changing both the amplitude of Vibration (**Amplitude**) and the number of steps which make up the motion (**Steps**). Change the amplitude to “0.6” (type **0.6** in the box to the right of **Amplitude** and press the **return** key). Next, click on **Make List** at the bottom of the dialog. This will give rise to a list of structures which follow the reaction coordinate down from the transition state both toward reactant and product. To avoid confusion, remove original molecule from the screen. Click on “ene reaction 1-pentene” (the vibrating molecule) and close it () along with the **IR Spectra** dialog.
 - Enter the **Calculations** dialog and specify an 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 **Apply Globally** is checked before you exit the dialog. Next, bring up 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** at the bottom of the dialog, select **density** for **Surface** and **none** for **Property** in the **Add Surface** dialog which results. Check “Static Isovalue” and select **bond** from the menu below. Click on **OK**. Click on **Add** again. Select **density** for **surface** and **potential** for **Property**. Check “Static Isovalue”, select **bond** in the menu and click on **OK**. Leave the **Surfaces** dialog on screen.
 - Submit for calculation. Name it “ene reaction 1-pentene sequence”. Once the job has completed, enter the **Surfaces** dialog and, on 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”.

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

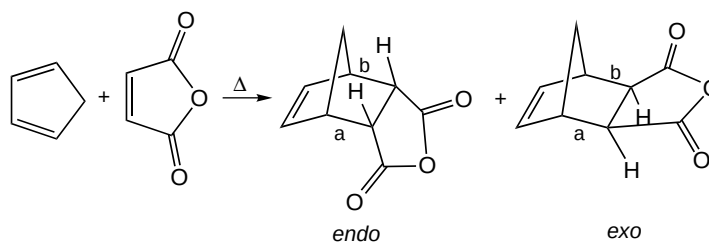
Hartree-Fock calculations are generally not able to furnish accurate estimates of absolute activation energies. This requires methods which take electron correlation into account. Perform single-point energy calculations using the B3LYP/6-31G* density functional model on both 1-pentene and on the ene reaction transition state (using geometries previously obtained from the 3-21G calculations) to get an estimate of activation energy.

10. Open “ene reaction 1-pentene” and make a copy (). Name it “ene reaction 1-pentene_B3LYP”.
11. Enter the **Calculations** dialog, and specify calculation of an energy using the B3LYP/6-31G* density functional model. Be certain to *uncheck* **IR** (below “Compute”). Submit the job.
12. While you are waiting for it to complete, bring “1-pentene_B3LYP” onto the screen (). Enter the **Calculations** dialog, and specify an energy calculation using the B3LYP/6-31G* density functional model. Also select **3-21G** from the menu below “Start from”. This designates that a 3-21G equilibrium structure is to be provided prior to the density functional calculation. Submit the job.
13. When both calculations have completed, obtain the activation energy (difference in total energies between 1-pentene and the ene reaction transition state).
14. Remove the molecules and any remaining dialogs from the screen.



5 mins

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 known to be the *endo* adduct, whereas it seems likely that the less-crowded *exo* adduct is the thermodynamic product.

1. Build the *endo* Diels-Alder adduct of cyclopentadiene and maleic anhydride (see figure above) and minimize (to C_s symmetry). Click on **V**.
2. Select **Measure Distance** from the **Geometry** menu () 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” (1.540Å) given in a box to the right of “Value”. Change this to 1.5Å by typing **1.5** inside the box. Type **2.7** (2.7Å) into the box to the right of “To”. Finally, type **13** into the box to the right of “Steps”. What you have now specified is that bond “a” will be constrained first to 1.5Å, then to 1.6Å, then to 1.7Å, etc., and finally to 2.7Å.

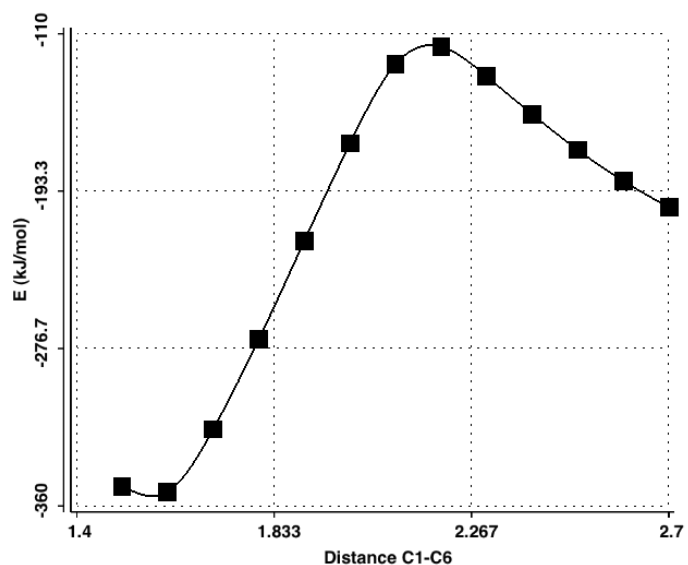
You need to repeat the process for bond “b”. Click on this bond (the **Constraint Properties** dialog will now refer to the



- constraint on bond “b”), and type **1.5** and **2.7** into the boxes to the right of “Value” and “To”, respectively (the value for “Steps” will already be set to 13). What you have done is to request that bonds “a” and “b” both be constrained from 1.5Å to 2.7Å in 13 equal steps. Dismiss the **Constraint Properties** dialog.
4. Bring up the **Calculations** dialog and select **Energy Profile** from the top menu below “Calculate”, and **Semi-Empirical** and **PM3** from the two bottom menus. *Click* on **OK** to remove the dialog and then select **Submit** from the **Setup** menu. Name it “cyclopentadiene+maleic anhydride endo”.
 5. When completed, the job will give rise to a new file “cyclopentadiene+maleic anhydride endo_prof” containing the 13 steps which make up the energy profile. This file will be open on screen.*
 6. Bring up the **Spreadsheet (Display menu)**, and *click* on **Add** at the bottom. Select **kJ/mol** from the **Energy** menu in the **Add Column** dialog, and *drag* **E** onto the spreadsheet. Close the **Add Column** dialog. Next, *click* on  and *click* on one of the two CC bonds varied in the energy profile. *Drag* “Distance Cx-Cy”** (near the center at the bottom of the screen) onto the spreadsheet. *Click* on . Finally, select **Plots...** from the **Display** menu to bring up the **Add Plot** dialog, and select **Distance (Cx-Cy)**** from among the items in the **X Axis** menu and **E (kJ/mol)** from the list of items beneath “Y Axis”. *Click* on **OK** to dismiss the dialog.

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

** The name of the text string following “Distance” will depend on which bond or constraint you select.



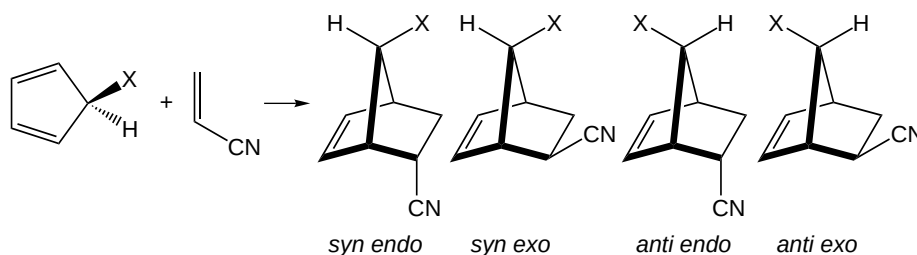
Identify both the reactant and transition state from the plot and estimate the activation energy for the cycloaddition reaction leading to the *endo* adduct.

7. Repeat steps 1 to 6 for the *exo* adduct. Compare the activation energy for *exo* addition to that for *endo* addition (above). According to your calculations, what should be the kinetic product?
8. Remove all molecules and any open dialogs from the screen.



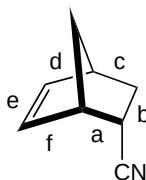
10 mins

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.

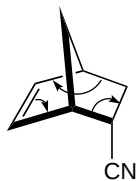
1. Construct the following substituted norbornene (the product of *endo* addition of cyclopentadiene and acrylonitrile). Click on and then on .



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. Click on .

3. Inside the **Calculations** dialog, specify calculation of transition state geometry using the semi-empirical AM1 model. Check **IR** (below “Compute”) to specify calculation of vibrational frequencies. This will allow you to verify that you have indeed located a “reasonable” transition state. Click on **OK**.
4. Submit the job. Name it “cyclopentadiene+acrylonitrile”. When it has completed, examine the resulting structure and calculated frequencies. Bring up the **IR Spectra** dialog (**Spectra** from **Display** menu and click on the **IR** tab) and make certain that there is one and only one imaginary frequency. Animate this motion to verify that it corresponds to motion along the reaction coordinate. When you are done, close the **IR Spectra** dialog.
5. Place the transition-state structure onto the clipboard. Position the cursor slightly above and slightly to the left of the model, then while holding down on either button in addition to the **shift** key, drag the mouse to a position slightly below and slightly to the right of the model, and finally release both the **shift** key and the button. Dotted lines will enclose the model. Select **Copy** from the **Edit** menu. Close “cyclopentadiene+acrylonitrile” .
6. Enter the builder . Click on **Custom** (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.



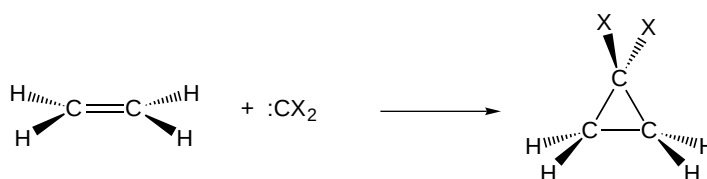
7. Select **New Molecule** (not **New**) from the **File** menu. The screen will clear. *Click* on **Custom** and then *click* anywhere on screen. Add fluorine to the other methylene group position.

Repeat the process two more times (starting with **New Molecule**), to add methyl *syn* and then *anti* on the methylene group. When you are done (four substituted transition states in total), *click* on **V**.
8. Enter the **Calculations** dialog and specify calculation of transition state geometry using the semi-empirical AM1 model. *Check IR* (below “Compute”). Finally, make certain that **Apply Globally** is *checked* before you exit the dialog. Submit the job (name it “Diels-Alder stereochemistry”). When it has completed, verify that the four structures actually correspond to transition states by examining the infrared spectra.
9. Enter the **Calculations** dialog and specify an energy calculation using the 3-21G Hartree-Fock model. Make certain that you remove the checkmark on **IR**, and that **Apply Globally** 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 **Add** at the bottom of the spreadsheet to bring up the **Add Column** dialog. Select **au** from the **Energy** menu, and *drag E* into the spreadsheet. Dismiss the **Add Column** dialog. Are your results consistent with the observed *syn/anti* selectivity in these reactions?
11. Remove all molecules from the screen.

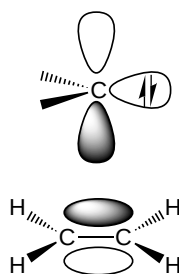


10 mins/40 mins

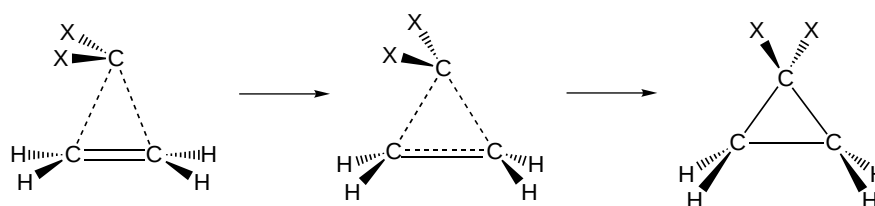
Carbene Additions to Alkenes



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-energy vacant orbital on the carbene, and not the high-energy filled orbital, to interact with the olefin π system during its approach.



Of course, this leads to a product with an incorrect geometry. It must be that the carbene “twists” by 90° during the course of reaction.

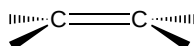


Here, you will use the 3-21G Hartree-Fock model to find the transition state and to analyze the motion of the fragments.

1. Bring up the organic model kit and build ethylene.
2. Select  from the model kit. Hold down the **option** key and *click* anywhere on screen. Your model now comprises two parts: “ethylene” and an sp^3 carbon. Ethylene should be “ghosted”

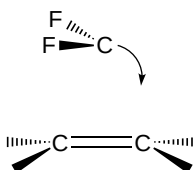


meaning that the sp^3 carbon is selected. Next select  from the model kit and *click* on two of the free valences on the sp^3 carbon. Finally, select  and, one after the other, *click* on the remaining two free valences on the sp^3 carbon. When you are done, *click* on . You are left with two fragments, ethylene and difluorocarbene. Orient the two as to be poised for reaction.*

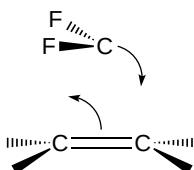


Recall that translations and rotations normally refer to the complete set of fragments. They can be made to refer to an individual fragment by first *clicking* on it. *Clicking* on “empty space” will reset the mode such that rotation and translation now refer to all fragments.

3. *Click* on  and then *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.



* 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.



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. *Click* on .

4. Enter the **Calculations** dialog, and specify calculation of a transition-state geometry using the 3-21G Hartree-Fock model. *Check IR* below “Compute”. This will allow you to verify that you have located a transition structure, and furthermore, allow animation of the motion along the reaction coordinate. Remove the dialog, and submit the job. Name it: “CF2+ethylene”.
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?
6. Animate the vibrational mode corresponding to the reaction coordinate. Bring up the **IR Spectra** dialog. *Double click* on the imaginary frequency at the top of the list of frequencies (this corresponds to motion along the reaction coordinate). Does the carbene reorient as it approaches the double bond, in line with the qualitative picture? When you are finished, turn “off” the animation by again *double clicking* on the imaginary frequency.
7. Select **Properties** from the **Display** menu. In turn, *click* on each of the four hydrogens in your transition state. As you do, the atom will be colored gold and the (**Atom Properties**) dialog will refer to the selected atom. Change the value in the menu to the right of “Mass Number” from “1” to “2”. When you have changed all four hydrogens to deuteriums, dismiss the **Atom Properties** dialog and resubmit the job. Execution should require only a few seconds. When complete, examine the new set of vibrational frequencies from the **IR Spectra** dialog. 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. Dismiss the **IR Spectra** dialog when you are done.

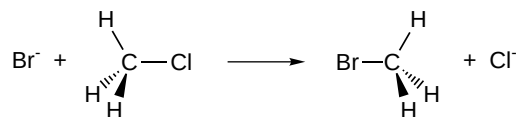
8 to 11 optional

8. Make a copy of “CF₂+ethylene” (); name it: “CF₂+cyclohexene”.
9. Select **Freeze Center** from the **Geometry** menu. One after the other, *click* on all atoms in your transition state except the two hydrogens 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 “frozen” (not to be moved during optimization). Bring up the organic model kit (*click* on ). Select sp³ carbon  from the model kit and connect the two free valences which you have not “frozen” by a chain of four “methylene groups” to make a cyclohexene ring. (You need to *click* on  to make the bond.) *Click* on . Note that the only four methylene groups which you have just added “move” and not the underlying transition state. This should provide an excellent guess at the transition state for difluorocarbene addition to cyclohexene based on the previous transition state for difluorocarbene addition to ethylene. *Click* on .
10. Enter the **Calculations** dialog, and specify calculation of transition-state geometry using the 3-21G Hartree-Fock model. Remove the checkmark from **IR** (below “Compute”). *Click* on **OK** to remove the dialog and submit the job.
11. When completed, examine the text output (**Output** under the **Display** menu), and note that the total number of optimization cycles is relatively small. This reflects the very good guess at the structure. Bring “CF₂+ethylene” back onto the screen () , and compare the geometries of the two transition states (corresponding to addition of difluorocarbene to ethylene and cyclohexene, respectively). Are they very similar as expected?
12. Remove both molecules from the screen.



5 mins

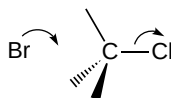
S_N2 Reaction of Bromide and Methyl Chloride



The S_N2 reaction is believed to pass through a transition state in which both entering and leaving groups are colinear, and the central carbon is in a trigonal bipyramid geometry. Here, you will use Spartan's energy profile facility to examine the reaction pathway for S_N2 displacement of chloride in methyl chloride by bromide, both in the gas phase and in water, and examine both the energetics of reaction and overall charge distribution.

1. Build methyl chloride. Next, select bromine from the model kit, hold down the **option** key 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 (after you are done, *click* on  to get out of “delete mode”). You are left with methyl chloride and bromide (bromine atom). Manipulate the two such that bromide is poised to “attack” methyl chloride from the backside (as in the transition state above). (Recall that, if you first *click* on the background, translations and rotations refer to both fragments. They can be made to refer to a single fragment by first *clicking* on the fragment.) **Do not minimize.** *Click* on .

Click on . *Click* on the bromine and, while holding down the **shift** key, *click* again on bromine and then on carbon. An arrow will be drawn from the bromine 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.

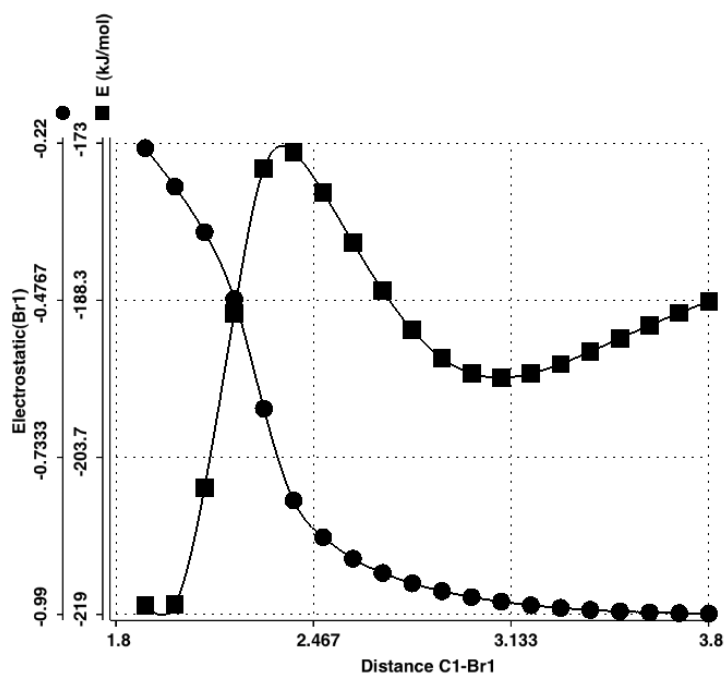




- Click on  at the bottom right of the screen. Your structure will be replaced by a “guess” at the transition state.*
2. Modify your structure so that it is more “reactant like”. Click on  and then on the CBr bond. Replace the current CBr distance in the box at the bottom right of the screen by **3.8** (3.8Å) and *press* the **return** key. You have now made a “complex” representing the “reactant”. **Do not minimize.**
 3. 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, select **Properties** from the **Display** menu and *click* on the constraint marker to bring up the **Constraint Properties** dialog. Change the value **3.8** (3.8Å) in the box to the right of “To” to **1.9** (1.9Å). Also, change the value in the box to the right of “Steps” to **20** (20 steps). You have requested a sequence of 20 structures in which the CBr bond is varied from 3.8Å to 1.9Å. These should pass through the transition state. Remove the dialog and *click* on .
 4. Enter the **Calculations** dialog, and select **Energy Profile**, **Semi-Empirical** and **AM1** from the menus below “Calculate”. Change **Total Charge** to **Anion**. Click on **OK**.
 5. Submit. Name it: “bromide+methyl chloride”. It will give rise to a series of calculations which will be placed in: “bromide+methyl chloride_prof”. Close “bromide+methyl chloride” (). Align the molecules in the list “bromide+methyl chloride_prof”. Select **Align Molecules** from the **Geometry** menu () , then in turn *click* on the three hydrogens, and finally *press* the **Align** button at the bottom right of the screen.
 6. Bring up the **Spreadsheet**, and *click* on **Add**. Select **kJ/mol** from the menu to the right of “Energy” in the **Add Column** dialog, and *drag* **E** to the spreadsheet. Dismiss the **Add Column** dialog. Next, enter the CBr distances into the

* This structure could have been constructed much more easily using the inorganic model kit to be introduced in **Chapter 7**.

spreadsheet. Click on , select the CBr distance and drag “Distance C1 - Br1” from the bottom of the screen into the spreadsheet. Next, enter the bromine charges in the spreadsheet. Select **Properties** in the **Display** menu and click on bromine to bring up the **Atom Properties** dialog. Drag “Electrostatic” (under “Charges”) into the spreadsheet. Finally, bring up the **Plots** dialog, and select **Distance (C1 - Br1)** from the **X Axis** menu, and both **E(kJ/mol)** and **Electrostatic (Br1)** from the list beneath “Y Axis”. Click on **OK**. One plot gives the energy of reaction, and the other the charge on bromine.



- Make another plot (energy vs. distance) using the aqueous phase energies in place of gas phase energies. You need to drag **Eaq** into the spreadsheet.
- Bring up the **Surfaces** dialog (**Display** menu). Click on **Add**. Select **density** from the **Surface** menu and **none** from the **Property** menu in the **Add Surface** dialog which results, and click on **OK**. Again click on **Add** and select **density** from the



- Surface** menu, and **potential** from the **Property** menu. *Click* on **OK**. Leave the **Surfaces** dialog on screen. Submit the job.
9. When completed, *double click* on the line: “density . . .” inside the **Surfaces** dialog. *Click* on  at the bottom left of the screen to see how the density changes during reaction.
 10. Turn “off” the density (*double click* on the line: “density . . .”) and turn “on” the electrostatic potential map (*double 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 plot you constructed in step 6. Recall that colors near red indicate maximum negative charge.
 11. Remove all molecules from the screen.

Chapter 6

Biologically Interesting Molecules

This chapter illustrates applications involving “biologically interesting” molecules, and introduces the peptide model kit.

At present time, calculations on “real” biopolymers (proteins and RNA/DNA strands among them) are limited to molecular mechanics models. However, large classes of organic molecules of biological interest, among them steroids, prostaglandins and vitamins, not to mention pharmaceuticals and pharmaceutical candidates, are amenable to investigation using quantum chemical models. The first three tutorials in this chapter give examples of such applications, and the last of these also provides a bridge between small molecules and biopolymers.

Polypeptides are considered in the fourth tutorial. 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.

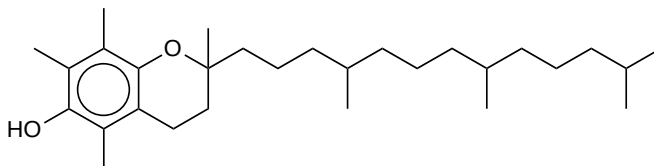
The last two tutorials draw on structures in the Protein Data Bank (PDB). These are intended only to showcase various aspects of protein and nucleotide structure displays.





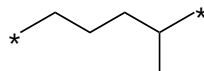
15 mins

Vitamin E

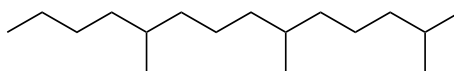


Vitamin E “defends” cells by reacting with oxidizing agents to give stable products that can then be safely excreted. Graphical models can help to account for this biological function, as well as to suggest why vitamin E requires a long hydrocarbon chain to accomplish its function.

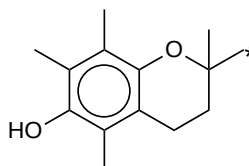
1. Construct the fragment shown below from five sp^3 carbons. (The *'d positions are open valences for later connections.) Put onto the clipboard (draw a selection box around the fragment by *dragging* the mouse while *pressing* either the right or left button in addition to the **shift** key, then select **Cut** from the **Edit** menu).



2. Select **Benzene** from the **Rings** menu. Add three sp^3 carbons () and an sp^3 oxygen () to the ring and join them () to form the bicyclic skeleton. Click on  and add four methyl groups and the hydroxy group. Click on .
3. Add the saturated carbon chain (to the skeleton).



Click on **Custom** in the model kit. The fragment constructed in step 1 will appear at the top. Click on the lefthand free valence in the fragment and then click on the appropriate free valence on the bicyclic skeleton (*'d in the figure below).



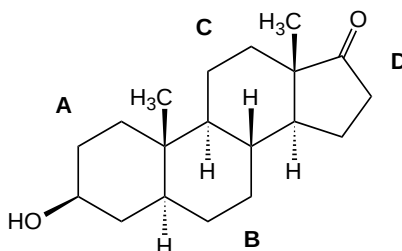


- Add the fragment two more times (**Custom** is still selected, as is the fragment attachment point). *Click* on the appropriate position in the molecule on screen, and then *click* again on the appropriate position in your new structure. When you are done, add a methyl group one position from the chain end. *Click* on  to produce a final structure. *Click* on .
4. Enter the **Calculations** dialog and specify calculation of an energy using the AM1 semi-empirical model. Select **Surfaces** and request an electrostatic potential map (**density** from the **Surface** menu and **potential** from the **Property** menu). Submit; name it “vitamin E”.
 5. When completed, examine the electrostatic potential map. (*Double click* on the line “density potential . . .” in the **Surfaces** dialog.) Note that the potential map suggests a molecule with a large non-polar region. This facilitates its incorporation into lipids.
 6. Perform an analogous (AM1 energy) calculation on the radical formed by removal of the hydroxyl hydrogen from vitamin E. Make a copy of “vitamin E” (). Name it “vitamin E radical”. *Click* on , and *click* on the hydroxyl hydrogen. *Click* on  and then on .
 7. Enter the **Calculations** dialog and change **Multiplicity** from **Singlet** to **Doublet**. Enter the **Surfaces** dialog. First, remove the request for the electrostatic potential map (*click* on the line “density potential . . .” and then *click* on **Delete**). Then, request a spin density surface (**spin** from the **Surface** menu and **none** from the **Property** menu). Submit the job.
 8. When completed, enter the **Surfaces** dialog and *double click* on the line “spin . . .”. Note that the unpaired electron is delocalized over the π system. This is why vitamin E forms a stable radical and is able to act as an effective “radical scavenger”.
 9. Remove both molecules from the screen.



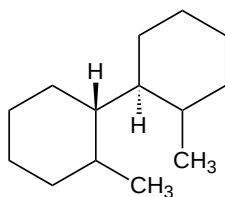
5 mins

Androsterone

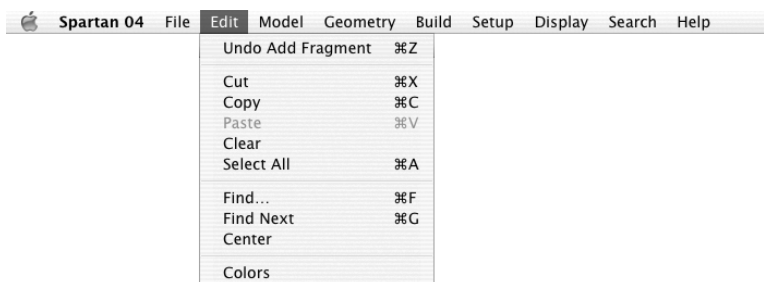


Construction of the steroid androsterone illustrates a number of “tactics” involved in building complex organic molecules. It also provides a good opportunity to compare space-filling models and electron density surfaces as measures of molecular size and shape.

1. Click on . Select **Cyclohexane** from the **Rings** menu, and click anywhere on screen to create the A ring.
2. **Cyclohexane** is still selected. The icon at the top of the model kit should indicate “eq” (*equatorial*) rather than “ax”(axial); attachment needs to be made using an *equatorial* free valence. If not, click on the icon to switch to “eq”. Click on an *equatorial* free valence of the A ring to join it to the C ring.
3. Rotate around the bond connecting the A and C rings to position the *axial* free valences on the connecting carbons “opposite” (180°) to each other. (This bond should be encircled by a red marker. If it is not, click on the bond.) To do so, press both the **spacebar** and the left button and drag the mouse up and down. *Equatorial* free valences on the cyclohexane carbons adjacent to those that connect the two rings are now positioned to form a third cyclohexane ring (the B ring).
4. Select sp^3 carbon () and click on the two opposing *equatorial* free valences of the connecting carbons. The resulting structure should appear as follows.



Click on and, one after another, *click* on the (*equatorial*) free valences that nearly overlap to create the B ring. Click on . Check to see that all rings are chairs and that the stereochemistry is as in the figure above. If not, then you have probably made an error. You can start over (select **Clear** from the **Edit** menu), or “undo” the last operation you performed (**Undo** from the **Edit** menu).



5. Next, form the D ring starting from the carbon that will become a carbonyl group. Select sp^2 carbon () from the model kit and *click* on the appropriate free valence on the C ring. Select sp^3 carbon () from the model kit and *click* first on the single free valence on the sp^2 carbon and then on a free valence of the sp^3 carbon just added.
6. Form a five-membered ring (the D ring) by first *clicking* on and then joining the free valence from the second sp^3 carbon added in the previous step and the appropriate *equatorial* free valence on the C ring. Click on .
7. Add two methyl groups. Select sp^3 carbon () from the model kit. Click on the *axial* free valence at the appropriate juncture the C and D rings, and then on the *axial* free valence at the proper juncture of the A and B rings.



8. Select sp^3 oxygen () from the model kit. Add hydroxy to the appropriate *axial* position on the A ring. Select sp^2 oxygen () from the model kit and *click* on the double free valence on the sp^2 carbon in the D ring. A carbonyl group will result. *Click* on  and then on .
9. 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 that appears. *Click* on **OK**. R/S labels will appear next to each of the chiral centers. (To remove the labels, select **Labels** from the **Model** menu.)
11. Select **Calculations...** from the **Setup** menu and specify calculation of an equilibrium geometry at the AM1 level. *Click* on **OK**. Submit. Name it “androsterone”.

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

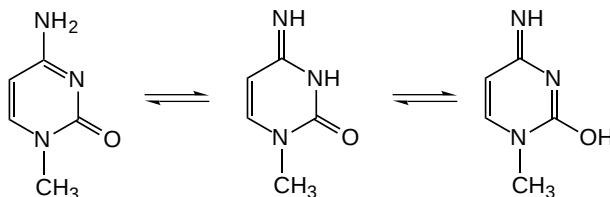
12. Select **Properties** (**Display** menu). The **Molecule Properties** dialog provides both the surface area and the volume of a space-filling (CPK) model. Write down both values. Leave the **Molecule Properties** dialog on screen.
13. Select **Surfaces** (**Setup** or **Display** menu). *Click* on **Add**. Select **density** from the **Surface** menu and **none** from the **Property** menu, and *click* on **OK**. Leave the **Surfaces** dialog on screen.
14. Submit. When completed, *double click* the line “density . . .” in the **Surfaces** dialog. *Click* on any portion of the density surface. The **Surface Properties** dialog which replaces the **Molecule Properties** dialog provides both the surface area and the volume of the electron density surface. How do these compare with quantities from the CPK model?
15. Remove androsterone from the screen.



5 mins/30 mins

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. Build 1-methylcytosine. Start with **Amide** from the **Groups** menu. Select planar trigonal nitrogen for the external amino group. Minimize (to C_s symmetry) and *click* on **V**.
2. Note that the word “Tautomer” appears at the bottom right of the screen, indicating that tautomers exist. Select **Tautomers** from the **Search** menu. Step through the tautomers using the **◀** and **▶** keys that appear at the bottom right of the screen. To put the tautomers in a list, *click* on **Make List** (also at the bottom right of the screen).
3. Enter the **Calculations** dialog with this list. Specify a single-point energy calculation using the 3-21G Hartree-Fock model. Select **AM1** from the menu below “Start from” to indicate that

* Note, however, that were the energy of an alternative tautomer only 10 kJ/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.



AM1 geometries will be employed.* Select **Submit** from the **Setup** menu. Name the job “cytosine tautomers”.

4. After the calculations have completed, bring up the spreadsheet and *click* on the line corresponding to the structure for cytosine that you originally built. *Click* on **Add** at the bottom of the spreadsheet. Select **kJ/mol** from the **Energy** menu in the **Add Column** dialog that appears and *drag rel. E* into the spreadsheet. Dismiss the dialog. Tautomer energies (relative to the “normal” form) appear in the spreadsheet. Are either of the alternatives close in energy to the normal form of cytosine?

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

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

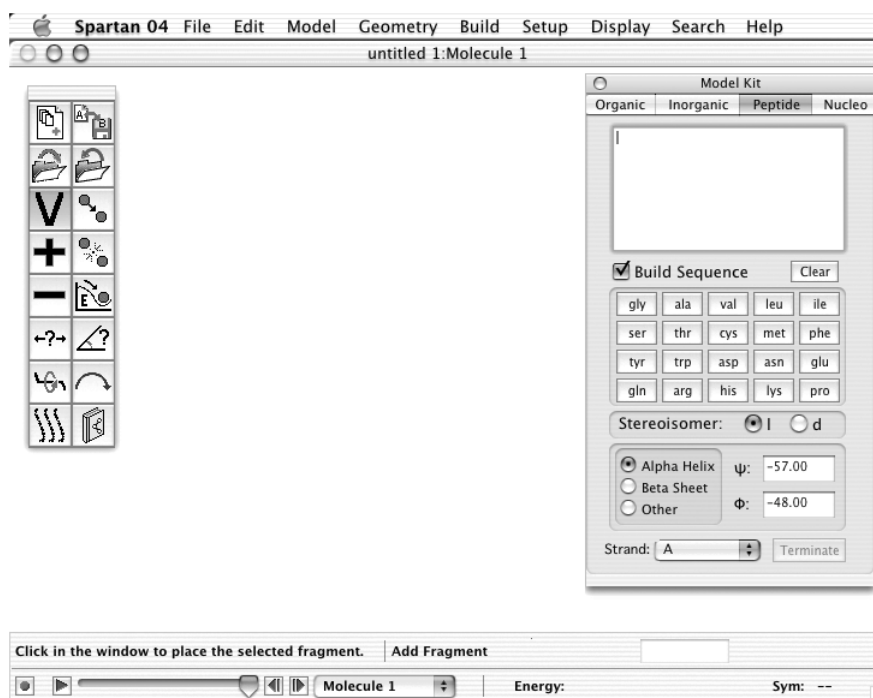
5. Make a copy of “cytosine tautomers” (⌘-C). Name it “cytosine tautomers_LMP2”. Enter the **Calculations** dialog with this copy and specify **Energy** from the menu below “Calculate” and **Møller Plesset, MP2** and **6-31G*** from the three bottom menus. *Check Localized* at the far right of the “Calculate” section. Finally, reset the menu below “Start from” to **Initial**. *Click* on **OK**. Submit the job.
6. When it completes, bring up the spreadsheet (it should contain the relative tautomer energies). Do the LMP2 results change any of the earlier conclusions?
7. Close whatever molecules 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 **Energy**) from the menu below “Calculate” and **Initial** (instead of **AM1**) from the menu below “Start from”.

Polyglycine

Triglycine and (optionally) decaglycine will be used to illustrate construction of simple amino acid sequences using Spartan'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 organic model kit.



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 organic or inorganic model kits.

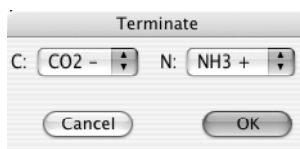
2. Check **Build Sequence** in the model kit, and then *click* three times on "gly" (glycine) from the selection of amino acid codes.



The structure of glycine will appear at the top of the model kit, and the sequence underneath **Build Sequence**.

gly-gly-gly

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 work with the non-zwitterionic structure. *Click* on **Terminate** in the model kit. A dialog will appear specifying available “C” and “N” terminating groups.



Select **CO₂H** from the **C** menu, and **NH₂** from the **N** menu. *Click* on **OK**. You have made the “neutral” form of triglycine. **Do not minimize.**

5. Select **New Molecule** from the **File** menu. Triglycine is still selected. *Click* anywhere on screen. *Click* on **Terminate** inside the model kit and this time select **CO₂H** and **NH₃ +** for “C” and “N” terminating groups, respectively. *Click* on **OK**. You have made the zwitterionic form of triglycine. **Do not minimize.**
6. *Click* on **V**. Both forms of triglycine now occupy the same list. Enter the **Calculations** dialog and specify an energy calculation using the 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. Make certain that **Apply Globally** is checked. *Click* on **OK** to remove the dialog and then select **Submit (Setup menu)**. Name the job “triglycine”.



7. After the two calculations complete, bring up the spreadsheet, *click* on the header cell of the leftmost empty column, and *click* on **Add** at the bottom of the spreadsheet. Specify **kJ/mol** from the **Energy** menu and *drag* both **E** and **Eaq** from the list of available properties at the top of the **Add Column** dialog that appears onto the spreadsheet. Dismiss the **Add Column** dialog.

Note, from the energies in the spreadsheet, that the “neutral” form of triglycine is favored in both the gas the “aqueous” phase, but that the energy difference to the zwitterionic form is greatly reduced by inclusion of solvent in the calculations.
8. Remove “triglycine” from the screen.

9 to 13 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.

9. 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 **CO2 D** and **NH3 +** for “C” and “N” terminating groups, respectively, and then *click* on **OK**. *Click* on **V**.
10. Enter the **Calculations** dialog and specify an AM1 energy 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.
11. 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**. Leave the **Surfaces** dialog on screen.

* The following instructions assume that this section follows the building of triglycine. If not, replace them by: “*Click* on **Sequence** and then *click* ten times on “gly”. *Click* on **Alpha Helix** and then *click* anywhere on screen. . .”.



12. Submit the job. Name it “decaglycine zwitterion”. Execution will take several minutes due primarily to calculation of the electrostatic potential map. When completed, again enter the **Surfaces** dialog. *Double 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 (yellow, green) represent neutral regions. What do you conclude about the environment in which decaglycine wishes to exist?
13. Remove decaglycine from the 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 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”. To simultaneously display both components, first *click* on  at the bottom left of the screen (it will become ) and then *check* both boxes to the right of the molecule names in the spreadsheet.
2. At the outset, both molecules are displayed as ball-and-spoke models, and it is difficult to locate propamidine inside the DNA strand. To remedy, first select **Global Model** from the **Model** menu. Then, select propamidine (*click* on its name in the spreadsheet) and **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

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

** Under “Tutorial” folder on the distribution CD.



is, display both as space-filling models. Another interesting display is to represent propamidine as a space-filling model and the DNA strand using “ribbons”. Select **Hide** and then **Ribbons** from the **Model** menu.

3. 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 **Apply Globally** at the bottom of the dialog is unchecked. Submit the job. When completed, turn “on” the electrostatic potential map by *double clicking* on the line “density potential . . .”. These kinds of displays may be used to supplement conventional models and provide insight into the possible relevance of charge-charge interactions on binding.
4. 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, select (*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 “Tutorial” folder on the distribution CD.

Chapter 7

Inorganic and Organometallic Molecules

This chapter shows how to construct inorganic and organometallic molecules using Spartan's inorganic 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 organic 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 inorganic 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 not proven to be suitable where transition metals are involved. The PM3 semi-empirical model, that 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.





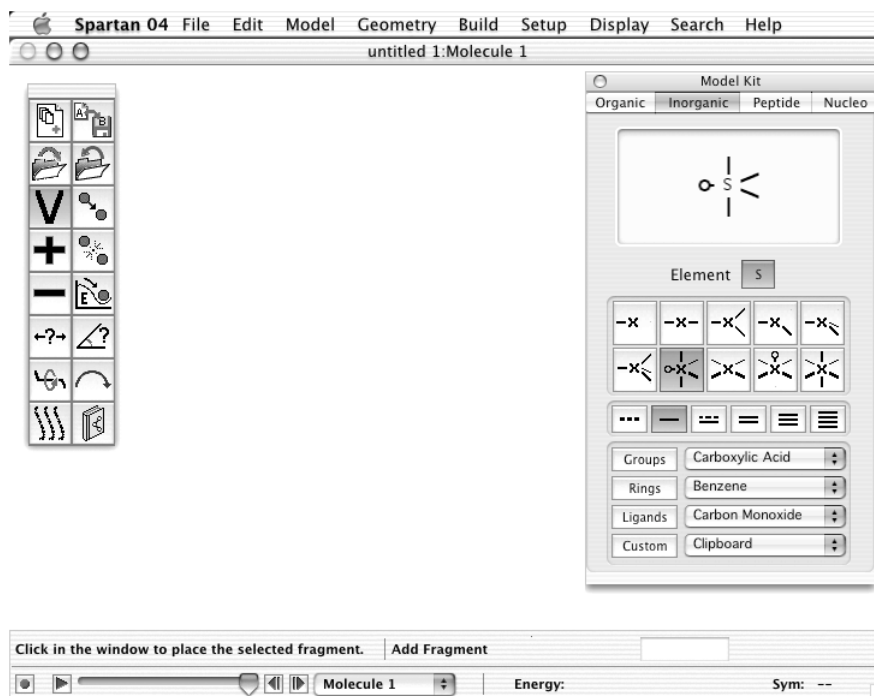
1 min

Sulfur Tetrafluoride



Even a simple hypervalent molecule such as sulfur tetrafluoride cannot be constructed using the organic model kit. This is because sulfur is not in its “normal” bent dicoordinate geometry, but rather in a trigonal bipyramid geometry with one of the *equatorial* positions vacant. SF₄ is, however, easily made with the inorganic model kit.

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



Functions at the top of the model kit allow selection of element, atomic hybrid and bond type. Further down the model kit are the **Rings**, **Groups** and **Custom** menus, that are the same as found in the organic model kit, and a **Ligands** menu. The last



- Position the cursor inside the box to the right of “Element” and *press* the left button to bring up a *Periodic Table* with main-group elements 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	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	Ac															

Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Move the cursor over **S** in the *Periodic Table* and release the button. Then select the five-coordinate trigonal bipyramid structure  from the list of atomic hybrids.



Move the cursor anywhere on screen and *click*. A trigonal bipyramid sulfur will appear.

- In a similar way, select **F** from 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.
- 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.
- Click* on . Molecular mechanics minimization will result in a structure with C_{2v} symmetry. *Click* on  to remove the model kit.

* Alternatively, move back to the organic model kit (*click* on the **Organic** tab at the top of the inorganic model kit) and select  from the list of atomic fragments.



6. Select **Calculations...** from the **Setup** menu. Specify calculation of equilibrium geometry using the Hartree-Fock 3-21G model.* *Click* on **OK**.
7. Submit the job. Name it: “sulfur tetrafluoride”. When completed, select **Properties (Display menu)**. *Click* on an atom, e.g., sulfur, and the electrostatic charge on that atom will appear in the (**Atom Properties**) dialog. To obtain the charge on another atom, simply *click* on it.** Inspect all the atomic charges on SF₄ (by *clicking* on the appropriate atoms). Note that sulfur carries a large positive charge. Close the **Atom Properties** dialog when you are done.
8. The usual picture is that the remaining *equatorial* position in sulfur tetrafluoride holds a non-bonded pair of electrons (a “lone pair”). To see to what extent this simple picture is accurate, examine the highest-occupied molecular orbital (HOMO) of SF₄.

Bring up the **Surfaces** dialog and *click* on **Add**. Select **HOMO** from the **Surface** menu (**none** from the **Property** menu) in the **Add Surface** dialog which appears and *click* on **OK**. Leave the **Surfaces** dialog on screen.
9. Submit the job. When the calculation has completed, enter the **Surfaces** dialog and *double click* on the line: “HOMO . . .”. Does the image you see clearly identify the orbital as corresponding to a lone pair on sulfur?
10. Remove sulfur tetrafluoride and any open dialogs from the screen.

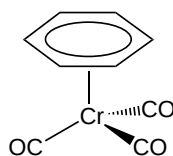
* The 3-21G(*) basis set, that incorporates a set of unoccupied d-type functions, is used in place of 3-21G for the sulfur atom.

** Electrostatic charges may be displayed for all atoms at once by selecting “Electrostatic Charges” in the **Configure Labels** dialog (**Configure...** from the **Model** menu).



2 mins/30 mins

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 inorganic model kit. Click inside the box to the right of “Element” and select **Cr** from the *Periodic Table* and the four-coordinate tetrahedral structure  from the list of atomic hybrids. Click anywhere on screen.
2. Select **Benzene** from the menu of available ligands in the **Ligands** menu.



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. Do not click on .
4. Select **New Molecule** from the **File** menu. Build benzene (**Rings** menu) and click on . Click on .
5. Select **Calculations...** (**Setup** menu). Specify calculation of equilibrium geometry with the semi-empirical PM3 model. Click on **OK**.



6. Select **Surfaces** (**Setup** or **Display** menu). Click on **Add** to bring up the **Add Surface** dialog. Specify **density** from the **Surface** menu, and **potential** from the **Property** menu, and click on **OK**. Leave the **Surfaces** dialog on screen.
7. Submit the job (two separate calculations). Name it “benzene chromium tricarbonyl”. When completed click on  at the bottom left of the screen. It will become  (multiple display mode). Then bring up the spreadsheet (**Spreadsheet** from the **Display** menu), and check the box to the right of the molecule name 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 for the organometallic).
8. Double click on the line “density potential . . .” inside the **Surfaces** dialog. Compare electrostatic potential maps for both free and complexed benzene, with attention to the “exposed face” on benzene.* Is the effect of the $\text{Cr}(\text{CO})_3$ 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. Make a copy of “benzene chromium tricarbonyl” (); name it “benzene chromium tricarbonyl BP”. Inside the **Calculations** dialog, specify an energy calculation using the BP/6-31G* density functional 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 open dialogs from the screen.

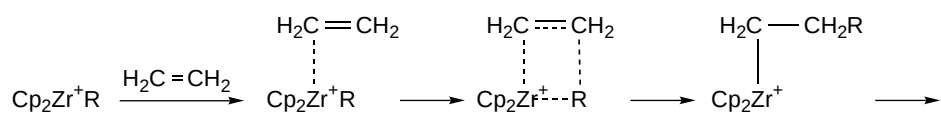
* Electrostatic potential maps (as well as other maps) for molecules in a single list will be put onto the same (color) scale. This allows comparisons to be made among different members.



10 mins/60 mins

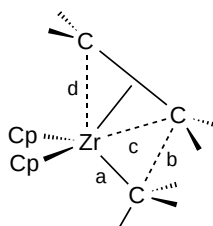
Ziegler-Natta Polymerization of Ethylene

Stable complexes of group IV transition metals may act as homogenous catalysts in alkene polymerization. The mechanism of so-called Ziegler-Natta catalysis remains somewhat uncertain, although it is believed to involve a cationic metallocene alkyl complex, e.g., Cp_2ZrR^+ , as the active species. This first complexes an olefin, which then inserts into the metal alkyl, leading to a new active metallocene in which the alkyl group is now extended by two methylene groups.



Here, you will use PM3 semi-empirical calculations to obtain a transition state for insertion of ethylene into $\text{Cp}_2\text{ZrCH}_3^+$ and, (optionally) following this, estimate the activation energy for the process using density functional calculations. While the “reaction” library could be used to provide a guess at the transition state, a different general technique will be employed here.

1. Bring up the inorganic model kit. Select **Zr** from the *Periodic Table* and four-coordinate tetrahedral  from the list of atomic hybrids. *Click* anywhere on screen.
2. Select **C** from the *Periodic Table* ( is still selected), and *click* on one of the free valences of the tetrahedral zirconium.
3. Select **Cyclopentadienyl** from the **Ligands** menu and, one after the other, *click* on two of the free valences on the tetrahedral zirconium.
4. Select **Ethylene** from the **Ligands** menu and *click* on the remaining free valence on zirconium.
5. Orient the methyl group and the ethylene ligand as shown at the top of the following page.



6. Constrain the four distances a, b, c, d (see figure above) to 2.35Å, 2.05Å, 2.60Å and 2.35Å, respectively. Select **Measure Distance** from the **Geometry** menu (or *click* on ) , then *click* on the appropriate bond (or two atoms), and finally *click* on  at the bottom right of the screen. The icon will change to  indicating that a (distance) constraint is to be applied. Replace whatever distance appears in the box to the left of  by the appropriate distance (see figure) and *press* the **return** key. When you have constrained all four bonds, *click* on  to produce a refined structure subject to the four distance constraints.
7. Enter the **Calculations** dialog, and specify the calculation of equilibrium geometry (*not transition-state geometry*) using the PM3 semi-empirical model. Set **Total Charge** to **Cation**. *Check Constraints* below “Subject to”. Exit the dialog and submit the job. Name it: “Cp2ZrMe+ethylene”. What you have done is to request a geometry optimization subject to the four bond length constraints specified in step 6. This should provide a reasonable starting point for transition-state structure optimization.
8. When the optimization has completed, enter the **Calculations** dialog a second time, and specify calculation of transition-state geometry using the PM3 semi-empirical model. Remove the checkmark beside **Constraints**. *Check IR* below “Compute” to specify calculation of vibrational frequencies. This will allow you to verify that you have in fact located a transition state.
9. Submit the job a second time. When completed, first examine the vibrational frequencies to verify that you have indeed located a transition state. Animate the motion corresponding to the imaginary frequency. Next, examine the final structure. Can you identify any unusual features?

10 to 12 optional (cannot be completed with the Essential Edition)

10. 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+ ethylene” (📄); name it “Cp₂ZrMe+ethylene_ BP”. 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 right of the “Calculate” section to specify use of a pseudopotential for Zr associated with the 6-31G* basis set. Remove the checkmark on **IR** (below “Compute”). **Total Charge** should still be set to **Cation**. Exit the dialog and submit the job.
11. Build both ethylene and Cp₂ZrCH₃⁺ (name them “ethylene_BP” and “Cp₂ZrMe+_BP”, 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 an energy with the BP/6-31G* density functional model. Select **PM3** from the menu below “Start From”. For “Cp₂ZrMe+_BP” (only) *check Pseudopotential*, and set **Total Charge** to **Cation**.
12. Submit both jobs. When they (and the transition-state calculation) have completed, calculate an activation energy for the insertion reaction.
13. Remove all molecules from the screen.

Section III

Features and Functions

This section describes the functions available under the menus incorporated into Spartan'04 for Macintosh, 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*” available from Wavefunction.

As with the tutorials (see **Section II**), the material in this section has been written assuming use of a two-button mouse in lieu of the Macintosh standard one-button mouse. Users wishing to employ a one-button mouse need to consult **Chapter 2** for the appropriate mouse/keyboard commands.





Chapter 8

The Spartan Menu

*This chapter describes operations under the **Spartan** menu. These allow monitoring and killing of executing jobs, setting of user preferences and exiting Spartan.*

Selection of **Spartan** leads to the following menu.



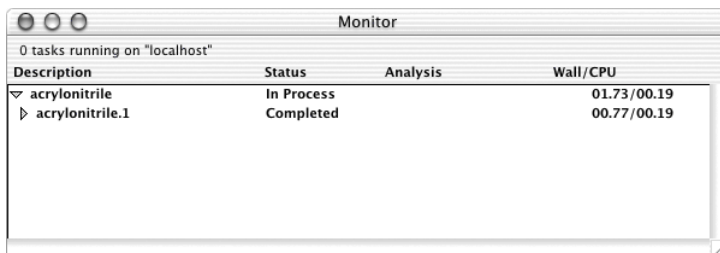
About Spartan...

Provides information about the user's release of Spartan'04 for Macintosh. This information should always be quoted when requesting program support.



Spartan Monitor

A monitor is available to oversee execution of jobs, to terminate executing jobs and to initiate execution of queued jobs. Selection leads to a window.



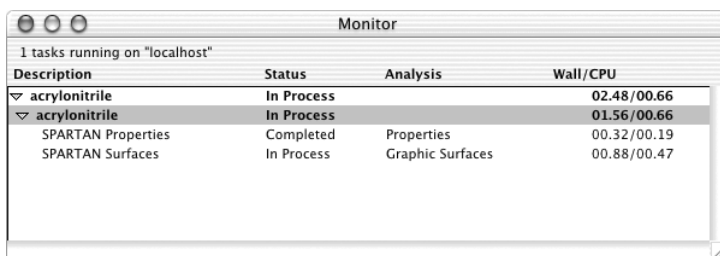
Monitor

0 tasks running on "localhost"

Description	Status	Analysis	Wall/CPU
▼ acrylonitrile	In Process		01.73/00.19
▶ acrylonitrile.1	Completed		00.77/00.19

Job requests appear under **Description**. **Status** displays the current state of each request. Additional information is found under **Analysis** and job times under **Wall/CPU**. Items that contain sub-tasks appear with a “twist-down” triangle in the left hand column.

To view the sub-tasks for an item, *click* on its “twist-down” triangle. *Clicking* on the triangle again will fold the sub-tasks back into its parent.

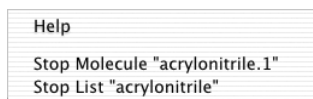


Monitor

1 tasks running on "localhost"

Description	Status	Analysis	Wall/CPU
▼ acrylonitrile	In Process		02.48/00.66
▼ acrylonitrile	In Process		01.56/00.66
SPARTAN Properties	Completed	Properties	00.32/00.19
SPARTAN Surfaces	In Process	Graphic Surfaces	00.88/00.47

An executing job may be killed by first selecting (*clicking* on) it in the monitor, holding down the right button to produce a menu,



Help
Stop Molecule "acrylonitrile.1"
Stop List "acrylonitrile"

and then selecting either **Stop Molecule “xyz”** or **Stop List “xyz”**. Where the molecule is the only member of a list, the two commands have the same effect. Where two or more molecules make up a list, selecting **Stop Molecule “xyz”** kills the currently executing molecule, but allows execution of all remaining molecules, while selecting **Stop**

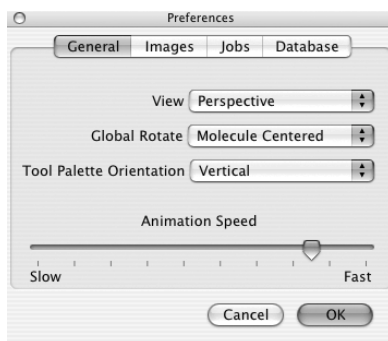


List “xyz” kills the currently executing molecule and does not allow execution of any remaining molecules.

In addition to “stop” commands (which remove the molecule or entire list of molecules from the queue) is a command **Start List “xyz”**, which starts execution of the job irrespective of queue limits (see **Preferences...** later in this chapter).

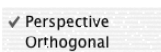
Preferences...

This allows setting a number of aspects of the user interface. Selection leads to a “tabbed” dialog.



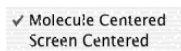
Upon initial entry, the **General** tab will be selected.

(i) **View**



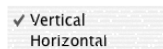
This controls the view of structural models and graphics images on screen. See **Chapter 11** for a discussion of viewing perspectives.

(ii) **Global Rotate**



This controls rotation of a set of molecules on screen. **Screen Centered** provides a single center for rotation of all molecules, and is useful for examining intermolecular complexes. **Molecule Centered** rotates each molecule about its individual center, and is useful for aligning molecules on screen.

(iii) Tool Palette Orientation

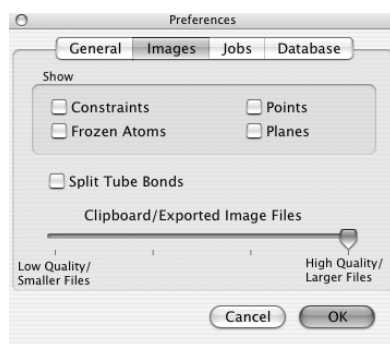


This controls the orientation of the tool palette. **Vertical** provides seven rows of two icons each and **Horizontal** provides two rows of seven icons each.

(iv) Animation Speed

A slider bar controls the (maximum) speed for vibrations and animations.

Clicking on the **Images** tab at the top of the dialog leads to a new dialog.



(i) Show

This provides check boxes that turn “on” (*checked*) or “off” display of constraint and frozen atom markers and points and planes.

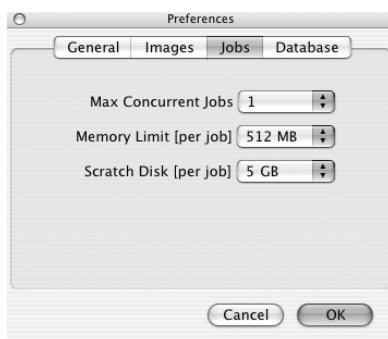
(ii) Split Tube Bonds

A check box splits tubes in tube and ball-and-spoke models to represent double and triple bonds.

(iii) Clipboard/Exported Image Files

A slider bar controls the quality (and size) of images exported or brought onto the clipboard.

Clicking on the **Jobs** tab at the top of the dialog leads to a new dialog.



(i) **Maximum Concurrent Jobs**

This sets the maximum number of jobs that can be run at one time. Default is one job/processor.

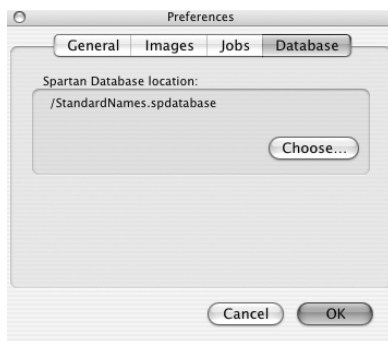
(ii) **Memory Limit [per job]**

This sets the maximum amount of memory (in MB) available to a single job. Default is 512 MB.

(iii) **Scratch Disk [per job]**

This sets the maximum amount of disk space (in GB) available to a single job. Default is 5 GB.

Clicking on **Database** at the top of the dialog leads to a new dialog.



This allows the user to choose the location where the Spartan Molecular Database is located.

Preferences dialogs are exited with all changes kept by *clicking* on **OK**; *clicking* on **Cancel** exits the dialog without instituting any changes.

Services

Hide Spartan

Hide Others

Show All

These are standard Mac OS 10 facilities.

Quit Spartan

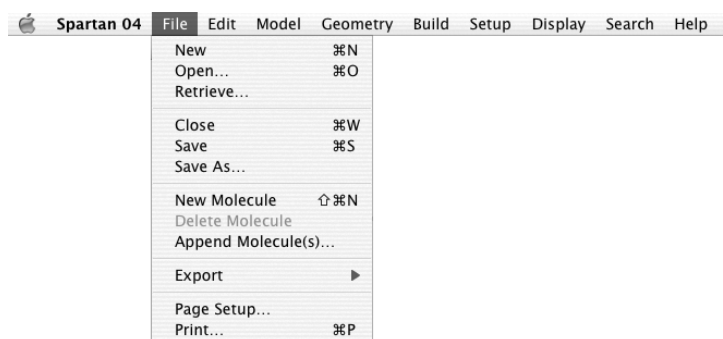
Exits, i.e., clears the screen and closes all open files. If there are any molecules (list of molecules) open with unsaved changes, the user will be presented with the opportunity to save them before exiting.

Chapter 9

The File Menu

*This chapter describes operations under the **File** menu. These permit initial entry into the builders, control reading of input to and writing of text and graphical output from the calculation modules, and provide printing of text and spreadsheet output as well as on-screen graphics.*

Selection of **File** leads to the following menu.



New

Creates a new single-membered molecule list (a “molecule”), and brings up a model kit for molecule building (for a discussion of builder functions, see **Chapter 13**).

Open...

Brings up a dialog from which the user may access a previously saved molecule (list of molecules).



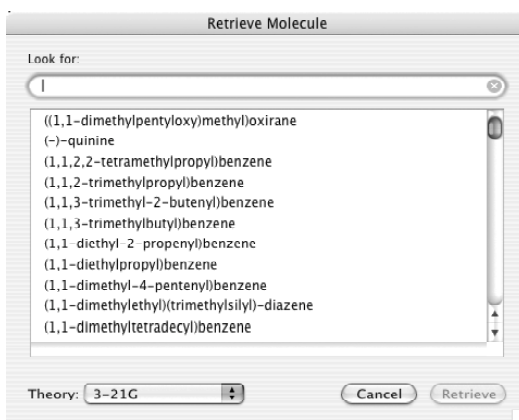
The **Enable** menu at the top of the dialog selects from among available file types.



Spartan for Macintosh is the default format. **Spartan for Windows** is for compatibility with Spartan'04 for Windows. **MacSpartan Molecule** is for backwards compatibility with earlier versions of Spartan for Macintosh. **SPARTAN Exchange** and **SPARTAN Collection** are compact single and multiple molecule formats compatible with SPARTANView. **All TEXT Files** allows reading from other sources. Presently SYBYL MOL and SYBYL MOL2, MacroModel, PDB and XYZ (3D), MDL SKC, TGF and SD (2D) and SMILES (1D) formats are (automatically) recognized.

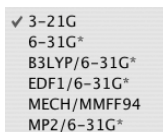
Retrieve...

Retrieves a molecule from the Spartan Molecular Database (SMD) from its name. Selection results in a dialog.



Typing a character string in the box at the top of the dialog and *pressing* the **return** key results in the names of all molecules containing this string being displayed in the window at the bottom of the dialog. *Clicking* on the molecule selects it, following which, *clicking* on **Retrieve** at the bottom of the dialog, retrieves it. Only one molecule may be retrieved at a time.

The **Theory** menu at the bottom of the dialog allows selection of theoretical model. Only one model may be searched at a time.



Close

Closes the current molecule (list of molecules) and any associated graphics.

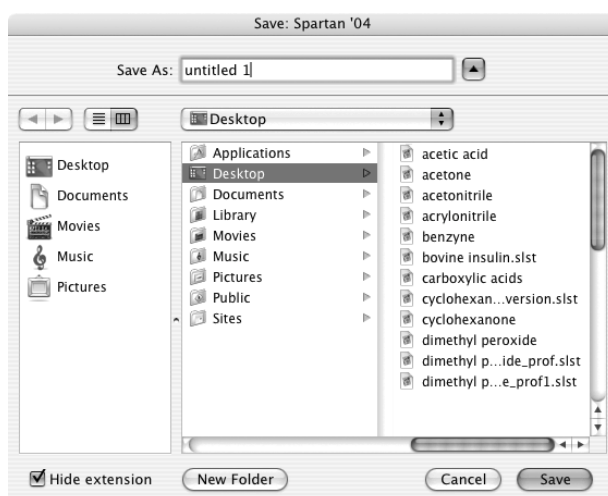
Save

Saves the selected molecule (list of molecules) and associated spreadsheet *exactly as it appears on screen*, that is, rendered in terms of a specific structure model and optionally with one or more graphical displays. Opening the molecule will bring it on screen exactly as it was last saved. If the molecule has not previously been saved, **Save** will behave as **Save As...** (see below) and will display a dialog to enter a file name; otherwise, the file will be saved under its previous

name. **Save** is particularly useful for storing predefined information for later display, as for example, in creating a “slide show”.

Save As...

Saves the current molecule (list of molecules), and associated spreadsheet *exactly as it appears on screen*, that is, rendered in terms of a specific structure model and optionally with one or more graphical displays, under a user-specified name. Selection of **Save As...**, results in a dialog.



New Molecule

Brings up a model kit and clears the screen. **New Molecule** is identical to **New**, except that the molecule is appended to the end of the current molecule list.

Delete Molecule

Deletes a molecule (or set of molecules in a list) that is (are) presently selected in a molecule list. The “last molecule” in a list may not be deleted and **Delete Molecule** is unavailable for lists containing only one molecule.



Append Molecule(s)...

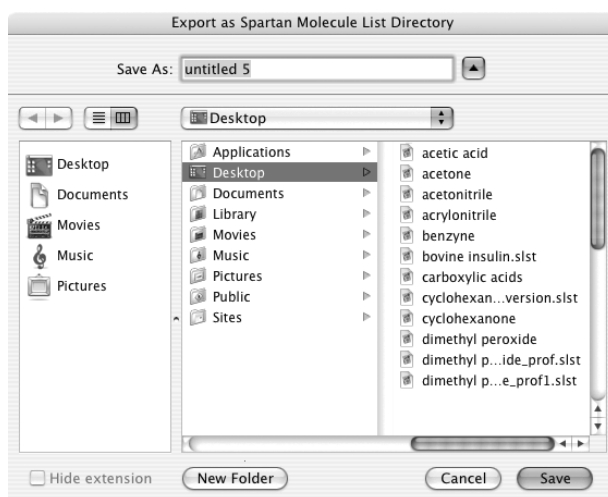
Appends a file which contains all information associated with a particular molecule (or list of molecules) onto the end of a list of molecules associated with the molecule which is presently selected. **Append Molecule(s)...** leads to a file browser (like that for **Open...** discussed earlier in this chapter) from which one or more molecules (or lists of molecules) needs to be selected.

Export

Exports data in various formats from the currently selected molecule to other programs. Selection of **Export** results in the following sub-menu.



Selection of any of these leads to a dialog.



This requests a name for the data once it has been converted to the appropriate format. Conversion is not restricted to structure. Rather, the text output and any graphical images will also be converted. If PICT or JPEG is selected, a snapshot of the selected molecule or the selected screen area will be saved to a file as a static image in PICT or JPEG format. Similarly, selection of QuickTime results in a snapshot of the individual frames which make up a complete list of molecules.

Page Setup...

Selection 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.

Print...

Selection causes whatever is presently displayed on screen to be printed (according to the specifications made in the last access to **Page Setup...**).

Chapter 10

The Edit Menu

*This chapter describes operations under the **Edit** menu. These provide for “undoing” some commands, cut, copy and paste operations involving the clipboard, finding text in the output and spreadsheet, centering molecules on screen and altering colors.*

Selection of **Edit** leads to the following menu.

Undo Add Fragment	⌘Z
Cut	⌘X
Copy	⌘C
Paste	⌘V
Clear	
Select All	⌘A
Find...	⌘F
Find Next	⌘G
Center	
Colors	

Undo/Redo

With few exceptions, this function “undoes” the last operation (only). Selection leads to **Undo** being replaced by **Redo** in the menu which may be used to “undo” the “undo”.

Cut

Deletes from the currently selected molecule all atoms highlighted or enclosed by the selection box (see below) and places these on the clipboard. Broken bonds are replaced by free valences. If no selection box has been specified, **Cut** deletes the entire molecule and places it on the clipboard.

A selection box is defined by first positioning the cursor above and to the left of the area to be selected, then moving the mouse while *pressing* either the left or right button in addition to the **shift** key below and to the right of the area to be selected, and finally releasing both the button and **shift** key.



Copy

Copies from the currently selected molecule all atoms highlighted or enclosed by the selection box onto the clipboard. Broken bonds are replaced by free valences. If no selection box has been specified, the entire molecule is copied to the clipboard. Highlighted text from the output window may also be brought onto the clipboard using **Copy**.

Information placed on the clipboard (a “snapshot”) may be brought into other documents (such as Microsoft Word®) by opening the other document and selecting **Paste** from its **Edit** menu. If the snapshot is a molecule, this may be copied onto the clipboard and be used (inside the builders) to initiate molecule construction or to add to or alongside of an existing molecule.

Only one snapshot at a time may be placed on the clipboard; selecting **Cut** or **Copy** again will replace a previous snapshot with a new image of the currently selected molecule. Note, however, that up to three previous clipboard entries are kept for use in the builders (see discussion in **Chapter 13**).

Paste

Pastes whatever is on the clipboard onto the screen. Functions in **View** and **Add Fragment** modes only (see **Custom** under **Organic Model Kit** in **Chapter 13**).

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. **Clear** is also used to remove rows and/or columns from a spreadsheet (see **Spreadsheet** in **Chapter 15**).

Select All

Designates the selection area as enclosing the entire selected molecule.

Center

Centers the selected molecule (or all molecules in a list) on screen, i.e., places the center of geometry at the center of the screen.

Find...

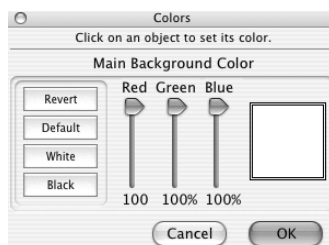
Finds text string in the output dialog or in the spreadsheet.

Find Next

Finds next occurrence of text string.

Colors

This allows default colors for atoms, bonds, surfaces (without mapped properties), contour and plot lines, as well as the background color to be altered. Selection leads to a dialog.



The background is initially selected. To change the color of another graphical object *click* on it.

In order to select a particular object, it may be necessary to orient the graphic on screen such that the object of interest does not overlap another object. Selection of atom and bond colors is best performed using ball-and-spoke models.

The selected object is identified at the top of the dialog and its color displayed in a square box at the right. At the left are four buttons, *clicking* on which accesses predefined colors: **Revert** (which reverts back to the color prior to the last selection), **Default** (which depends on the object selected), **White** and **Black**. Object color may also be set by adjusting the **Red**, **Green** and **Blue** slider bars in the center of



the dialog. Color changes apply to all objects of the same type, e.g., all carbon atoms, and not just the selected object.

Color selection may be performed for as many objects as desired. For each, simply *click* on the object and select the color. *Clicking* on **OK** sets all color choices and exits the dialog. *Clicking* on **Cancel** exits the dialog without instituting any color changes.

Chapter 11

The Model Menu

*This chapter 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. Finally, it describes procedures to allow model style to be applied globally (to all molecules in a list) and for molecules 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".

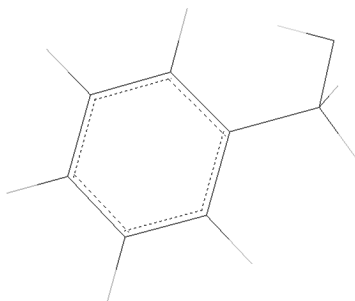


All structure models, as well as isosurfaces, property maps and slices may be presented either in orthogonal or perspective projections. While orthogonal projections are generally easier to work with, perspective views are valuable in helping to visualize spatially large molecules. Note, also that perspective projections are required for stereographic viewing (see **3-Dimensional Displays** in **Chapter 2**). Selection of orthogonal or perspective projection is done from **Preferences...** (**Spartan** menu; see **Chapter 8**). All figures drawn in this guide correspond to orthogonal projections.

Wire

This model represents the molecule as a wire frame.

Wire Model



The bonds are drawn in two colors, one for each of the two atoms making up the bond. Default atom colors are listed in **Table 11-1**. These may be changed using **Colors** (**Edit** menu; see **Chapter 10**).

Ball and Wire

This model, represents atoms by small balls and bonds by wires.

Ball-and-Wire Model

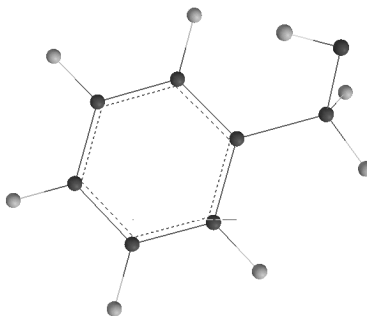




Table 11-1: Default Atom Colors

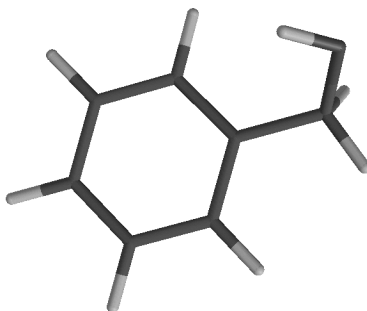
main group		main group con't	
Hydrogen	white	Strontium	red
Lithium	tan	Indium	tan
Beryllium	green	Tin	gray
Boron	tan	Antimony	tan
Carbon	gray	Tellurium	tan
Nitrogen	blue-gray	Iodine	tan
Oxygen	red	transition metals	
Fluorine	green	Scandium-Zinc	green
Sodium	yellow	Yttrium-Cadmium	green
Magnesium	blue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



Tube

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

Tube Model

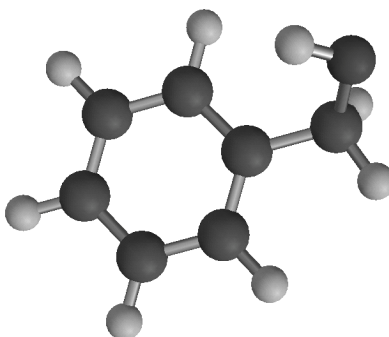


As in wire models, the bonds are drawn in two colors, one for each of the two atoms making up the bond. The choice between solid or split tubes for bonds are made in the **Images Preferences** dialog (**Preferences...** from the **Spartan** menu).

Ball and Spoke

This model represents atoms by small spheres the size and color of which depend on atom type, and bonds by solid or split tubes.

Ball-and-Spoke Model

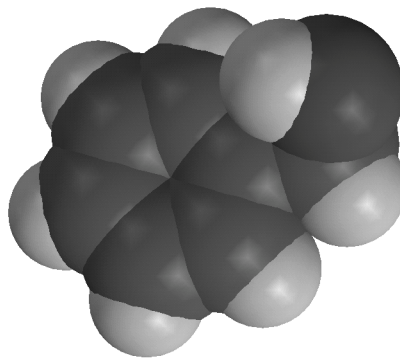


Bond color does not depend on the atoms, and may be changed using **Colors** (**Edit** menu; see **Chapter 10**). The choice between solid or split tubes for bonds are made in the **Images Preferences** dialog (**Preferences...** from the **Spartan** menu).

Space Filling

Space-filling (or CPK) models represent a molecule as a composite of spheres, the size and color of which depend on atom type.

Space-Filling Model



As the atom sizes have been chosen to reproduce experimental X-ray crystal packing data, space-filling models are intended to portray overall molecular size. Space-filling models closely approximate electron density surfaces. The volume and surface area of a space-filling model are available in the **Molecule Properties** dialog (**Properties** from the **Display** menu).

Hide

This removes the current model from among those described above from the screen, and is used to simplify displays where structure models may lead to unnecessary crowding. It is particularly useful for polypeptides and polynucleotides where ribbons may provide a clearer overall picture. A model may be restored by selecting it from the **Model** menu. In the case of screen displays involving more than one molecule, switching to another molecule following selection of **Hide** may result in “loss of a molecule”. It can be recovered by reselecting the “lost” molecule using the **Page Up** or **Page Down** key until its name appears in the window title bar, followed by switching on a model.



Global Model

If *checked*, this signifies that all molecules in a list will share a common model type (that of the currently selected molecule). This includes presentation of hydrogens, atom and other labels and ribbon displays. **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 will be moved (translated, rotated) together. **Coupled** is automatically turned “on” following molecule alignment (see **Align Molecules** in **Chapter 12**). **Coupled** acts in a toggle manner, i.e., repeated selection couples and decouples the motions of 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. **Hydrogens** acts in a toggle manner, i.e., repeated selection turns “on” and “off” the display of hydrogens.

Labels

If *checked*, this signifies that any labels associated with the model as specified in **Configure...** are to be displayed in the model. **Labels** acts in a toggle manner, i.e., repeated selection turns “on” and “off” display of labels and other requested information. **Labels** is automatically turned “on” following selection of **Configure...**

Ribbons

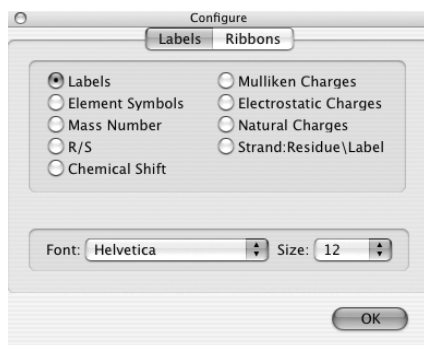
If *checked*, this signifies that ribbons are to be displayed along with the selected model. (If only ribbons are desired, for example, in displaying polypeptides and polynucleotides, select **Hide** for the model.) **Ribbons** acts in a toggle manner, i.e., repeated selection turns “on” and “off” display 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°. **Hydrogen Bonds** acts in a toggle manner, i.e., repeated selection turns “on” and “off” display of hydrogen bonds.

Configure...

This sets the type of atom label under **Labels** as well as controls the “coloring” of ribbons. Selection leads to a “tabbed” dialog.

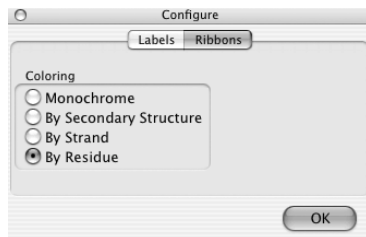


Upon initial entry, the **Labels** tab will be selected.

Labels refers to default atom labels (an elemental symbol plus a number), **Element Symbols** refers to elemental symbols only, **Mass Number** refers to atomic mass, **R/S** refers to R/S designation and **Chemical Shift** refers to NMR chemical shift. **Mulliken**, **Electrostatic** and **Natural Charges** refer to atomic charges from Mulliken, electrostatic fit and natural bond orbital procedures and **Strand:Residue\Label** identifies atoms in particular strands in particular residues of polypeptides.

Type font and size used for labels may be selected from the menus to the right of **Font** and **Size**, respectively.

Clicking on the **Ribbons** tab at the top of the dialog leads to a new dialog.



This allows ribbon coloring to be selected from among the following: **Monochrome**, **By Secondary Structure**, **By Strand** or **By Residue**.

Either **Configure** dialog is removed by *clicking* on **OK**. Note, that **Labels** (from the **Model** menu) will be turned “on” following *clicking* on **OK**, meaning that labels will be attached to the model. To remove them, select **Labels** from the **Model** menu.

Chapter 12

The Geometry Menu

*This chapter 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, ligand 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
Define Point
Define Plane
Freeze Center
Set Torsions
Align Molecules

All functions under the **Geometry** menu require selecting one or more atoms, bonds, points, planes and/or constraint markers. 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 marker results in two atoms being identified by gold spheres, an angle constraint marker in three atoms identified, and a dihedral constraint marker in four atoms being identified. As points and planes are selected, the magenta marker will be changed to gold.

Measure Distance

This obtains and displays the distance (in Ångstroms) between two atoms, whether or not they are bonded. In some cases, **Measure Distance** also allows a distance to be set. Finally, it permits a distance to be constrained. Selection of **Measure Distance** results in a message at the bottom left of the screen.

Select two atoms, a bond, ...

This directs you to *click* on two atoms or, if the atoms are bonded, on the interconnecting bond, or on the constraint marker. Once accomplished, this results in the atoms being colored gold and in the distance being displayed in the box immediately to the right of “Distance” at the bottom right of the screen. For bonded atoms, both of which are not incorporated into the same ring, the distance may be changed by changing the value inside the box (you need to *press* the **return** key after you edit the value). Finally, a distance may be constrained during geometry or transition-state geometry optimization, or generation of a conformer distribution or an energy profile. This is accomplished by *clicking* on the  icon at the bottom right of the screen (which will then turn to ). A previously defined constraint can be removed by *clicking* on  (which will then turn back to ). A new constraint value may be specified by changing the value inside the box (you need to *press* the **return** key after you edit the value).

Any distance constraint may be turned into a so-called NOE (Nuclear Overhauser Effect) constraint. This indicates that a (non-bonded) distance is to be kept below a certain threshold value (the constraint value). NOE's are set in the **Constraint Properties** dialog (available from **Display** menu (see **Chapter 15**).

Points and planes are treated like atoms, except that only a single plane may be used in a distance measurement and that distances involving points, ligand points and/or planes may not be set or constrained.



Measure Angle

This obtains and displays the angle (in degrees) involving three atoms or two connected bonds. In some cases, **Measure Angle** also allows an angle to be set. Finally, it permits an angle to be constrained. Selection of **Measure Angle** results in a message at the bottom left of the screen.

Select three atoms, two adjacent bonds, ...

This directs you to *click* on the appropriate atoms or bonds in the proper order, or on the constraint marker. Once accomplished, this results in the three atoms being colored gold and in the angle being displayed in the box immediately to the right of “Angle” at the bottom right of the screen. In the case where all three atoms are not incorporated into a ring, the angle may be changed by changing the value inside the box (you need to *press* the **return** key after you edit the value). Finally, an angle may be constrained during geometry or transition-state geometry optimization, or generation of a conformer distribution or an energy profile. This is accomplished by *clicking* on the  icon at the bottom right of the screen (which will then turn to ). A previously defined constraint can be removed by *clicking* on  (which will then turn back to ). A new constraint may be specified by changing the value inside the box (you need to *press* the **return** key after you edit the value).

Points and planes are treated like atoms, except that only a single plane may be used in an angle measurement and that angles involving points, ligand points and/or planes may not be set or constrained.

Measure Dihedral

This obtains and displays the dihedral angle (in degrees) involving four atoms or three connected bonds. 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 last two bonds) specified. In some cases, **Measure Dihedral** allows a dihedral angle to be set. Finally, it permits a dihedral angle to be constrained. Selection of **Measure Dihedral** results in a message at the bottom left of the screen.



Select four atoms, three adjacent bonds, ...

This directs you to *click* on the appropriate atoms or bonds in the proper order, or on the constraint marker. Once accomplished, this results in the four atoms being colored gold and in the dihedral angle being displayed in the box immediately to the right of “Dihedral” at the bottom right of the screen. In the case where no more than two atoms are incorporated into a single ring, the dihedral angle may be changed by changing the value inside the box (you need to *press* the **return** key after you edit the value). Finally, a dihedral angle may be constrained during geometry or transition-state geometry optimization, or generation of a conformer distribution or an energy profile. This is accomplished by *clicking* on the  icon at the bottom right of the screen (which will then turn to ). A previously defined constraint can be removed by *clicking* on  (which will then turn back to ). A new constraint value may be specified by changing the value inside the box (you need to *press* the **return** key after you edit the value).

Points and planes are treated like atoms, except that only a single plane may be used in a dihedral angle measurement and that dihedral angles involving points, ligand points and/or planes may not be set or constrained.

Define Point/Define Ligand Point

This defines and displays a point as the geometric (unweighted) center of a selected group of atoms. Selection of **Define Point/Define Ligand Point** results in a message at the bottom left of the screen.

Select atoms to define a centroid. Repeat an atom to end.

This directs you to select atoms by *clicking* on them, with the end of the group signaled by *clicking* a second time on the last atom selected. A point will be placed at the centroid of the selected atoms, and displayed as a magenta asterisk. 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** 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 13**).

To remove a point or a ligand point, select **Delete** from the **Build** menu (or *click* on the  icon in the **Tool Palette**) and then *click* on the point.

Define Plane

This defines and displays a reference plane passing through three atoms (or a least-squares fit to four or more atoms). Selection of **Define Plane** results in a message at the bottom left of the screen.

Select atoms to define a plane. Repeat an atom to end.

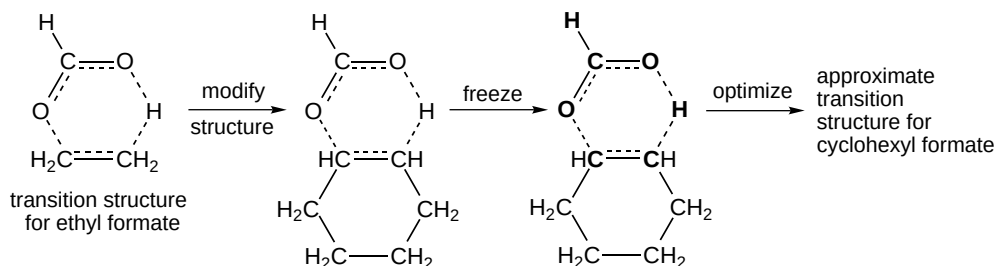
This directs you to select (three or more) atoms by *clicking* on them, with the end of the group signaled by *clicking* a second time on the last atom selected. The resulting plane will either pass through three atoms or (in case more than three atoms were selected) will be a least-squares fit. This plane, which is indicated as a magenta colored disk, can be treated as an “atom” for the purpose of distance (“distance to plane”) and angle (“angle with plane”) measurements. As many planes as desired can be defined.

To remove a plane, select **Delete** from the **Build** menu (or *click* on the  icon in the **Tool Palette**) and then *click* on the plane.

Freeze Center

This “freezes” one or more atoms during structure minimization (in build mode), or (optionally) during geometry or transition-state optimization, or during generation of a conformer distribution or an energy profile using methods under the **Calculations** dialog. Freezing inside the **Calculations** dialog needs to be explicitly indicated (see **Chapter 14**).

Atom freezing is especially useful in a number of situations, among them guessing transition structures for closely-related reactions. For example, a good guess at the transition state for pyrolysis of cyclohexyl formate may be obtained by modifying the transition state for pyrolysis of ethyl formate, freezing all but the modified sections (designated in **bold** in the figure on the following page) and then performing geometry optimization instead of transition-state optimization.*



Selection of **Freeze Center** results in a message at the bottom left of the screen.

Select atom to freeze / thaw.

This directs you to *click* on one or more atoms to designate them as frozen. Frozen atoms are marked with magenta “anchors” (⊥). They may be thawed by again *clicking* on them. Functions in the **Freeze** and **Thaw** menus at the bottom right of the screen allow for freezing all atoms (**All**), freezing only heavy (non-hydrogen) atoms (**Heavy Atoms**), thawing all atoms (**All**) or thawing only heavy atoms (**Heavy Atoms**).

Set Torsions

Flexible bonds and rings to be considered during a conformational search as well as default step size for each “motion” are automatically set. **Set Torsions** allows these default selections to be altered.** Selection results in a model in which flexible bonds are marked by a

* An example is provided in “**Carbene Additions to Alkenes**” in **Chapter 5**.

** Other parameters involved in conformational searching may be adjusted from their default values using the **Options** box in the **Calculations** dialog (see **Calculations...** under the **Setup** menu in **Chapter 14**). **Appendix C** provides a listing of conformational searching options.



gold cylinder and flexible rings are marked by a gold circle around one or more atoms. In addition, a message appears at the bottom left of the screen.

Select bond or atom.

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 either 2 or 3 for a single bond (step size of 180° and 120°, respectively) and 3 for a flexible ring.* Other integer values may be entered into the box, followed by *pressing* the **return** 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.

A selected bond or ring atom may be deselected by *double clicking* on it. *Double clicking* on a bond or ring atom which is not currently selected (or has been deselected) selects it with default rotation values.

Align Molecules

This aligns molecules in a list by best matching the coordinates of two or more selected atoms. Alignment is based on atom labels. Labels will be the same for all molecules generated as a result of a conformational search or from an energy profile, but will generally not be the same for user defined lists. Here, the labels on individual molecules may need to be altered using the **Atom Properties** dialog (see **Chapter 15**).

Selection results in a message at the bottom left of the screen.

Select atoms to align.



Atoms may be selected by *clicking* on them. *Clicking* a second time also selects the atom but instructs the alignment procedure to ignore the label, that is, simply demands that any atom be in the selected position. *Clicking* a third time deselects the atom.

non-selected $\xrightarrow{\text{click}}$ selected $\xrightarrow{\text{click}}$ selected as "wild card" $\xrightarrow{\text{click}}$ non-selected

Selected atoms are marked by a single red circle if the label is to be considered, and by two concentric red circles if the label is to be ignored. Note, that at least three (non-colinear) atoms need to be selected for alignment to be meaningful, and it is recommended that no more than ten 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**.

Chapter 13

The Build Menu

*This chapter 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.



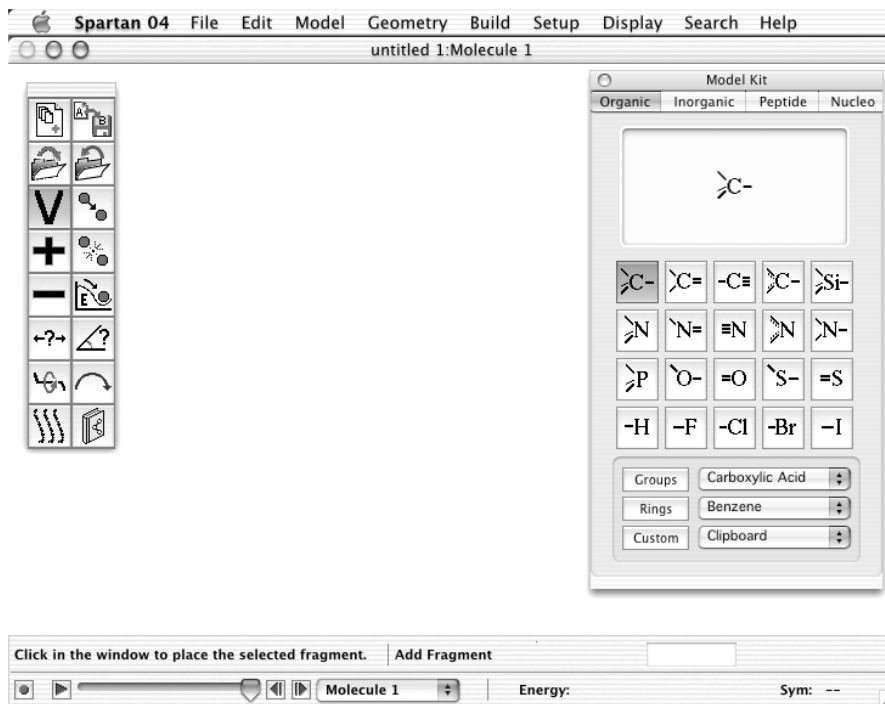
Selection of **Add Fragment** results in display of one of four model kits*: an organic model kit for most organic molecules, an inorganic model kit for inorganic and organometallic molecules, and specialized model kits for polypeptides and polynucleotides. The organic and inorganic model kits utilize “atomic fragments”, functional groups and rings (and ligands in the inorganic model kit), while the peptide model kit uses amino acids as building blocks, and the nucleotide model kit uses 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.

* The model kits are also brought onto screen from **New** or **New Molecule** (**File** menu; see **Chapter 9**).

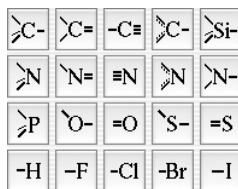
Organic Model Kit

The organic model kit, which contains a suite of molecule building/editing tools specifically designed to construct most organic molecules, appears at the right of a screen that has been cleared of all molecules except that under construction.*



(Other molecule building functions are accessed by pull-down menus and by icons in the **Tool Palette**.)

A selection of “atomic fragments” displayed as icons, is provided in the middle of the model kit.



* The screen is blank following selection of **New** or **New Molecule** from the **File** menu. Re-entry into the builder with an existing structure (**Add Fragment** from the **Build** menu), results in this structure being displayed.



These correspond to:

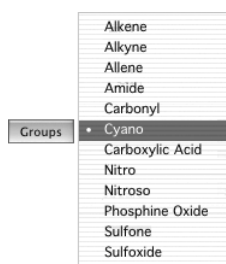
C(sp ³)	C(sp ²)	C(sp)	C(aromatic)	Si(sp ³)
N(sp ³)	N(sp ²)	N(sp)	N(aromatic)	N(planar)
P(sp ³)	O(sp ³)	O(sp ²)	S(sp ³)	S(sp ²)
H	F	Cl	Br	I

An “atomic fragment” is chosen by positioning the cursor on top of its icon and *clicking*; the selected icon is highlighted and its structure is displayed at the top of the model kit. Once selected, the atomic fragment can be used to initiate building (*clicking* anywhere on screen), to add alongside of an existing structure (*clicking* anywhere on screen while holding down on the **option** key), or to add to an existing structure (*clicking* on the tip of 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.

Two fragment collections are located further down the model kit.

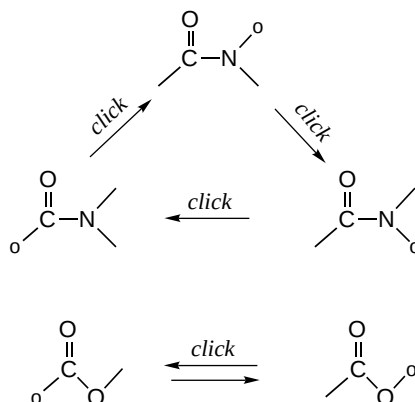
(i) **Groups**

Clicking on the menu entry to right of **Groups** accesses a menu of functional groups.



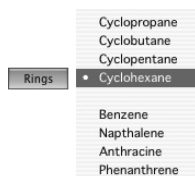
Once selected, the name of the group replaces the full menu, and its structure appears at the top of the model kit. This group may then be used to initiate building (*clicking* anywhere on screen), to add alongside of an existing structure (*clicking* anywhere on screen while holding down on the **option** key), or to add to an existing structure (*clicking* on the tip of a free valence). The amide and carboxylic acid groups have different types of free

valences. The free valence that will be used to connect these groups to the molecule is marked with an “o”, and circulates among the different positions with repeated *clicking* inside the icon display area.



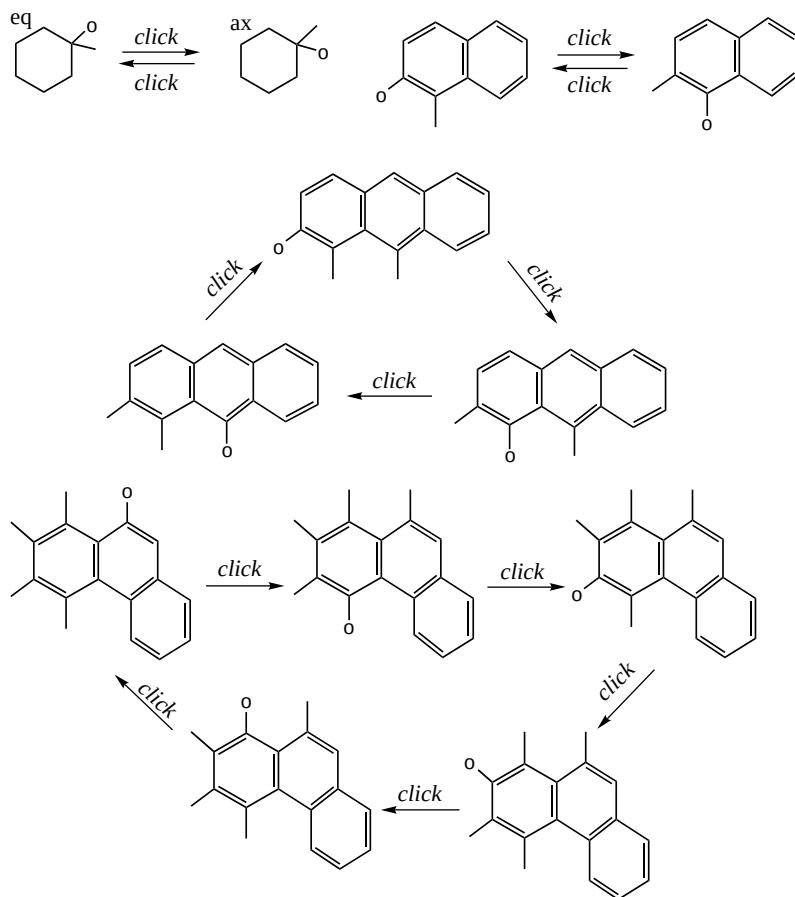
(ii) Rings

Clicking on the menu entry to the right of **Rings** accesses a menu of hydrocarbon rings.



Once selected, the name of the ring replaces the full menu, and its structure appears at the top of the model kit. This ring may then be used to initiate building (*clicking* anywhere on screen), to add alongside of an existing structure (*clicking* anywhere on screen while holding down on the **option** key), or to add to an existing structure (*clicking* on the tip of a free valence). Cyclohexane, naphthalene, anthracene and phenanthracene rings have different types of free valences. The free valence that will be used to connect these rings to the molecule is marked with an “o”, and circulates among the different positions with repeated *clicking* inside the icon display

area. Selection of an *axial* or *equatorial* free valence in cyclohexane is indicated by a label “ax” or “eq” appearing alongside the icon.



Note that all rings provided in this menu are hydrocarbons. Heteroatoms may be substituted using Spartan’s atom replacement features available in the organic and inorganic model kits (see **General Molecule Building Functionality** following).

(iii) Custom

This provides access to a molecule or molecule fragment that has been placed on the clipboard, via a **Cut** or **Copy** operation (**Edit** menu; see **Chapter 10**). Once selected, the molecule (or molecular fragment) will be displayed

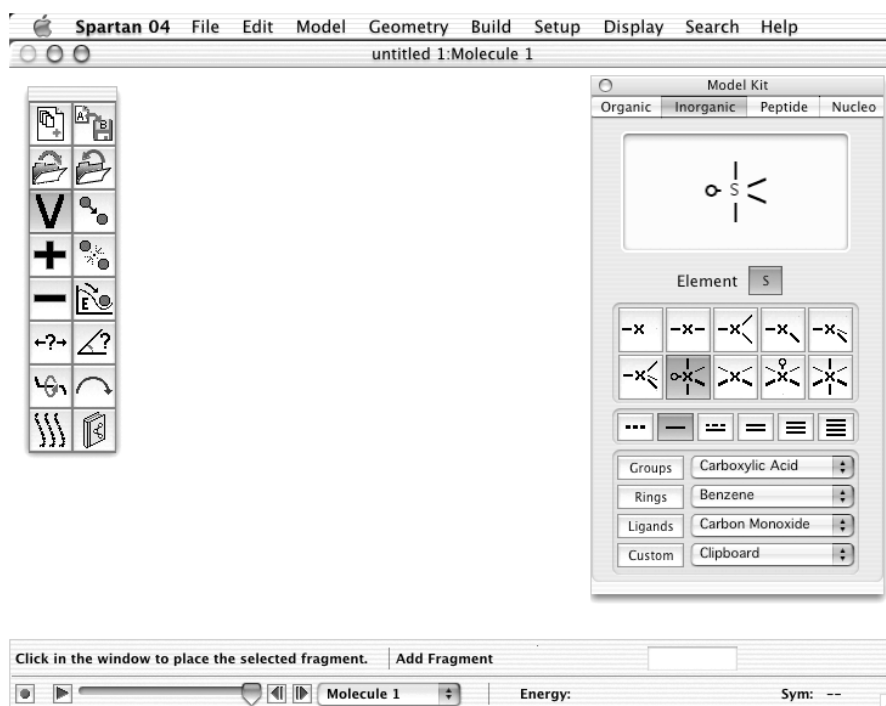


as a manipulatable model at the top of the model kit. It can be used to initiate building (*clicking* anywhere on screen), to add alongside of an existing structure on screen (*clicking* anywhere on screen while holding down on the **option** key), or to add to an existing structure (*clicking* on the tip of a free valence). In the last case, the attachment point can be selected by *clicking* on the appropriate free valence in the model (at the top of the model kit).

Four entries (current and three previous entries) may be stored on (and accessed from) the clipboard. Selection is from the menu to the right of **Custom** in the model kit.

Inorganic Model Kit

The inorganic model kit allows construction of a much wider class of molecules than permitted using the organic model kit. These include inorganic and organometallic species, as well as organic molecules that violate conventional bonding rules. Unlike the organic model kit, the inorganic model kit purposefully provides no valence checking. The inorganic model kit is reached by *clicking* on the **Inorganic** tab that is located at the top of the organic (or peptide or nucleotide) model kit. (Return to the organic, peptide or nucleotide model kit is accomplished by *clicking* on the **Organic**, **Peptide** or **Nucleotide** tab in the inorganic model kit.)



Near the top of the model kit to the right of “Element” is a box that displays the atomic symbol for an element. Other elements may be selected by positioning the cursor on this box and *pressing* the left button. This brings up a *Periodic Table*, in which elements are color coded according to type: hydrogen (grey), alkali and alkaline earth (yellow), main group (grey), transition metals (green), lanthanides (violet), actinides (blue) and noble gases (orange).

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	Ac															
Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu				
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr				

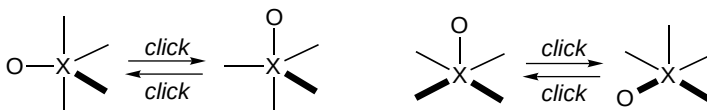
Element selection follows by moving the cursor while *pressing* the left button) over the desired element and then releasing the button. The *Periodic Table* disappears and the element symbol appears to the right of “Element”.

In the middle of the model kit is a listing of “atomic hybrids”. *Click* on one to select.

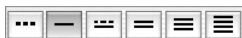


Selection of both element and atomic hybrid results in display of a structure at the top of the model kit. This may be used to initiate building (*clicking* anywhere on screen), to add alongside of an existing structure (*clicking* anywhere on screen while holding down on the **option** key), or to add to an existing structure (*clicking* on the tip of a free valence)

Two of the hybrids may bond either *axially* or *equatorially*. Selection of the appropriate bonding point, indicated by an open circle, is effected by repeatedly *clicking* on the icon.



All atoms are initially connected with single linkages. Bond types may be changed by first selecting (*clicking* on) the desired bond type,



and then *double clicking* on the appropriate bond. Bond types may also be changed from a contextual menu, by first positioning the cursor over the bond, then holding down either left or right button, and finally selecting a bond type from the menu that results.



Note that, no valence checking is performed in the inorganic model kit. The user is free to construct any arrangement of atoms. Note, that the molecular mechanics force field used for energy minimization



in the builder may not be “well parameterized” for all bond types, and caution is advised.

Three fragment collections are located inside the model kit. In addition, custom fragments may be accessed from the clipboard.

(i) **Groups**

This has already been described for the organic model kit.

(ii) **Rings**

This has already been described for the organic model kit.

(iii) **Ligands**

This provides access to a number of pre-built ligands, useful in the construction of inorganic and especially organometallic molecules. Its operation is analogous to that for the **Groups** and **Rings** menus. *Clicking* on the menu entry to the right of **Ligands** accesses a menu of groups.



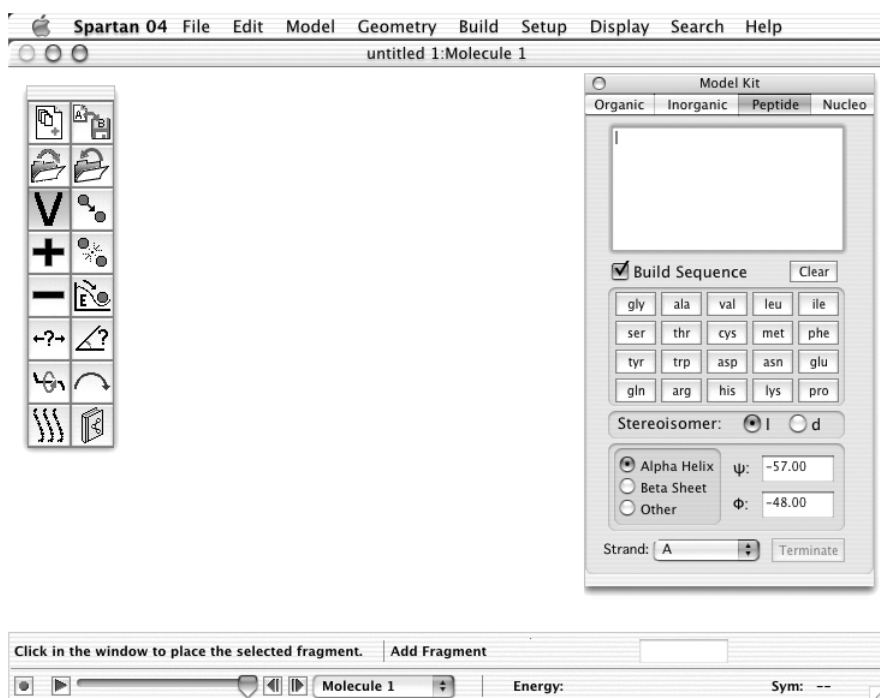
Once selected, the name of the selected ligand replaces the full menu, and a ligand icon appears to the right. This ligand may then be used to initiate building (*clicking* anywhere on screen), to add alongside of an existing structure on screen (*clicking* anywhere on screen while holding down on the **option** key), or to add an existing structure (*clicking* on the tip of a free valence).

(iv) **Custom**

This has already been described for the organic model kit.

Peptide Model Kit

Spartan provides a separate model kit for construction of polypeptides. It is reached by *clicking* on the **Peptide** tab that is located at the top of the organic and inorganic model kits. (Return to the organic, inorganic or nucleotide model kit is accomplished by *clicking* on the **Organic**, **Inorganic** or **Nucleotide** tabs, respectively, in the peptide model kit.)



At the middle of the peptide model kit is a listing of amino acids.

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

A box immediately above the codes displays an icon of the selected amino acid. Also, the name of the amino acid and its three-letter code are displayed. Amino acids replace “atoms”, functional groups, rings and ligands as the basic building blocks in the peptide model kit. Note, that most modifications of peptides, aside from modifications in amino acid sequence and in overall conformation, need to be carried out using the organic or inorganic model kits.



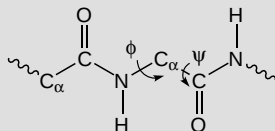
There are two different modes of operation: single amino acid mode and polypeptide mode. The former is used to initiate building with a single amino acid, to add a single amino acid alongside of an existing structure or to add a single amino acid to an existing structure, while the latter is used to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

Peptide construction 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 name and structure of the amino acid appears in the box above the codes, and the letter code appears as part of a string separated by “-” in a box below **Build Sequence**. 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. At any time, the sequence can be altered by changing the text in the box above **Build Sequence**. 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 nonexistent 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 is specified by *clicking* on one of **Alpha Helix**, **Beta Sheet** or **Other**. For the first two, preset angles are available. Specification of **Other**, requires that angles be entered into the boxes to the right of ψ and ϕ .

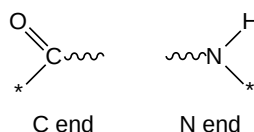


Dihedral angles ϕ and ψ are defined for each pair of amino acids according to the following diagram.

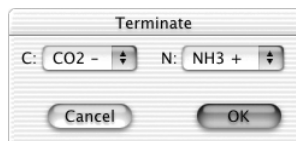


Certain combinations of ϕ and ψ lead to stable arrangements corresponding to helices and beta sheets. A plot of energy vs. ϕ and ψ is known as a Ramachandran plot.

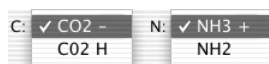
- (iii) Termination. The peptide (or single amino acid) is not yet terminated, and the two ends are still set up for addition of further amino acids, i.e.,



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



This incorporates two menus for specifying “C” and “N” terminating groups, respectively.



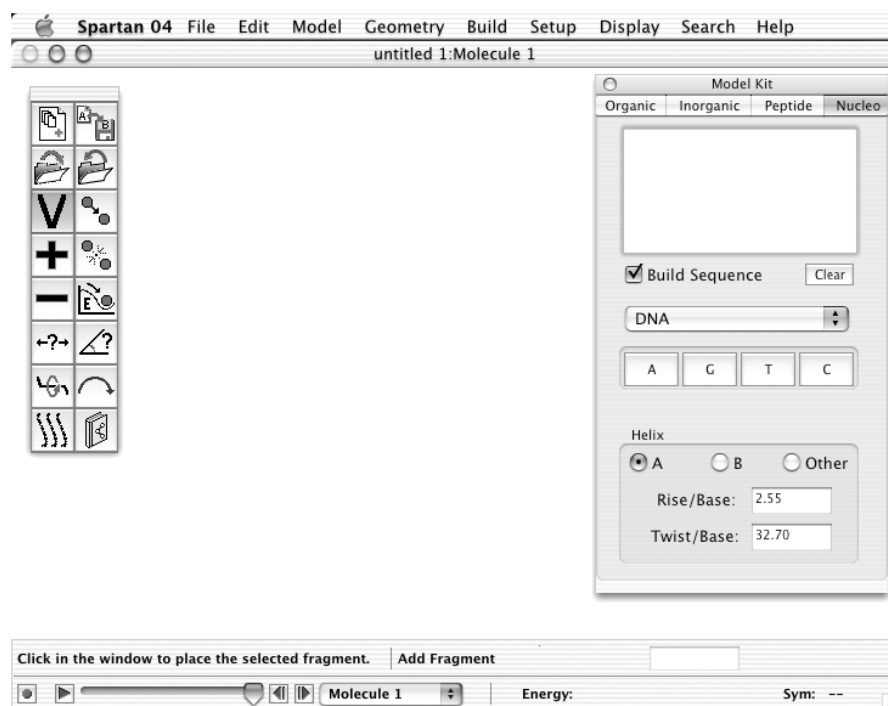
Select one entry from each and then *click* on **OK** to close the dialog and terminate the polypeptide. *Clicking* on **Cancel** exits the dialog without termination. Terminating groups can be elaborated as needed in the organic or inorganic model kits.



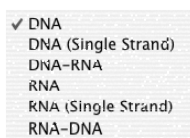
The peptide may be used either to initiate building, by *clicking* anywhere on screen, added alongside of an existing structure, by *clicking* anywhere on screen while holding down the **option** key, or to be joined onto an existing structure by *clicking* on a free valence. Attachment is made from the “N end”, unless the valence corresponds to an “unterminated” peptide fragment, in which case the end is that required to make an amide bond.

Nucleotide Model Kit

Finally, Spartan provides a model kit for construction of polynucleotides. It is reached by *clicking* on the **Nucleotide** tab that is located at the top of the organic, inorganic and peptide model kits. (Return to the organic, inorganic or peptide model kit is accomplished by *clicking* on the **Organic**, **Inorganic** or **Peptide** tab, respectively, in the nucleotide model kit.)



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



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, in which uracil (U) has been substituted for thymine (T).



Nucleotide bases replace “atoms”, functional groups, rings and ligands as the basic building blocks in the nucleotide model kit. Because these other building blocks are missing, most modifications of nucleotides, aside from modifications in base sequence and helical structure, need to be carried out using either the organic or inorganic model kits.

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

Polynucleotide construction is accomplished in two steps:

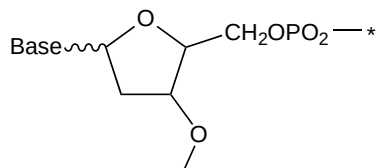
- i) Specification of base sequence. This is accomplished by *clicking* in order on the base codes. In response to each selection, the letter code appears as part of a string separated by “-” in a box below **Build Sequence**. The sequence can be altered by editing the contents of the box. Existing base 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 or B. These correspond to “standard” A and B helices, respectively. Selecting **Other** allows user modification of the rise (in Å) per base (**Rise/Base**) and twist (in degrees) per base (**Twist/Base**) for either A or B helices.

At this point, the polynucleotide can be placed on to a blank screen by *clicking* anywhere on screen, placed alongside of an existing structure by *clicking* on screen while holding down the **option** key, or joined onto an existing structure by *clicking* on a free valence. In the latter case, attachment is made from the “phosphate” end.

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).



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, ring, or ligand added to the molecule is automatically selected.)
- (ii) Simultaneously *pressing* the **spacebar** and the left mouse button while *dragging* the mouse, for bond rotation, or the **spacebar** 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 organic model kit or an atom icon in the inorganic model kit is highlighted, replaces this atom by the selected atom icon. Atom replacement functions differently in the organic and inorganic model kits. In the organic 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 inorganic 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 available in the peptide and nucleotide model kits.

Chirality Inversion

Double clicking on an atom while *pressing* the **Ctrl** key inverts the chirality ($\text{R} \rightarrow \text{S}$ or $\text{S} \rightarrow \text{R}$). This function is available in all model kits, but may not be used in some ring systems where unacceptable structures may result. 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 that actually alter molecular geometry are unavailable.

Initial entry into build mode is by way of **New** under the **File** menu (see **Chapter 9**). **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 (organic and inorganic model kits only). If a model kit is already on screen, *clicking* on an atomic fragment, atom, etc., icon, or on the **Groups**, **Rings**, **Ligands** or **Custom** button 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* anywhere on screen while holding down the **option** key, 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. Selection results in message at the bottom left of the screen.

Select an object to delete.

Subsequent *clicking* on an atom or a free valence results in this atom and all of its associated free valences or a free valence being removed. A miss will be signaled by a “beep”; try again. Free valences for any

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



atoms to which the deleted atom was connected are restored. Note that atom deletion may result in one or more detached fragments.

Delete may also be used to remove a point or plane, as well as curves and entire plots (see **Plots...** in **Chapter 15**), in addition to “reaction arrows” used to specify transition states (see **Transition States** in **Chapter 16**).

Deletion may be terminated by selecting any button or menu in the model kit, or by selecting any menu or icon in the main window.

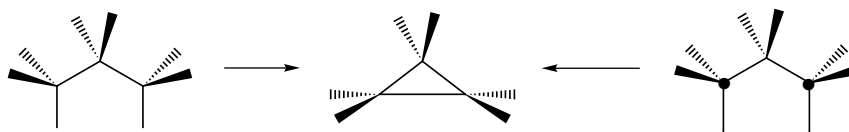
Make Bond

This allows free valences on different atoms to be bonded. Selection results in a message at the bottom left of the screen.

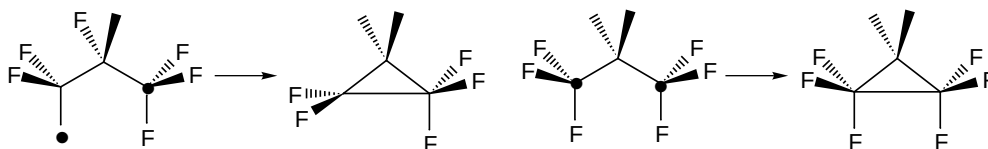
Select two unfilled valences to define bond.

Subsequent *clicking* on two free valences (on two different atoms) will cause these atoms to be linked by a single bond. Alternatively, *clicking* on each of two atoms will bond them, and *clicking* on a free valence on one atom and *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 attempt to bond an atom to itself will result in 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.





Note that free valences can be “consumed” (allowing construction of “hypervalent” arrangements) by adding hydrogens ( from the model kit) prior to bond formation.

Bond creation can be terminated by selecting any button, or menu in the model kit, or by selecting any menu or icon in the main window.

Break Bond

This allows breaking an existing bond resulting in one or more sets of 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 removal; the free valences on the respective atoms will automatically be restored. A miss will be signaled by a “beep”; try again. Note that bond deletion may result in detached fragments, which can either be manipulated in concert or independently of one another.

Bond deletion can be terminated by selecting any button or menu, in the model kit, or by selecting any menu or icon in the main window.

Minimize

The initial molecular geometry resulting from building may not be suitable, and it will generally be advantageous to perform preliminary structure refinement using molecular mechanics. The minimizer built into Spartan is based on the MMFF94 force field. This results in a refined structure, as well as the final mechanics strain energy and symmetry point group at the bottom of the screen. Minimization may be terminated at any time by *clicking* on **Stop** at the bottom right of the screen. Termination brings the program back into the previous mode.



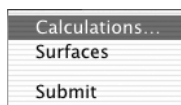
Chapter 14

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.*

*The **Setup** menu is also used to 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. Finally, the **Setup** menu is used to submit 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...

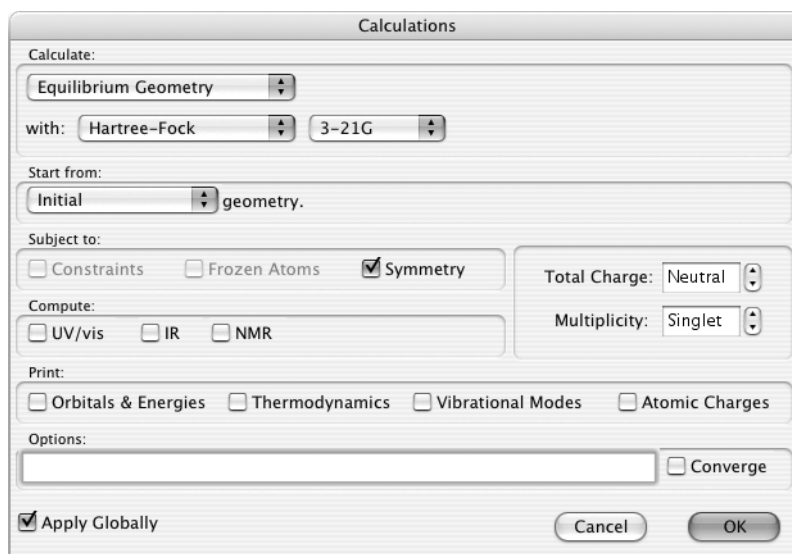
Calculations modules perform: molecular mechanics calculations using the SYBYL and MMFF force fields; MNDO (MNDO/d where second-row and heavier elements are involved), AM1 and PM3 semi-empirical calculations, including PM3 calculations on transition-metal inorganic and organometallic systems; Hartree-Fock 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 Macintosh 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 for Macintosh 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.

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



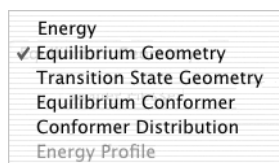
This contains a number of pull-down menus, checkboxes and text boxes:

(i) **Calculate**

This section contains a series of menus and checkboxes 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:

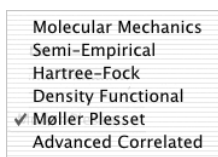




Energy applies to all methods. **Equilibrium Geometry**, **Equilibrium Conformer**, **Conformer Distribution** and **Energy Profile** apply to all methods except MP3, MP4, CCSD, CCSD(T), G3, G3(MP2), CIS(D) and related high-order correlated methods. **Transition State Geometry** applies to all methods except molecular mechanics methods and MP3, MP4, CCSD, CCSD(T), G3, G3(MP2), CIS(D) and related high-order correlated methods. Additionally, MP2 methods based on localized orbitals are available for energy calculations only, and the MMFFaq method (MMFF corrected for solvent using the SM50R model) is available only for equilibrium conformer and conformer distribution only (it provides only energy and not geometry corrections).

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 correlation 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, although they are presently limited to energy calculations only for excited states. **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:



For excited-state species:

Density Functional
✓ Config. Interaction

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

Molecular Mechanics

✓ MMFF
SYBYL
MMFFaq

Semi-Empirical

✓ AM1
PM3
MNDO

Density Functional

BP
BLYP
EDF1
✓ B3LYP
LOCAL

Møller-Plesset

✓ MP2
MP3
MP4

Advanced Correlated*

✓ CCSD
CCSD(T)
G3
G3(MP2)

Configuration Interaction

✓ CIS
CIS(D)

Either restricted or unrestricted SCF 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 semi-empirical methods, a basis set needs to be specified.*** For Hartree-Fock methods:

-
- * A number of other advanced correlated methods are available, and may be requested from the **Options** box: CCSD(2), OD, OD(T), QCCD, QCCD(2), QCISD, QCISD (T) and G2.
- ** Only unrestricted methods are presently available for Møller-Plesset and advanced correlated calculations on systems with unpaired electrons.
- *** A number of other basis sets are available, and may be requested from 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, are with “+” or “++” inserted before G; cc-pVDZ and cc-pVQZ.



STO-3G
✓ 3-21G
6-31G*
6-31G**
6-31+G*
6-311G*
6-311+G**

3-21G refers to use of the 3-21G basis set 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 simply “**model**”. The nomenclature adopted here 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 referred to as 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 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. **Density** 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, consult on-line help (**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 required, to compute the IR spectrum prior to calculation of an intrinsic reaction coordinate.) The full sequence of steps: reactant → transition state → product,

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



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.

(ii) **Start from**

Calculations using one model may be preceded by equilibrium geometry calculations using another model. (This feature does not apply to transition-state geometry calculations.) Choices depend on the model selected:

molecular mechanics

✓ Initial
MMFF Conformer
MMFFaq Conformer

semi-empirical

✓ Initial
MMFF
MMFF Conformer
MMFFaq Conformer

Hartree-Fock

✓ Initial
MMFF
AM1
PM3
MMFF Conformer
MMFFaq Conformer

density functional, Møller-Plesset,
advanced correlated

✓ Initial
MMFF
AM1
PM3
3-21G
6-31G*
MMFF Conformer
MMFFaq Conformer

In addition, geometry optimization may be preceded by a search for the lowest-energy MMFF or MMFFaq conformer. Selection of either leads to an additional menu specifying the model to be employed for geometry optimization:

molecular mechanics

not available

semi-empirical

not available

Hartree-Fock

☒ MMFF
☐ AM1
☐ PM3

density functional, Møller-Plesset,
advanced correlated

☒ MMFF
☐ AM1
☐ PM3
☒ 3-21G

(iii) **Subject to**

Spartan allows calculations to be carried out in the presence of geometrical constraints or with atoms which have been frozen in place. In addition, the program 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 energy calculations. See **Chapter 12** for information about constraining geometrical parameters. **Constraints** is available (highlighted) only if geometrical constraints have previously been specified. By default, **Constraints** is *unchecked*.

NOE data are not treated as constraints during optimization, but rather as “post-calculation filters” in establishing conformer distributions. They will be used wherever specified irrespective of whether or not **Constraints** is *checked*.

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 energy calculations. See **Chapter 12** for information about freezing atoms. **Frozen Atoms** is available (highlighted) only if frozen atoms have previously been specified. By default, **Frozen Atoms** is *unchecked*.



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 spectral quantities. Other quantities such as the dipole moment and LogP* that are “less costly” are calculated automatically, whereas calculation of still others may be requested from the **Options** box (see discussion following).

UV/vis

If *checked*, specifies that an excited-state energy calculation will be performed (following a ground-state calculation) and that state-to-state energy differences will be reported. A UV/visible spectrum may be displayed from the **UV/vis** dialog accessible from **Spectra** under the **Display** menu (see **Chapter 15**).

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).

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

* 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 15**).



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 15**).

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 15**) as well as from the **Atom Properties** dialog (**Display** menu). ^{13}C (proton decoupled) and ^1H (shifts only) spectra may be displayed from the **NMR** dialog accessible from **Spectra** under the **Display** menu (see **Chapter 15**). 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 molecular charge. The default setting **Neutral** may be changed either by *clicking* on  to the right of the box, and selecting **Anion**, **Dianion**, **-3**, etc. and **Cation**, **Dication**, **3**, etc., respectively, from the menu which appears, or by replacing any menu entry by a numerical value. **Total Charge** is ignored for molecular mechanics calculations.

* 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.



(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. The numerical value of multiplicity corresponds to the number of unpaired electrons +1: 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 discussion following). By default, all entries are *unchecked*.

Orbitals & Energies

If *checked*, writes the molecular orbitals and orbital energies to the output. Note, that HOMO and LUMO energies are also available from the **Molecule Properties** dialog under the **Display** menu (see **Chapter 15**), as well as in the spreadsheet (see **Chapter 15**).

Thermodynamics

If *checked*, writes thermodynamic quantities to the output. Requires that vibrational frequencies have been calculated. Selected thermodynamic quantities are also available in the spreadsheet (see **Chapter 15**).

Vibrational Modes

If *checked*, writes vibrational frequencies and normal modes to the output. Requires that vibrational frequencies have been calculated.

Atomic Charges

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



(viii) **Options**

Additional computational methods and/or 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.

(ix) **Converge**

If *checked*, invokes procedures to assist in convergence. Use of **Converge** will generally increase computation time, and it should be selected only in response to experiencing convergence difficulties. **Converge** does not apply to molecular mechanics calculations. By default, **Converge** is *unchecked*.

(x) **Apply Globally**

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

The **Calculations** dialog may be exited by *clicking* on **Cancel** or **OK** at the bottom right of the dialog. (**OK** will be deactivated if the job is already executing.) *Clicking* on **OK** overwrites any previous information. *Clicking* on **Cancel** exits the **Calculations** dialog without saving any changes.

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



The **Task** menu is the same but the **Type of Calculation** menu is restricted to molecular mechanics, semi-empirical and Hartree-Fock models. There is no **State** menu.



Molecular Mechanics
Semi-Empirical
Hartree-Fock

The **Basis Set** menu (Hartree-Fock models only) is identical. Pseudopotentials are not available. Additionally, intrinsic reaction coordinate (**IRC**) 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 for Macintosh provides for graphical display of the molecular orbitals, the electron density, the spin density (the difference in electron densities arising from the α and β spin manifolds) for open-shell systems, 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 removed 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 14-1**. Surfaces (like other graphical objects) may also be rendered in perspective (see **Chapter 11**) and in stereo (see **Chapter 2**).

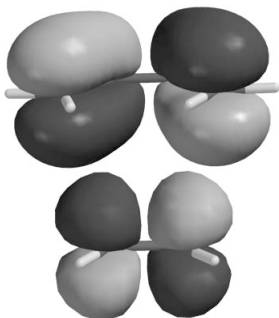
Additionally, any one of the quantities listed above (except the electron density) may be mapped onto any surface (except a molecular orbital surface). For example, the electrostatic potential may be mapped onto a surface of electron density, yielding an electrostatic potential map, that portrays both 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.

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 14-1**.



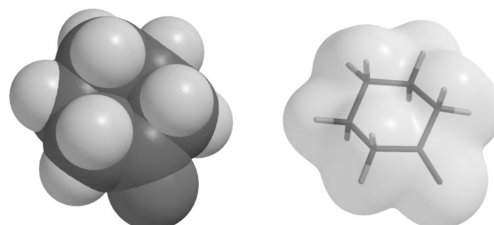
Figure 14-1: Examples of Graphical Displays Available in Spartan

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



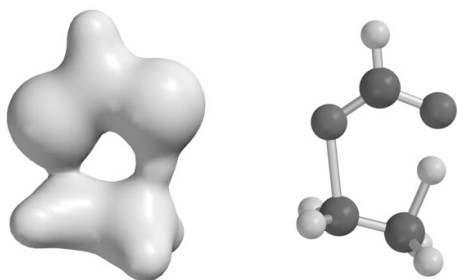
showing interaction of the HOMO of 1,3-butadiene and the LUMO of ethylene.

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



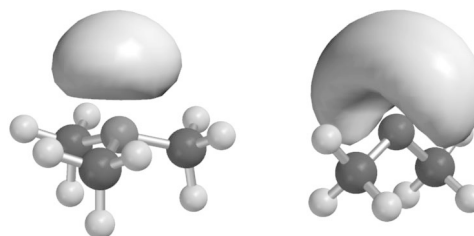
showing overall molecular size and shape.

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



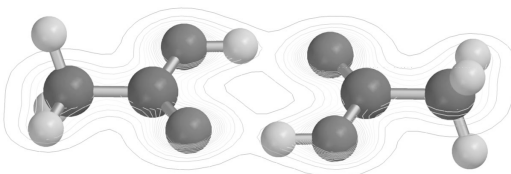
showing bonding in the transition state.

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



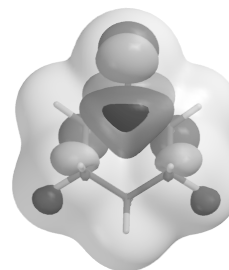
showing the lone pairs on nitrogen and oxygen, respectively.

Electron density slice for acetic acid dimer,



showing hydrogen bonding.

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

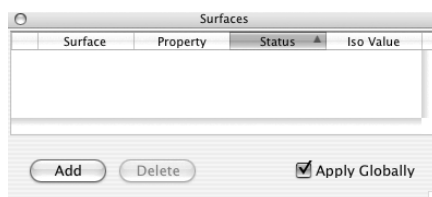


showing accessibility for nucleophilic attack.

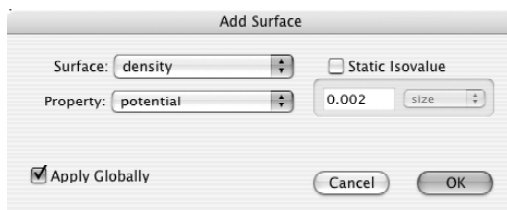
Several different surfaces, maps and slices may be simultaneously displayed. This allows visual comparison of different surfaces, of different properties or both. In addition, any of the usual structure representations (skeletal, ball-and-stick, tube, ball-and-spoke and space-filling models) may be displayed 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 is provided in “***A Guide to Molecular Mechanics and Quantum Chemical Calculations***”.

Selection of **Surfaces** results in the following dialog.

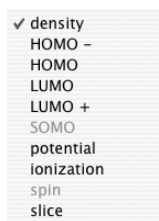


The box at the top of the dialog is used to identify graphical surfaces for later calculation and display. The **Add** button at the bottom of the dialog is used to specify new graphical surfaces. *Clicking* on it leads to the **Add Surface** dialog.



(i) **Surface**

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



Available surfaces 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**). Selection of two of the entries, “**HOMO-**” and “**LUMO+**”, results in display of a box alongside of the entry, e.g.

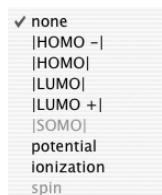


This contains a decrement value from the HOMO and increment value from the LUMO. Default values (-1 for HOMO and +1 for LUMO) may be changed, meaning that any molecular orbital may be specified. Numbers may also be directly entered.

Slice designates 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 absolute value of 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.



Alpha and **Beta** buttons will be displayed if **Multiplicity** (**Calculations** dialog) is not **Singlet**, or if the **Scf** keyword has been set to **unrestricted** (**Options** in the **Calculations** dialog; see **Appendix C**), and is available (highlighted) only if **HOMO-**, **HOMO**, **LUMO** or **LUMO+** has been selected for **Surface** or for **Property**. **Alpha** and **Beta** designate that the molecular orbital either to be displayed as a surface or mapped onto a surface will come from the α and β spin manifolds, respectively. *Clicking* on **Alpha** turns it “on” and turns **Beta** “off” and vice versa.

(iii) **Static Isovalue**

If *checked*, signifies that a single isosurface (or a property map based on a single isosurface) is to be calculated, rather than a series of data values from which different isosurfaces may be constructed. “Static Isovalue” mode offers significant computation and storage savings, in particular, for electrostatic potential maps. By default, **Static Isovalue** is *unchecked*.

Entries following **Static Isovalue** depend on the surface.

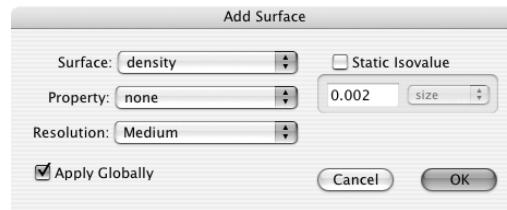
surface	menu entry	isovalue
density	size	0.002 electrons/au ³
	bond	0.080 electrons/au ³
	custom	>0
HOMO, HOMO-, LUMO, LUMO+	default	0.032
	custom	>0
spin	default	0.002 electrons/au ³
	custom	>0
potential	-20	-20 kcal/mol
	-10	-10 kcal/mol
	-5	-5 kcal/mol
	custom	any value



(iv) **Apply Globally**

If *checked*, signifies that the requested surfaces will be calculated for all members of the list. By default, **Apply Globally** is *checked*.

An extended **Add Surface** dialog appears if the **option** key is held down while selecting **Add** from the **Surfaces** dialog.



This incorporates an additional menu that allows for selection of surface resolution.



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

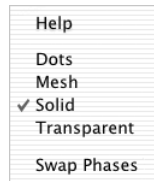
Following surface, property and (optionally) spin and resolution selection, *clicking* on **OK** adds the requested graphic to the list and removes the **Add Surface** dialog. *Clicking* on **Cancel** does not add a graphic to the list but removes the **Add Surface** dialog. This process may be repeated as required. An existing graphic may be deleted by first *clicking* on its entry in the list and then *clicking* on **Delete**.

The **Surfaces** dialog is also used to display calculated graphics. To display a graphic, *click* inside the box to the left of its surface designation in the **Surfaces** dialog. Alternatively, *double click* on the line describing the surface. A check mark will appear inside the box. To remove a displayed graphic, *click* again inside the box (or *double click* on the line). The checkmark will disappear.

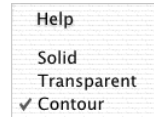


The property in a property map may be turned “on” and “off” using the **Surface Properties** dialog (see **Properties** in **Chapter 15**).

Surfaces and property maps will initially be displayed as opaque solids. A contextual menu may be used to select another display style (a series of dots, a mesh or a transparent solid). Position the cursor over the graphic, and hold down either the left or right button. Select the appropriate entry from the menu that appears immediately below the cursor, and release the button.



Slices will initially be displayed as a series of contours. A contextual menu may be used to select another display style (a solid or transparent series of “fringes”). Position the cursor over the frame bounding the slice and hold down either the left or right button. Select an appropriate entry from the menu which appears immediately below the cursor, and release the button.

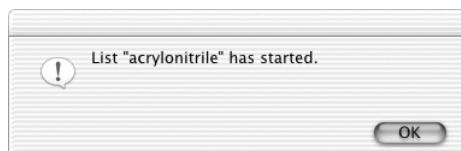


Surface, property map and slice styles may also be changed using the **Surface Properties** dialog (see **Properties** in **Chapter 15**).

Only one copy of the **Surfaces** dialog may appear on screen and its contents and any actions refer to the currently selected model.

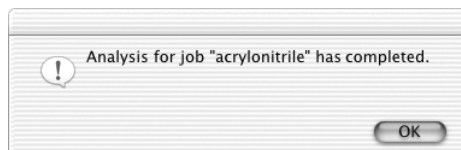
Submit

Following specification of a molecular mechanics or quantum chemical calculation, and/or request for graphics, the required calculations need to be requested using **Submit**. If the job has not previously been named, selection of **Submit** triggers a request for a name* (see **Save As** in **Chapter 9**). After a name has been provided, a dialog appears indicating that the job has been submitted.



Click on **OK** to remove it. After a job has started, and until it has completed, all associated files will be designated “read only”. You can “follow” the job from the **Output** window (see **Output** in **Chapter 15**) or from the **Monitor** (see **Spartan Monitor** in **Chapter 8**).

Another dialog appears following completion of a calculation.



Click on **OK** to remove it.

* If the molecule is in the Spartan Molecular Database, its name will be suggested as a possible file name.

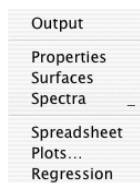


Chapter 15

The Display Menu

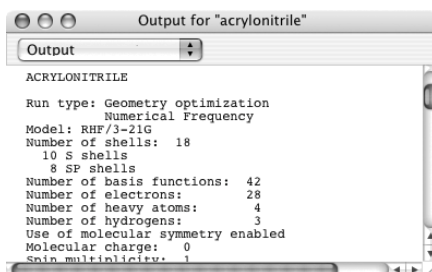
*This chapter describes functions available under the **Display** menu. These provide for spreadsheet, text and graphical displays following molecular mechanics or quantum chemical calculations, as well as for regression analysis on tabulated data.*

Selection of **Display** leads to the following menu.



Output

Selection of **Output** opens a window.



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



Output provides normal output for the selected molecule and **List Output** provides an overview of execution status for all jobs in the list. The window can be *scrolled* in the usual manner. The contents of the **Output** window (only) are automatically updated during execution, making it possible to monitor a job in progress.



Text in the **Output** window may be brought onto the clipboard using **Copy** (see **Chapter 10**).

Selection of **Output** while holding down on the **option** key leads to a dialog with more output choices.



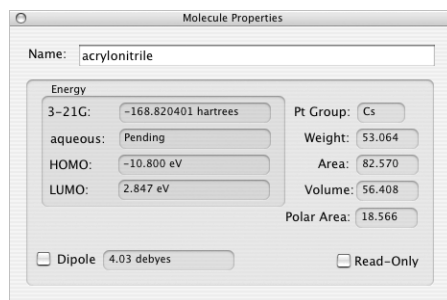
Verbose Output provides additional details for calculations. It is often of value in tracing execution errors. **Archive** and **Property Archive** contain a listing of quantities generated during the calculations.

Properties

Dialogs are available 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. Only one “properties” dialog may appear on screen and its contents and any actions refer to the currently selected attribute of the currently selected molecule.

(i) Molecule Properties

Unless an atom, bond, surface, constraint, plot axis or curve has previously been selected, selection of **Properties** leads to the **Molecule Properties** dialog.

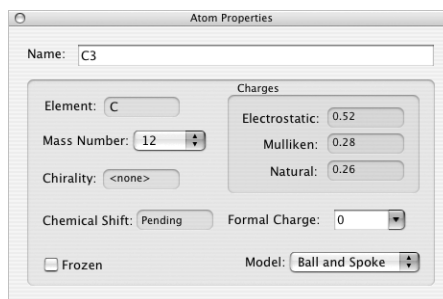


This displays total energy (in au), heat of formation in the case of a semi-empirical calculation (in kcal/mol), or

strain energy in the case of a molecular mechanics calculation (in kJ/mol), aqueous phase energy (the sum of the gas-phase total energy, heat of formation or strain energy and the solvation energy, and in same units as the gas-phase quantities), HOMO and LUMO energies (in eV), dipole moment (in debyes), molecular weight (in amu), surface area, polar surface area (area taken up by nitrogen, oxygen and any attached hydrogens) and volume of a space-filling model (in Å², Å², and Å³, respectively) and point group. The dialog also allows for changing the default molecule name that is given in the text output.

(ii) **Atom Properties**

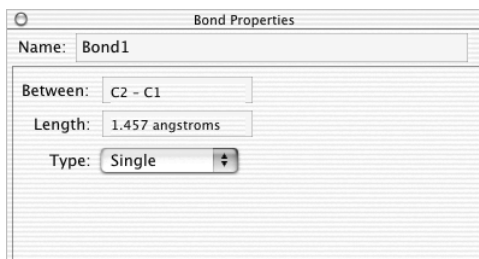
Selection of an atom with a “properties” dialog on screen, or selection of **Properties** following selection of an atom, leads to the **Atom Properties** dialog.



This displays the element symbol and allows for changing element as well as the mass number. To change element, *click* inside the box and select from the *Periodic Table*. It also displays R/S chirality, and Mulliken, electrostatic-fit and natural charges (in electrons), the NMR chemical shift (in ppm relative to an appropriate standard; see **Appendix E**) and allows for freezing the atom. The dialog allows for setting formal charges and for changing the default atom name, which is used as a label. This is important for molecule alignment (see **Align Molecules** in **Chapter 12**). Finally, the dialog allows changing the model.

(iii) Bond Properties

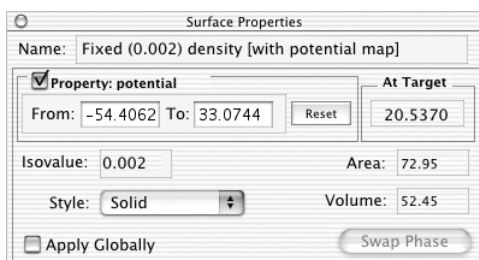
Selection of a bond with a “properties” dialog on screen, or selection of **Properties** following selection of a bond, leads the **Bond Properties** dialog.



This displays the labels for the two atoms involved in the bond as well as the bond length (in Å). It also provides for changing bond type (see **Inorganic Model Kit** in **Chapter 13**) and the default bond name.

(iv) Surface Properties

Selection of graphical surfaces (isosurface or slice) with a “properties” dialog on screen, or selection of **Properties** following selection of a graphical surface, leads to the **Surface Properties** dialog.

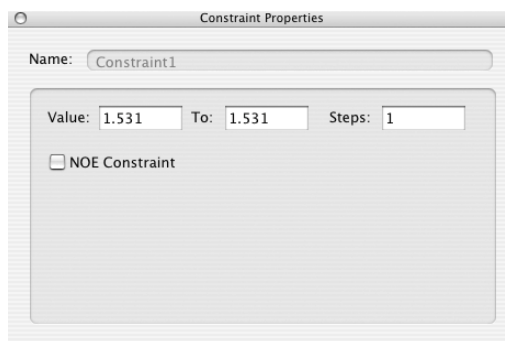


This displays the area (in Å²) and volume (in Å³) of the selected surface. It also allows for turning “on” and “off” and setting the range of a property map, for changing the isovalue except where **Static Isovvalue** has been specified (see **Surfaces** in **Chapter 14**), for altering display style, and (in the case of molecular orbital surfaces) for

swapping the phase. Finally, it reports the property value at the cursor position on a property map.

(v) **Constraint Properties**

Selection of a constraint vector with a “properties” dialog on screen, or selection of **Properties** following selection of a constraint marker, leads to the **Constraint Properties** dialog.



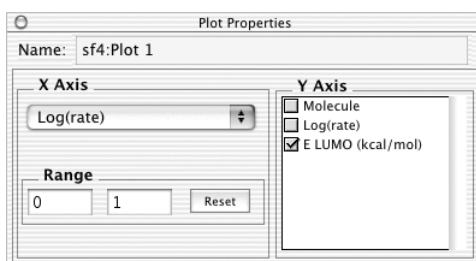
This allows setting the value of the constraint, designating the constraint as an NOE constraint and changing the default constraint name. To set a constraint value, type into the box to the right of “Value:”. To designate the constraint as an NOE, *check* the box to the left of “NOE”.

The dialog also allows specification of a series of constraints to generate an energy profile (see **Calculations...** in **Chapter 14**). The starting value of the constraint is given in the box to the right of “Value”, and the ending value of the constraint is given in the box to the right of “To”. The number of members in the series is given in the box to the right of “Steps”. Upon initial entry, the number in the box to the right of “To” will be set to the number to the right of “Value”, and “Steps” will be set to **1** (1 step). These may be altered as required by typing the desired numbers into the appropriate boxes. Note, that a series 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.

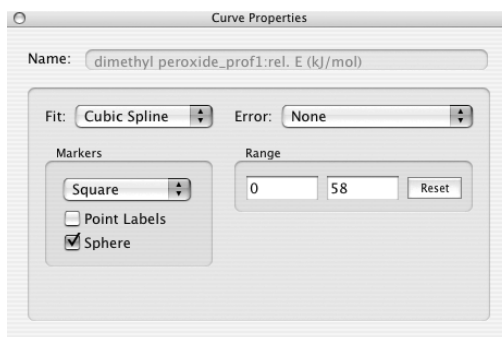
(vi) **Plot Properties and Curve Properties**

Plots created using data in the spreadsheet may be edited using controls in these two closely-related dialogs. With a plot on screen, selecting **Properties** followed by *clicking* on the plot frame, leads to the **Plot Properties** dialog.



The **X Axis** menu and the “Y Axis” list duplicate functionality under the **Add Plot** dialog (see discussion later in this chapter). They allow for specification of a molecular property to serve as the X axis of the plot and one or more properties to serve as the Y axis of the plot. 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 Axis” list). In addition, the default range for the X axis (from the minimum to the maximum value of the property) may be altered by changing the values inside the boxes underneath “Range”. Any of these adjustments have an immediate effect on the displayed plot.

Clicking on an individual curve in the plot leads to the **Curve Properties** dialog.



This allows for changing the presentation format for the selected curve. This includes designation of the kind of “Markers” for the individual data points, request for “Point Labels” (molecule names associated with the data points), and designation of the kind of “Fit” to the data points. 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 in the spreadsheet) and for adjusting the “Range” of values of the data.

Surfaces

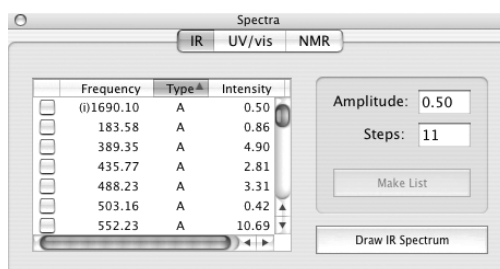
This has already been described in **Chapter 14**.

Spectra

Spartan’04 for Macintosh 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 14**.) Access is via a series of tabbed dialogs under **Spectra**.

IR

Clicking on the **IR** tab leads to the **IR Spectra** dialog that 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.



The dialog contains an ordered (smallest frequency first) listing of frequencies (in cm^{-1}) together with their symmetry labels and intensities. Imaginary frequencies, e.g., corresponding to the reaction coordinate for a transition state, will appear first in the list, and will be indicated as such at the right of the frequency. A frequency is selected for animated display by *clicking* on the box to the left of its value (or by *double clicking* on the value). *Clicking* again on the box or *double clicking* on the value deselects it. Only one vibration at a time may be selected (animated).

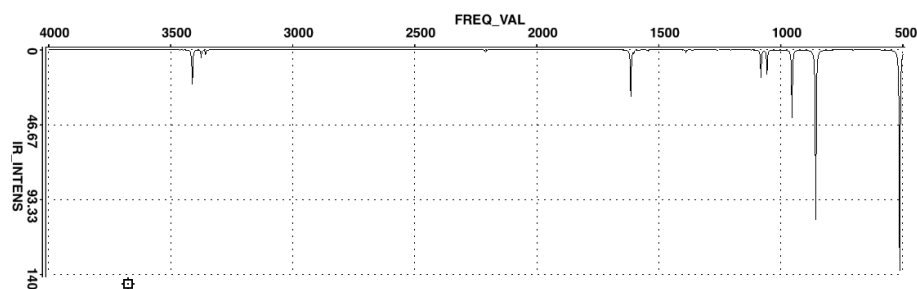
The amplitude of vibrational motion may be changed from the default amplitude (0.5Å that is much larger than appropriate for vibrational motion at room temperature) by altering the contents of the box to the right of “Amplitude” and *pressing* the **return** key. The default number of steps (11 frames) may be changed by altering the contents of the box to the right of “Steps” and *pressing* the **return** key.* The greater the number of frames, the slower will animation occur. Additional control of animation speed is provided under **General Preferences** in the **Spartan** menu (see **Chapter 8**).

Make List at the bottom of the dialog creates a list containing a sequence of structures corresponding to motion along the selected vibrational mode. The amplitude of the motion and the number of “steps” in the sequence are specified (prior to selecting **Make List**) by the entries in the boxes to the right of “Amplitude” and “Steps”, respectively. The original molecule is not closed, so that several sequences (corresponding to different vibrations) can be created.

* It is recommended that the number of steps be odd ensuring that the center point corresponds to the actual equilibrium or transition-state structure.



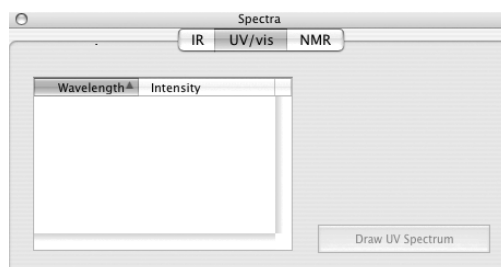
A spectrum may be drawn by *clicking* on **Draw IR Spectrum**.



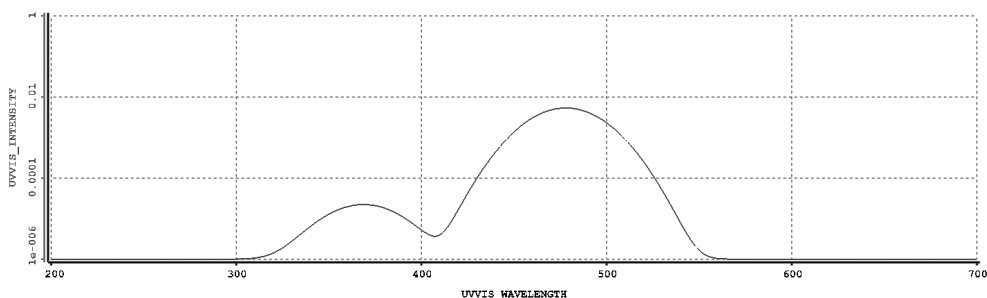
The default range, from 4000 cm^{-1} to 500 cm^{-1} , corresponds to that commonly obtained experimentally, and may be changed by bringing up the **Properties** dialog (**Display** menu), *clicking* on the horizontal axis to bring up the **Plot Properties** dialog and editing the values under **Range**. 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  and then *clicking* on the spectrum.

UV/vis

Clicking on the **UV/vis** tab leads to the **UV/vis Spectra** dialog.



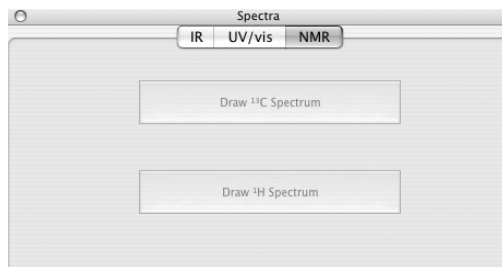
This lists excitation energies (from lowest to highest) together with intensities. A UV/visible spectrum may be drawn by *clicking* on **Draw UV Spectrum**.



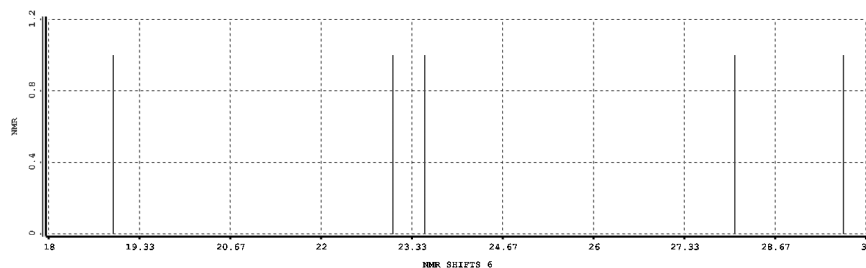
The default range, from 200 nm to 700 nm, corresponds to that commonly obtained experimentally, and may be changed by bringing up the **Properties** dialog (**Display** menu), *clicking* on the horizontal axis to bring up the **Plot Properties** dialog and editing the values under **Range**. The spectrum 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  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 ^{13}C Spectrum/Draw ^1H Spectrum** inside the dialog.





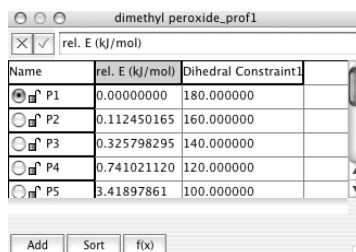
The default range may be changed by bringing up the **Properties** dialog (**Display** menu), *clicking* on the horizontal axis to bring up the **Plot Properties** dialog and editing the values under **Range**.

^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  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**.



Name	rel. E (kJ/mol)	Dihedral Constraint1
P1	0.0000000	180.000000
P2	0.112450165	160.000000
P3	0.325798295	140.000000
P4	0.741021120	120.000000
P5	3.41897861	100.000000

The resulting (spreadsheet) dialog comprises a series of “cells” made by the intersection of rows (corresponding to the different molecules in the list) and columns (corresponding to different molecular properties). The spreadsheet can be expanded or contracted as required for display of all relevant information by positioning the cursor on  at the lower right corner of the spreadsheet, *pressing* either the left or right button and moving the mouse.

The default molecule name in the leftmost column of the spreadsheet may be replaced by *clicking* inside the appropriate cell, typing a new name in the text box at the top of the spreadsheet and *pressing* the **return** key.

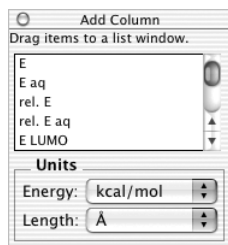


Molecule selection follows either by *clicking* on the button at the right of the spreadsheet cell containing the molecule name, or by using the  and  keys or the scroll bar at the bottom left of the screen. Molecule selection results in deselection of the previously selected molecule.

By default, only a single molecule from a list (the “selected” molecule) will be displayed on screen. However, several molecules from a list may be displayed at once and may be manipulated either independently or in concert (see **Coupled** in **Chapter 11**). Multiple display mode is specified by *clicking* on  at the bottom left corner of the screen (it will turn to ). In this mode, a molecule is designated for display by *checking* the box immediately to the left of its name 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”).

Upon initial entry, all columns in the spreadsheet are blank, except the leftmost column which contains the “name” of the molecule. Data may be entered in one of several ways:

- (i) Molecular properties from the **Add Column** dialog. A number of “important” molecular properties may be easily entered into the spreadsheet by *clicking* on **Add** at the bottom of the spreadsheet. This leads to the **Add Column** dialog.



Columns (molecular properties) are added by *dragging* (moving the mouse while holding down on the left mouse button) them in turn from this dialog into the spreadsheet. Note that “Energy” and “Length” units need to be specified.

* Note, that check boxes () replace buttons () in the spreadsheet when “multiple molecule mode” is selected in place of “single molecule mode”.



A subset of the quantities available in the **Add Column** dialog may also be added via a contextual menu. To access, *click* on the column header, select **Add Column** from the menu that appears and then the desired quantity from the sub menu. Note that energy and length units are those previously set in the **Add Column** dialog.

- (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 the column header, type a name in the box at the top of the spreadsheet and either *press* the **return** key or *click* inside the ☒ box at the top left of the spreadsheet (*Clicking* inside the ☐ box at the top left of the spreadsheet cancels the entry.) To enter data, first select (*click* on) an individual spreadsheet cell, then type into the box at the top of the spreadsheet, and finally either *press* the **return** key or *click* inside the ☒ box.
- (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 take the form “name=formula”, where “formula” is made up of arithmetic operations (**Table 15-1**), specialty functions (**Table 15-2**), quantities resulting from molecular mechanics or quantum chemical calculations (**Table 15-3**), conversion factors and constants (**Table 15-4**) 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* the **return** key following entry of the expression into a cell. Examples of user-defined expressions are provided in **Table 15-5**.



Table 15-1: Arithmetic and Boolean Operations and Mathematical Functions

arithmetic operations + addition - subtraction * multiplication / division ^ raise to a power	boolean operations > greater than >= greater than or equal to < less than <= less than or equal to == equal to != not equal to or & and
mathematical functions ABS(x) absolute value ACOS(x) inverse cosine ASIN(x) inverse sine ATAN(x) inverse tangent COS(x) cosine EXP(x) exponential LN(x) natural logarithm LOG(x) log (base 10) SIN(x) sine SQRT(x) square root TAN(x) tangent	

Table 15-2: Specialty Functions

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



Table 15-3: 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 ($\text{\AA}^2$)
CPKVOLUME	volume of a space-filling model ($\text{\AA}^3$)
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) ($\text{\AA}^2$)
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 ($\text{\AA}^3$)
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 ($\text{\AA}$)
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 (eV)
HOMOBETA(-n)	energy of the n^{th} orbital below the HOMO in the β spin manifold (eV)
ISOTOPE(i)	mass number of atom i
LENGTH (i)	length of bond i ($\text{\AA}$)
LOGPC	LogP from Crippen model
LOGPV	LogP from Villar model
LUMO(+n)	energy of the n^{th} orbital above the LUMO (eV)
LUMOBETA(+n)	energy of the n^{th} orbital above the LUMO in the β spin manifold (eV)
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 15-4: 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 15-5: User Defined Expressions

$E/\text{area} = @ENERGY/@AREA$	energy divided by surface area
$RelE = @ENERGY - @REF(6, @ENERGY)$	energy relative to energy of molecule in row 6
$E_q = @EXP(-@ENERGY/592.1)$	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



- (iv) Molecular and atomic properties by *dragging* into the spreadsheet. A number of properties that require user specification may be *dragged* into the spreadsheet. These include bond distances, angles and dihedral angles (available from **Measure Distance**, **Measure Angle** and **Measure Dihedral** under the **Geometry** menu; see discussion in **Chapter 12**), and atomic charges (available from the **Atom Properties** dialog; see discussion earlier in this chapter). The user first needs to select the function, e.g., **Measure Distance**, then the specific quantity, e.g., the distance between atoms C1 and C2, and then *drag* the label at the bottom of the screen, e.g., **Distance C1-C2**, into the spreadsheet. This action generates an entire column of values based on atom labels for the selected molecule in the list. Only 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 this action likely to lead to the desired result.

Columns may be deleted from the spreadsheet by first *clicking* on the column header and then selecting **Clear** from the **Edit** menu. Column deletion is also available from a contextual menu. *Click* inside the header cell of the column to be deleted and select **Delete Column** from the menu that results.

As each row in a spreadsheet corresponds to a molecule in a list, 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 9**), or by appending one or more existing molecules (**Append Molecule(s)...** from the **File** menu; **Chapter 9**). Additionally, one or more molecules can be *dragged* from one spreadsheet onto another (see **List-to-List Operations** in **Chapter 2**). In this mode, the **shift** (range selection) and **⌘** (multiple selection) keys operate in the usual manner.

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



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 (see **Chapter 9**), or by first *clicking* on the molecule name in the spreadsheet (leftmost column) and then selecting **Clear** from the **Edit** menu (see **Chapter 10**). Here, too the **shift** and **⌘** keys function in the usual manner.

Rows in the spreadsheet may be sorted according to the numerical values in any column by first *clicking* on the column header and then *clicking* on **Sort** at the bottom of the spreadsheet. The rows are placed in ascending order, smallest (least positive) value at the top, largest (most positive) value at the bottom. To sort in descending order, hold down the **option** key and *click* on **Sort**. **Sort** is also available from a contextual menu. *Click* on a column header and select **Sort** from the menu that results.

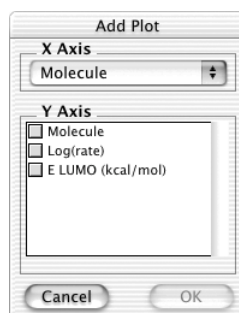
Totals and averages of column values may be obtained by first *clicking* on **Add** at the bottom of the spreadsheet, and *dragging* “Totals” and/or “Averages” from the dialog which results into the spreadsheet.

A button at the bottom of the spreadsheet toggles between numerical representation of data “**f(x)**” and formula presentation “**=?**”. This facility is also available from a contextual menu. *Click* on a column header and select **Show Formulas** from the menu that results.

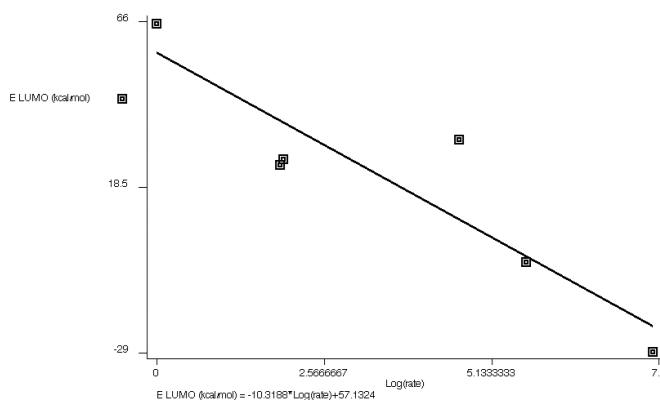
The spreadsheet may be printed by first selecting it and then selecting **Print** from the **File** menu .

Plots...

Plots may be constructed from data in a spreadsheet and a variety of simple “curves” may be fit to these data. Selection of **Plots...** leads to the **Add Plot** dialog.



This incorporates a menu designating the molecular property to be displayed along 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 plot, select an item from the **X Axis** menu, then *click* on one or more boxes to the left of the descriptors under “Y Axis” (or *double click* on their descriptors). (Repeated *clicking* on the box or *double clicking* on the descriptor turns it “on” and “off”.) The dialog is removed from the screen by *clicking* on **OK**. *Clicking* on **Cancel** also removes the dialog, but any plots that have been designated are not displayed.



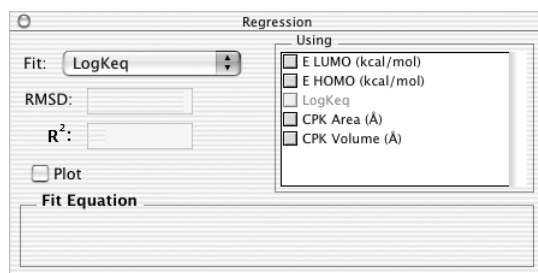
As with any other graphical object, the plot can be moved about the screen. Select (*click* on) either the frame or on one of the curves (it will turn gold), move the mouse with the right button depressed. The plot may also be scaled (expanded or shrunk) by first selecting either the frame or one of the curves, holding down both the  key and the right button while moving the mouse “up and down” (alternatively, use the scroll wheel if available). The plot may not be rotated.

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 **Curve Properties** dialog (see discussion earlier in this chapter).

An individual curve or the entire plot may be deleted by first selecting **Delete** from the **Build** menu (or *clicking* on ) and then *clicking* on either an individual curve or on the plot frame, respectively.

Regression

A linear regression analysis can be performed on data in the spreadsheet, RMSD and R^2 statistics reported and a plot made showing the quality of fit. Selection of **Regression** leads to the **Regression** dialog.



This incorporates a menu on the left, from which a single entry (corresponding to a column in the spreadsheet) is to be designated, and a list of entries on the right (corresponding to the columns in the spreadsheet). Analysis proceeds by selecting the quantity to be fit from the **Fit** menu, and then designating (*clicking* on) one or more entries from the list below “Using” as the variables. This accomplished, the “quality” of the fit in terms of RMSD and R^2 statistics will be reported in the dialog as will the actual fitting function. Different selections from the “Using” list can be made “on-the-fly” in order to obtain a best fit. A plot of the fitting function vs. the quantity to be fit (from the **Fit** menu) may be drawn by *checking* the box to the left of **Plot**.

The dialog (but not the plot) can be removed from the screen by *clicking* on **OK**. *Clicking* on **Cancel** removes the dialog in addition to the plot.

Chapter 16

The Search Menu

*This chapter describes functions available under the **Search** menu. These provide 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 Spartan Molecular Database of calculated molecular structures, energies and properties, a facility for guessing transition state geometries and a procedure for identifying tautomers.

Database
Transition States
Tautomers

Database

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.

Future extensions of SMD will include transition-metal inorganic and organometallic compounds and transition states as well as calculations using higher-level models, and will also allow users to add their own entries.

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.

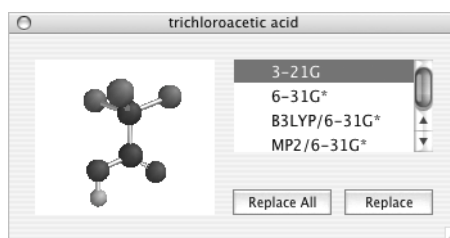
SMD may be used to replace a structure with a database entry corresponding to a particular quantum chemical model, and to locate entries in the database (corresponding to one or more quantum chemical models) that contain a particular substructure. SMD may also be searched by molecule name (see **Retrieve** under the **File** menu; **Chapter 9**).

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.

 trichloroacetic acid

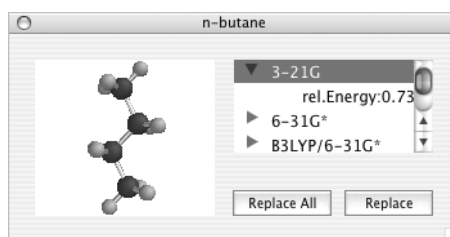
Details are provided by *clicking* on  to the immediate left of the molecule name (it then changes to ). This brings up a dialog that comprises a viewing screen on the left and a list of quantum chemical models for which database entries exist on the right.



Upon initial entry, the topmost entry in the list is highlighted 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). Initially, the selected molecule is “tumbling”. To stop the tumbling, simply rotate it. Model style may not be changed. A different database entry (corresponding in this case to a different quantum chemical model) may be selected by *clicking* on 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 10**). 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 quantum chemical model designation. *Clicking* on this icon leads to an expanded entry which allows access to these higher-energy conformers, as well as provides their relative energies (in kJ/mol).

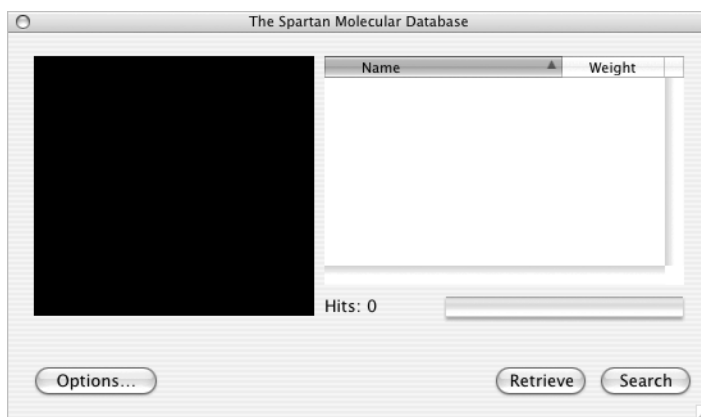


Entries are selected as before, at which time they may be examined in the viewing screen or used to replace the on-screen molecule.

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 controlled from the **SMD** dialog that is brought onto the screen by selecting **Database**. This 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’s file system.



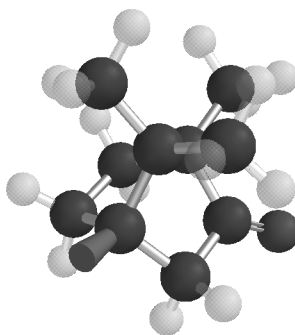
A substructure is specified by selecting (*clicking on*) one or more (ghosted) hydrogens in the structure model*. These will be replaced by orange cones. *Clicking* again will remove the designation and return the hydrogens. As many attachment points as desired may be specified. Anything may be “grown” off an attachment point

* If no attachment points are specified, a search for an “exact” match is carried out.

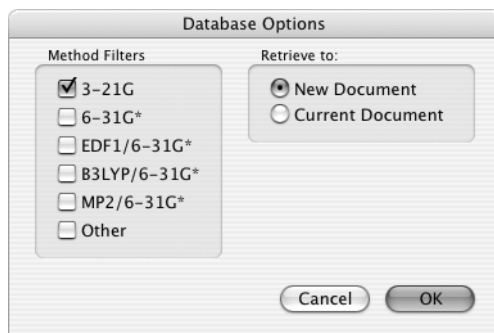


(including hydrogen). The coordination of the atom where attachment is made is maintained. Note, that positions that are not identified as attachment points are assumed to be hydrogens.

For example, to search for camphor derivatives resulting from substitution on the sp^3 carbon at the bridgehead position adjacent to the carbonyl group, it is necessary to *click* on the hydrogen at this position. The structure display will now appear as follows, with an “orange cone” replacing the hydrogen.



Prior to starting the actual search, it is necessary to specify which theoretical model or set of models is to be included. This is accomplished by *clicking* on the **Options** button at the bottom left of the dialog. This brings up the **Database Options** dialog.

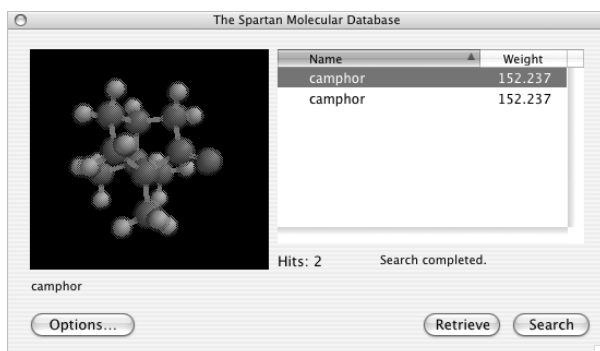


Checking the appropriate boxes specifies the appropriate model(s).

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*).

Specification of **Other** provides access to data with theoretical models other than those explicitly referenced in the dialog. *Clicking* on **OK** removes the dialog. (*Clicking* on **Cancel** 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). The search can be terminated at any time by *clicking* on the **Stop** 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-spoke model is displayed in the window at the left of the dialog, and its name appears immediately below the window.



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 Spartan's 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 **Database Options** dialog (see previous). Selection of destination is accomplished by *toggling*

* 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.



between **New Document** and **Current Document**. Selection of the latter results in the retrieved molecules being appended to the end of the current molecule list.

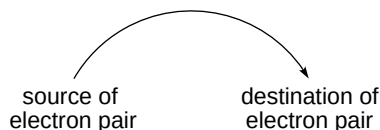
Retrieval is accomplished by first selecting (*clicking on*) one or more hits in the box and then *pressing* the Retrieve button at the bottom of the **SMD** dialog. The **Shift** and **Ctrl** keys may be used to specify retrieval of multiple hits. A block of entries may be specified by *clicking* on 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 the **Stop** button to the right of the **Retrieve** button at the bottom of the **SMD** dialog.

Transition States

Spartan provides a facility for guessing the geometries of transition states based on the similarity of the reaction of interest with one or more entries in a database. While there is always the possibility of an “exact hit”, in which case the guess will be the “exact transition state”*. More commonly, a hit will not be found, 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 that are common, and will optimize the remaining parts (using molecular mechanics). Because conformational searching is not performed, 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 may be easier to start from the “unimolecular side” (the product) where stereochemistry is defined.

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

Input to Spartan’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 an electron pair. The direction of electron flow follows customary practice:



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

* 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 quantum chemical models, although these will gradually be supplemented by transition states from higher-level models.



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.

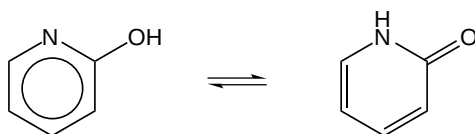
Select atom, bond or SHIFT-click two atoms as head.

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, hold down the **shift** key and then, one after the other, *click* on the two atoms that are to be bonded. Together, 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 “arrows” may be removed by selecting **Delete** (**Build** menu) or by *clicking* on  and then *clicking* on the arrow. (You need to again select  to continue “arrow” selection.) After all reaction arrows have been designated, *clicking* on  at the bottom right of the screen leads directly to the transition state guess (which replaces your original structure). The original structure (with arrows in place) may be returned by selecting **Undo** from the **Edit** menu.

Tautomers

Spartan provides a facility for automatically generating isomers arising from (rapid) transfer of hydrogens among heteroatoms, that is, so-called tautomers. Tautomer generation 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.



The algorithm incorporated into Spartan is limited to tautomers involving nitrogen, oxygen, phosphorous and sulfur. It locates all possible tautomers, but makes no attempt either to remove duplicates or to remove tautomers that are likely to be highly unfavorable.*

The existence of tautomers is automatically sensed by Spartan, and is signaled by the word “Tautomer” being displayed at the bottom right of the screen. (No further action needs to be taken if tautomers are not of interest.) If tautomers exist, individual structures may be examined or a complete list of structures generated by selecting **Tautomers**. Following this, *clicking* on and buttons at the bottom right of the screen moves forward and backward through the list of tautomers. *Clicking* on **Make List** (also at the bottom right of the screen) leads to a full list of tautomers, which can then be handled in the same way as any other (unsaved) document. Caution: the list of tautomers may contain duplicates.

* Of course, once a complete list of tautomers has been generated it is straightforward to calculate their relative energies using any of Spartan’s quantum chemical models.



Chapter 17

The Help Menu

This chapter describes on-line help.

On-line help facilities are available under the **Help** menu.



Spartan Help

This provides information relating to application of computational methods in general, and to methods available in Spartan'04 for Macintosh in particular, as well as technical details regarding the program's operation.

The following topics make up on-line help (the Essential Edition contains a subset):

- Using the Mouse
- Keyboard Functions
- Calculation Options
- Relative Computation Times
- General Operating Features
- Selecting a Model
- Memory Usage

Help files are HTML documents.





Appendix A

Capabilities and Limitations

Essential Edition of Spartan'04 for Macintosh

Spartan'04 for Macintosh is available in two versions: a “full” version that is referred to as Spartan'04 or simply Spartan and a lower-cost version, that 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 and to calculate and display UV/visible and NMR Spectra.

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. The MMFF molecular mechanics energy may be corrected for the effects of aqueous solvation by way of the SM50R model². (A correction to geometry is not presently available.) This is particularly useful for identifying “good conformers” in water. There are no atom limits for molecular mechanics calculations.

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
------------------------------------	-----

Hartree-Fock Models^{1,3,4}

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-pVDZ⁵, cc-pVTZ⁵ and cc-pVQZ⁴) basis sets supplemented by additional polarization and/or diffuse functions. Also available are pseudopotentials for calculations on molecules incorporating heavy atoms.⁵

Preset limits for Hartree-Fock calculations are enumerated below.

maximum number of atoms	200
maximum number of basis functions	2000

Density Functional Models^{1,3,5}

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^{1,3,5}

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^{1,3,5}

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^{1,3,5}

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 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 Truhlar⁶ (available for H, C-F, S-Cl, Br and I), and added to gas-phase total energies obtained at other levels of calculation.

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 spectra⁵ (Hartree-Fock, local density and density functional models only) and NMR spectra⁵ (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. G.D. Hawkins, C.J. Cramer and D.G. Truhlar, *J. Phys. Chem.*, **101**, 7147 (1997).
3. For a review of the quantum chemical methods used in Spartan'04 for Macintosh (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).
4. 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.
5. Not available in Essential Edition.
6. C.C. Chambers, G.D. Hawkins, C.J. Cramer and D.G. Truhlar, *J. Phys. Chem.*, **100**, 16385 (1996).





Appendix B

Menus*

Spartan

About Spartan...	Provides information about Spartan'04 for Macintosh, Wavefunction and Q-Chem
Preferences...	Selects modes for model display and other defaults
Spartan Monitor	Monitors job progress and allows for killing
Quit Spartan	Exits Spartan

File

New (⌘N)	Brings up a model kit for molecule building
Open... (⌘O)	Opens a molecule (or set of molecules)
Retrieve...	Retrieves a molecule from the Spartan Molecular Database by name
Close (⌘W)	Closes a molecule (or set of molecules)
Save (⌘S)	Saves a molecule (or set of molecules)
Save As...	Saves a molecule (or set of molecules) under a user-specified name
New Molecule (⇧⌘N)	Adds a molecule to an existing list; brings up a model kit for molecule building
Delete Molecule	Deletes a molecule (or set of molecules) from a list
Append Molecule(s)...	Appends a molecule (or set of molecules) to the end of a list
Export	Writes molecule or graphics information in one of several formats for reading by other programs.

* ... following the menu name indicates modal operation.



Page Setup...

Setup for printing

Print... (⌘P)

Prints on-screen display

Edit

Undo (⌘Z)

Undoes the last operation (selected operations only)

Cut (⌘X)

Deletes a portion of the selected molecule (or the entire molecule)

Copy (⌘C)

Copies the current molecule or any portion of the main window to the clipboard

Paste (⌘V)

Pastes the contents of the clipboard to the screen (build mode only).

Clear

Clears the molecule from screen (build mode only)

Select All (⌘A)

Selects all atoms in the selected molecule.

Find... (⌘F)

Finds a text string in the output dialog or in the spreadsheet

Find Next (⌘G)

Finds the next occurrence of a text string

Center

Centers the molecules on screen

Colors

Selects screen and model colors

Model

Wire

Displays structure as wire-frame model

Ball and Wire

Displays structure as ball-and-wire model

Tube

Displays structure as tube model

Ball and Spoke

Displays structure as ball-and-spoke model

Space Filling

Displays structure as space-filling (CPK) model

Hide

Hides structure model from view

Global Model

Applies model type and labels of current molecule to all molecules in the same list.



Coupled	Couples motions of all molecules in the same list
Hydrogens	Toggles hydrogens “on” and “off”
Labels	Toggles labels “on” and “off”
Ribbons	Toggles ribbons “on” and “off”
Hydrogen Bonds	Toggles hydrogen bonds “on” and “off”
Configure...	Specifies labels for atoms and ribbon coloring

Geometry

Measure Distance	Displays and/or sets distance between two atoms and allows introduction of a distance constraint
Measure Angle	Displays and/or sets angle involving three atoms or two bonds and allows introduction of an angle constraint
Measure Dihedral	Displays and/or sets dihedral angle involving four atoms or three bonds and allows for introduction of a dihedral angle constraint
Define Point/ Define Ligand Point	Defines a point or ligand point as a geometric mean of a set of atoms
Define Plane	Defines a plane made by three atoms or least-square fit to four or more atoms
Freeze Center	Freezes selected atomic positions
Set Torsions	Alters default bond and ring settings for conformational searching
Align Molecules	Aligns molecules in a list according to a set of user-selected atoms

Build

View	“Neutral” mode; allows display of more than one molecule on screen and removes the model kit if present
Add Fragment (Σ E)	Adds atomic fragment, functional group or ring
Delete	Deletes atoms, bonds, points, planes
Make Bond	Makes a bond between two free valences
Break Bond	Breaks a bond
Minimize	Performs molecular mechanics energy minimization

Setup

Calculations...	Sets up molecular mechanics and quantum chemical calculations as well as request for molecular properties and spectra
Surfaces	Sets up generation of and displays isosurfaces, property maps and contour plots (same entry as in Display menu)
Submit	Submits a job for execution

Display

Output	Displays text output
Properties	Reports total energy, dipole moment, atomic charges, and property value on surface
Surfaces	Sets up generation of and displays isosurfaces, property maps and contour plots (same entry as in Setup menu)
Spectra	Displays IR, NMR and/or UV/visible spectra and animates vibrational modes (associated with IR spectra).
Spreadsheet	Displays spreadsheet



Plots...	Creates plots from the data in the spreadsheet
Regression	Performs regression analysis from data in the spreadsheet

Search

Database	Performs substructure search on the Spartan Molecular Database
Transition States	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
Tautomers	Generates tautomers

Help

Spartan Help (# ?)	Provides information about selecting computational methods and using Spartan
--------------------	--







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>AM1</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 1.0×10^{-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>

Molecular Mechanics and Semi-Empirical Calculations

Keywords unique to molecular mechanics and semi-empirical calculations are as follows:

keyword	value	description
PlanarAmine	–	forces nitrogen in aniline derivatives to be planar
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 3C (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
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).

$$1 \text{ Å} = 0.1 \text{ nm} = 1.889762 \text{ au}$$

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 kJ/mol, but are also available in au, kcal/mol and eV.

Solvation energies are provided in the same units as those for the underlying (gas-phase) calculations.

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).

Absorption Maxima

λ_{max} is given in wavenumbers (cm⁻¹).

Chemical Shifts

Chemical shifts are given in parts per million (ppm) relative to standard. Standards are listed in **Appendix E**.



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 for these nuclei with these Hartree-Fock models are in ppm relative to the appropriate standard. Chemical shift values for other nuclei or for Hartree-Fock models with other basis sets are reported as absolute values.





Appendix F

Citation

The proper citation for Spartan'04 for Macintosh is as follows:

Spartan'04 for Macintosh
Wavefunction, Inc.
Irvine, CA

Except for molecular mechanics and semi-empirical models, the calculation methods used in Spartan'04 for Macintosh 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. 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.





Appendix G

Installing a Network HASP

Spartan 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 (Windows) server. This allows Spartan to be run on a specified number of “client” machines (Macs) 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 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).
6. If client computers are on a different subnet from the license server, a “nethasp.ini” file must be created and deposited in the “/etc” directory (this will require administrator privileges on each client).

Additional:

7. 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>

Index

Note: Items in **bold type** refer to entries in Spartan's menus.

A

- About Spartan**; Spartan menu, about Spartan
- Absorption maximum ($\lambda_{\max}$), units 246
- Add Column dialog 51,206
- Add Fragment**; Build menu, add fragment 35,169
- Add Plot dialog 52,212
- Add Surface dialog 30,191
- Align Molecules**; Geometry menu, align molecules 51,151
- AM1 227
- AM1 calculations, on
acetaldehyde 62
acetone 62
acetophenone 62
allyl vinyl ether 55
androsterone 99
benzaldehyde 62
tert-butylaldehyde 62
3-cyano-4-methylcyclohexenyl radical 38
decaglycine 104
formaldehyde 62
hexafluoroacetone 62
- S_N2 reaction of bromide and methyl chloride 90
- transition state for Diels-Alder cycloaddition of cyclopentadiene and acrylonitrile 83
- transition state for Diels-Alder cycloaddition of 5-fluorocyclopentadiene and acrylonitrile 84
- transition state for Diels-Alder cycloaddition of 5-methylcyclopentadiene and acrylonitrile 84
- trifluoroacetaldehyde 62
- trifluoroacetone 62
- trifluoroacetophenone 62
- vitamin E 96
- vitamin E radical 96
- AM1 parameters 227
- Amino acids, in peptide builder ... 162
- Angles
constraining 147
measuring 146
entering in spreadsheet 207
units 245
- Animation speed, setting 211
- Append Molecule(s)**; File menu, append molecule(s) 131
- Apple key 13ff



- Apply globally
 calculations 50,185
 surfaces 65,191
- Archive 195
- Area 197,198
- Atomic charges
 displaying 143,197
 electrostatic 230
 for S_N2 reaction of bromide
 and methyl chloride 91
 for sulfur tetrafluoride 113
 Mulliken 230
 natural 230
 units 246
- Atomic fragments, in entry
model kit 153
- Atomic hybrids, in expert
model kit 160
- Atomic radii,
 used in space filling models... 141
- Atomic weight 87,197
- Atom colors 139
- Atom labels 25,143
- Atom Properties dialog 29,197
- Atom replacement 32,168
- B**
-
- B3LYP/6-31G* calculations on
 dimethylperoxide 60
 1-pentene 78
- transition state for ene reaction
 of 1-pentene 78
- Ball and Spoke;** Model menu,
ball and spoke 24,140
- Ball-and-spoke model 24,140
- Ball and Wire;** Model menu,
ball and wire 24,138
- Ball-and-wire model 24,138
- Boltzmann equation 69
- Bond density, for
 S_N2 reaction of bromide and
 methyl chloride 91
 transition state for ene
 reaction 1-pentene 77
- Bond distances
 constraining 146
 measuring 146
 entering in spreadsheet 207
 units 245
- Bond Properties dialog 198
- Bonds
 rotation 168
 stretching 168
- BP/6-31G* calculations, on
 benzene 118
 benzene chromium tricarbonyl.118
 bis(cyclopentadienyl)(methyl)
 zirconium cation 118
 ethylene 118



transition state for ethylene insertion into <i>bis</i> (cyclopentadienyl) (methyl) zirconium cation	118
Break Bond; Build menu, break bond	171
Builders in Spartan'04 inorganic	158ff
organic	154ff
nucleotide	165ff
peptide	162ff
Building acetaldehyde	62
acetic acid	64
acetone	62
acetophenone	62
acrylonitrile	21,50
allyl vinyl ether	54
androsterone.....	97
benzaldehyde	62
benzene	114
benzene chromium tricarbonyl.....	114
benzoic acid	64
benzyne	41
<i>bis</i> (cyclopentadienyl) (methyl) zirconium cation	118
<i>tert</i> -butylaldehyde	62
2-butyne	42
camphor	35
chloroacetic acid	64
3-cyano-4-methylcyclohexenyl radical.....	38
cyclohexane	45
cyclohexanone	32
decaglycine	104
decalin.....	45
dichloroacetic acid	64
1,1-dicyanoethylene	50
1,2-dicyanoethylene	50
Diels-Alder cycloaddition of cyclopentadiene and maleic anhydride.....	79
dimethylcyclohexane	44
dimethylperoxide	57
ethinamate	36
ethylene.....	118
formaldehyde	62
formic acid	64
hexafluoroacetone	62
2-hexene.....	67
2-hydroxypyridine	69
2-methylnorbornane	68
1-pentene	75
pivalic acid.....	64
2-pyridone.....	69
S _N 2 reaction of bromide and methyl chloride	89
sulfur tetrafluoride	111
tetracyanoethylene	50
transition state for Diels-Alder cycloaddition of cyclopentadiene and acrylonitrile	82
transition state for Diels-Alder cycloaddition of 5-fluorocyclopentadiene and acrylonitrile.....	83
transition state for Diels-Alder cycloaddition of 5-methylcyclopentadiene and acrylonitrile.....	84
transition state for difluorocarbene addition to cyclohexene	88
transition state for difluorocarbene addition to ethylene.....	85
transition state for ene reaction of 1-pentene	75
transition state for ethylene insertion into <i>bis</i> (cyclopentadienyl)	



(methyl) zirconium cation	116	Carbonyl compounds	
trichloroacetic acid	64	hydration of	61
tricyanoethylene	50	nucleophilic reactivity	33
trifluoroacetaldehyde	62	Carboxylic acids, acidities of	64
trifluoroacetone	62	CCSD, CCSD(T), CCSD(2)	
trifluoroacetophenone	62	models	229
triglycine	102	Center ; Edit menu, center	135
vitamin E	95	Charge	183
vitamin E radical	96	Chemical shifts	
Build menu		displaying	143,197
add fragment	35,169	requesting	183
break bond	171	standards	247
delete	38,169	units	246
make bond	35,170	Chirality	
minimize	23,171	displaying	35,143,197
view	23,169	inverting	14,15
C		CIS, CIS(D) models	230
¹³ C chemical shifts, for		Citation, for Spartan'04 for	
cyclohexane	45	Macintosh	249
decalin	46	Clear ; Edit menu, clear	22,98,134
dimethylcyclohexane	45	Clipboard	
2-hexene	67	copying to	95,133,134
2-methylnorbornane	68	use of in organic and	
¹³ C spectrum, of decalin	46	inorganic model kits ..	95,157,161
Calculate	26,175	Close ; File menu, close	31,120
Calculation options	178,259	Colors ; Edit menu, colors	135
Calculations ; Setup menu,		Colors	
calculations	25,174	atom	139
Calculations dialog	26,175	bond	138
Calculations dialog, essential			
edition	185		



- setting 135
- Colors dialog 135
- Compute 42,182
- Configure**; Model menu,
configure 24,143
- Configure Labels dialog 24,143
- Configure Ribbons dialog 144
- Conformational search, on
allyl vinyl ether 54
3-cyano-4-methylcyclohexenyl
radical 38
ethinamate 37
- Conformer distribution 54
- Constraint Properties dialog .. 58,199
- Constraints, turning on 181
- Contextual menus 15,31
- Control key 13
- Convergence difficulties 185
- Copy**; Edit menu, copy 134
- Correlated models available in
Spartan'04
CCSD, CCSD(T), CCSD(2) .. 229
OD, OD(T) 229
QCISD, QCISD(T) 229
QCCD, QCCD(2) 229
- Coupled**; Model menu,
coupled 66,142
- CPK models 141
- Ctrl key; *see* Control key
- Cubic spline 52,66
- Curve Properties dialog 53,200
- Custom menu 95,157,161
- Cut, Edit** menu, cut 133
- D**
-
- d and l amino acids, in peptide
builder 163
- Database Options dialog 70,219
- Database**; Search menu,
databases 215ff
- Define Ligand Point**; Geometry
menu, define ligand point 148
- Define Plane**; Geometry
menu, define plane 149
- Define Point**; Geometry
menu, define point 148
- Delete**; Build menu, delete 38,169
- Delete Molecule**; File menu,
delete molecule 55,130
- Density 179,246
- Density functional calculations;
See B3LYP/6-31G* calculations,
BP/6-31G* calculations



Density functional models available in Spartan'04	spreadsheet..... 50,205
B3LYP 228	surfaces 30,201
BLYP 228	E
BP 228	Edit menu
EDF1 228	center 135
local 228	clear 22,134
range of applications 228	colors 135
Density functional models 228	copy 134
Dialogs, in Spartan'04 18	cut 133
Dihedral angles	find 135
constraining 148	find next 135
entering in spreadsheet 207	paste 134
measuring 147	redo 133
units 245	select all 134
Dipole moments	undo 22,133
display of 29,196	Electron density
for acrylonitrile 29	for androsterone 99
units 245	units 246
Dipole moment vector 29,196	Electrostatic charges 230
Display menu	Electrostatic potential map, for
output 27,195	acrylonitrile 30
plots 53,212	benzene 115
properties 28,196	benzene chromium tricarbonyl 115
atom properties 197	decaglycine 104
bond properties 197	S _N 2 reaction of bromide
constraint properties 198	and methyl chloride 91
curve properties 199	transition state for ene
molecule properties 196	reaction of 1-pentene 77
plot properties 199	vitamin E 96
surface properties 198	Element symbol, display of 143
Spectra 42,201	Ending jobs 122
IR 201	End key 16
UV/vis 203	
NMR 204	
regression 213	



Energy		new molecule	50,130
conversions	246	open	35,127
display of	196	page setup	132
units	245	print	132
		retrieve	128
Energy profile	58	save	129
		save as	35,129
Entropy	183,230		
Equilibrium conformer	37	Font, selection for labels	143
Equilibrium geometry	26	Force fields	227
Excited-state models available		Four (4) key	18
in Spartan'04		Fourier fit	59
CIS, CIS(D)	230	Fourier series, for describing	
TDDFT	230	torsional potential	57
Export ; File menu, export	131	Free valence	22,155
F			
File formats		Freeze Center ; Geometry	
JPEG	131	menu, freeze center	88,149
MacroModel	128,131	Frequencies	
PDB	128,131	displaying	201
PICT	131	units	246
QuickTime movie	131	Frozen atoms, turning on	181
SDF	128		
SKC	128	G	
SMILES	128	G2, G3, G3(MP2) models	229
Spartan collection	128,131	Geometry menu	
SPARTAN exchange	128,131	align molecules	51,152
SYBYL MOL and MOL2 .	128,131	define ligand point	148
TGF	128	define plane	149
File menu		define point	148
append molecule(s)	130	freeze center	87,149
close	31,129	measure angle	25,146
delete molecule	55,130	measure dihedral	25,147
export	130		
new	21,127		



measure distance	25,146	benzyne	41
set torsions	150	<i>tert</i> -butylaldehyde	62
Global minimum	36,216	2-butyne	42
Global Model ; Model menu,		chloroacetic acid	65
global model	142	3-cyano-4-methylcyclohexenyl	
Global rotate	13,14,123	radical	38
Graphics module	231	cyclohexanone	33
Graphical surface selection	34,195	dichloroacetic acid	65
Groups	22	1,1-dicyanoethylene	50
H		1,2-dicyanoethylene	50
Hartree-Fock calculations; <i>See</i>		formaldehyde	62
HF/3-21G(*) calculations,		formic acid	65
HF/6-31G* calculations		hexafluoroacetone	62
Hartree-Fock models, range		1-methylcytosine	100
of application	228	1-pentene	78
Heat of formation		pivalic acid	65
displaying	196	tetracyanoethylene	50
units	245	transition state for Diels-Alder	
Help menu, Spartan help	225	cycloaddition of	
Help menu (monitor)	122	5-fluorocyclopentadiene	
HF/3-21G calculations, on		and acrylonitrile	84
acetaldehyde	62	transition state for Diels-Alder	
acetic acid	65	cycloaddition of	
acetone	62	5-methylcyclopentadiene	
acetophenone	62	and acrylonitrile	84
acrylonitrile	26,50	transition state for	
allyl vinyl ether	55	difluorocarbene addition to	
benzaldehyde	62	cyclohexene	88
benzoic acid	65	transition state for	
		difluorocarbene addition to	
		ethylene	87
		transition state for ene reaction	
		of 1-pentene	76
		trichloroacetic acid	65
		tricyanoethylene	50
		trifluoroacetaldehyde	62
		trifluoroacetone	62
		trifluoroacetophenone	62
		triglycine	103
		sulfur tetrafluoride	113



HF/6-31G* calculations, on	Inorganic model kit	158
cyclohexane		45
decalin	Intrinsic reaction coordinate	179
dimethylcyclohexane		44
1,2-dimethylperoxide	IRC	179
2-hexene	IR Spectra dialog	42,201
2-methylnorbornane		68
Hide ; Model menu, hide	IR Spectrum, requesting	182
		141
Hide Others ; Spartan menu,	Isotopes	87,197
hide others		125
Hide Spartan ; Spartan menu,	Isovalue, fixed	190
hide Spartan		125
Home key	J	
HOMO energy, displaying	Jobs	
HOMO, for sulfur tetrafluoride ...	maximum concurrent jobs	124
	maximum memory/job	124
HOMO-LUMO gap	maximum scratch disk/job	124
		49
Hydrogen Bonds ; Model	Jobs Preferences dialog	124
Menu, hydrogen bonds	JPEG	131
		143
Hydrogen bonds, displaying . 108,143	K	
Hydrogens, removing from	Keystroke equivalents	11,233ff
model; Model menu, hide		122
	Killing jobs	79
Hydrogens ; Model menu,	Kinetic product	
hydrogens		142
I	L	
Imaginary frequency	Labels ; Model menu, labels ...	25,142
		77
Infrared spectrum, for	Labels	
benzyne	atoms	143
2-butyne	charges	143
	chemical shifts	45,143
	element symbols	143



font	143	Mass number	
ribbons	144	changing	87,197
R/S	35,143	displaying	197
size	143		
Least squares	53,63,66	MDL file formats	128,131
Ligand points, defining	148	Measure Angle; Geometry	
Ligands	114,161	menu, measure angle	25,147
Linear synchronous transit	222	Measure Dihedral; Geometry	
LMP2/6-31G* calculations,		menu, measure dihedral	25,147
on 1-methylcytosine	101	Measure Distance; Geometry	
Localized	178	menu, measure distance	25,146
LogP	182	Mechanics models inSpartan'04..	227
LUMO, for cyclohexanone	33	Menus	11,233
LUMO energy, for		Minimize; Build menu,	
acrylonitrile	51	minimize	23,171
1,1-dicyanoethylene	51	MNDO	227
1,2-dicyanoethylene	51	MNDO/d	227
tetracyanoethylene	51	MNDO/d parameters	227
tricyanoethylene	51	MNDO parameters	227
LUMO energy, displaying	196	MMFF	227
LUMO map, for cyclohexanone		MMFFaq	176,227
displaying	33	MMFF calculations,	
units	245	allyl vinyl ether	54
M		3-cyano-4-methylcyclohexenyl	
MacroModel file format	128,131	radical	38
Make Bond; Build menu,		ethinamate	37
make bond	35,170	Model	4



- Model menu
- ball and spoke 24,140
 - ball and wire 24,138
 - configure 24,143
 - coupled 67,142
 - global model 141
 - hide 141
 - hydrogen bonds 143
 - hydrogens 142
 - labels 25,142
 - ribbons 142
 - space filling 24,141
 - tube 24,140
 - wire 24,138
- MOL, MOL2 file formats 128,131
- Molecular mechanics calculations;
See MMFF calculations
- Molecular mechanics models
- overview 4
 - range of application 227
- Molecular models
- 3D 18
 - atom colors 139
 - ball-and-spoke 24
 - ball-and-wire 24
 - bond colors 138
 - coupling of motions 142
 - CPK 141
 - global model 141
 - hiding 141
 - hydrogen bonds 143
 - hydrogens 142
 - labels 24,143
 - molecule centered 123
 - orthogonal view 123
 - perspective view 123
 - ribbons 142
 - rotation of 13,14
 - scaling 13,14
 - screen centered 123
 - space filling 24
 - split tubes 124,140
 - translation 13,14
 - tube 24
 - wire 24
- Molecular size 99,197
- Molecular volume 99,197
- Molecule builders
- amino acids 162
 - atomic fragments 153
 - atomic hybrids 160
 - atom/hybrid replacement .. 32,168
 - bond rotation 168
 - bond stretching 168
 - bond types 160
 - breaking bonds; Build menu,
break bond 171
 - chirality inversion 14,15,168
 - clipboard 157
 - custom 157
 - delete; Build menu, delete 169
 - going between builders
..... 158,162,165
 - groups 22,155
 - inorganic model kit 158
 - ligands 114,161
 - making bonds; Build menu,
make bond 170
 - manipulating molecular
fragments 14,15
 - minimizing; Build menu,
minimize 171
 - nucleotide bases 166
 - nucleotide model kit 165
 - organic model kit 154
 - peptide model kit 102,162
 - Periodic Table*... 159



rings 32,156
sequencing polypeptides/
polynucleotides 163,166
terminating polypeptides 163,164

Molecule centered rotation 13,14

Molecule Properties dialog 29,196

Molecule selection 13,14

Møller-Plesset models available in
Spartan'04 for Macintosh

LMP2 229

MP2 229

MP3 229

MP4 229

Monitor dialog 122

Mouse 13ff

Mulliken charges 230

Multiplicity 38,184

N

New; File menu, new 21,127

New Molecule; File menu,
new molecule 50,130

NMR Spectra dialog 204

NMR spectra
plotting 204
requesting 183

NOEs, setting 146,199

O

OD, OD(T) models 229

Open; File menu, open 35,119

Open valence 22,147

Option key..13ff,89,155,156,158,160

Orbital energies, units 245

Organic model kit 154

Orthogonal view 123

Output; Display menu, output .27,195

Output window 27,195

P

Page Setup; File menu,
page setup 132

Page Up/Down keys 16

Partial surface area 209

Partial volume 209

PDB file format 128,131

Paste; **Edit** menu, paste 134

Peptide model kit 102,162

Periodic Table 112,159

Perspective view 123

Picking 13,14



PICT	131	Printing	
Plot Properties dialog	199	atomic charges	184
Plots ; Display menu, plots	52,212	on-screen graphics; See File menu, print	
PM3	227	orbitals and orbital energies ...	184
PM3 calculations, on		spreadsheet	212
benzene	114	thermodynamic quantities	184
benzene chromium tricarbonyl	114	vibrational modes	184
bis(cyclopentadienyl) (methyl)		Properties ; Display menu,	
zirconium cation	118	properties	28,196ff
Diels-Alder cycloaddition of		Property archive	195
cyclopentadiene and maleic		Pseudopotential	179
anhydride	80	Q	
ethylene	118	QCCD, QCCD(2) models	229
transition state for ethylene		QCISD, QCISD(T) models	229
insertion into		Quantum chemical models,	
bis(cyclopentadienyl)		overview	4ff
(methyl) zirconium cation	117	QuickTime	131
PM3 parameters	227	Quit Spartan ; Spartan menu,	
PNG	131	Quit Spartan	11,125
Polar surface area	196,209	Quitting Spartan	11,125
Preferences ; Spartan menu,		R	
preferences	123	Redo ; Edit menu, redo	133
Preferences dialog (database)	125	Regression ; Display menu,	
Preferences dialog (general)	123	regression	63,213
Preferences dialog (images)	124	Regression dialog	63,213
Preferences dialog (jobs)	125	Retrieve ; File menu, retrieve	128
Preferences, setting	123		
Print ; File menu, print	132		



- Ribbons**; Model menu, ribbons .. 142
- Rings 82
- Rotation about single bonds 168
- Rotation, of molecules on screen..13,14
- R/S Chirality 14,15,35,143,197
- S**
-
- Save**; File menu, save 129
- Save As**; File menu, save as ... 35,130
- Save As dialog 26,130
- Scaling 13,14
- Screen centered rotation 13,14
- Scroll wheel 14
- SD file format 128,131
- Search menu
 database 37,68,70,215ff
 tautomers 100,224
 transition states 75,222
- Select All**; Edit menu, select all... 134
- Selection box 95,133
- Semi-empirical calculations;
See AM1 calculations; PM3
calculations
- Semi-empirical models
 available in Spartan'04 for
 Macintosh 227
- range of application 228
- Services**; Spartan menu, services 125
- Set Torsions**; Geometry menu,
set torsions 150
- Setup menu
 calculations 26,174
 submit 26,193
 surfaces 30,186
- Shift key 13ff
- Show All**; Spartan menu,
show all 125
- Single-point energy 38
- Size restrictions in Spartan'04 for
Macintosh
 advanced correlated models... 229
 density functional models 228
 excited state models 230
 Hartree-Fock models 228
 molecular mechanics models . 227
 Møller-Plesset models 229
 semi-empirical models 228
- SKC file format 128,131
- SM50R iii,177
- SM5.4 174,230
- SM5.4, calculations for
 reaction coordinate for S_N2
 addition of bromide to
 methyl chloride 91
- SM5.4, parameters 230



- SMD; See Spartan Molecular Database
- SMD dialog 70,218,220
- SMD preview dialog 37,217
- SMILES file format 131,215
- Solvation
- for SN2 addition of bromide
 - to methyl chloride 91
 - SM0R model iii,177
 - SM5.4 model 230
- SOMO, for 3-cyano-4-methylcyclohexenyl radical 40
- spacebar 13ff
- Space-Filling**; Model menu, space-filling 24,141
- Space-filling model 24,141
- Spartan'04 for Macintosh
- advanced correlated models... 229
 - changing colors 18
 - contextual menus 15
 - density functional models 228
 - dialogs 18
 - essential edition 227
 - excited state models 230
 - exiting 11
 - file formats 128,131
 - graphics 230
 - Hartree-Fock models 228
 - keyboard functions 16
 - keystroke equivalents 12
 - keywords 185,239ff
 - killing jobs 18,122
 - list-to-list operations 17
 - mechanics models 227
 - menus 11
 - molecule selection 13,14
 - Møller-Plesset models 229
 - monitor 122
 - monitoring jobs 18,122
 - new features iii
 - options 185,239ff
 - overview 3
 - properties 230
 - quitting 11
 - semi-empirical models 227
 - setting preferences 18
 - spectra 230
 - starting 11
 - submitting jobs 193
 - tool palette 12
 - using the mouse 13
- Spartan Help**; Help menu, Spartan help 225
- Spartan menu
- About Spartan 121
 - Hide Others 125
 - Hide Spartan 125
 - Preferences 123
 - Quit Spartan 125
 - Services 125
 - Show All 125
 - Spartan Monitor 122
- Spartan Molecular Database
- content 215
 - generation of 216
 - name search of 128
 - replacement from 65,216
 - substructure search of .. 69,70,218
- Spartan Molecular Database dialog 70,218,220



Spartan Monitor ; Spartan menu, Spartan monitor	122	Stopping jobs	122
Spectra ; Display Menu, spectra	42,201	Strain energy display of	196
Spin density, for 3-cyano-4-methylcyclohexenyl radical	40	units	245
vitamin E radical	96	Subject to	181
Spin density map, for 3-cyano-4-methylcyclohexenyl radical	40	Submit ; Setup menu, submit ..	26,193
Spin multiplicity	38,184	Submit dialog	193
Spreadsheet ; Display menu, spreadsheet	50,205	Submitting jobs	193
Spreadsheet adding columns	206ff	Surface area of CPK model	196
deleting columns	211	of graphical surface	198
deleting rows (molecules)	211	partial	209
entering numerical data	62,65,206	polar	196,209
expressions	207	units	245
printing	212	Surface Properties dialog	31,198
sorting	62,212	Surfaces ; Display menu, surfaces; Setup menu, surfaces	30,186,201
summarizing columns	212	Surfaces dialog	30,188
Spreadsheet dialog	50,205	SYBYL	227
Start from	38,180	SYBYL MOL and MOL2 file formats	128,131
Starting jobs	123	Symmetry, using	182
Starting Spartan'04 for Macintosh ..	11	T	
Stereo display	18	Tautomers ; Search menu, tautomers	100,224
Stereographic monitor	iv	TDDFT (time-dependent density functional) models	230



Terminate dialog	103,164	UV/vis spectrum	
Theoretical model	4	plotting	203
Thermodynamic product	79	requesting	182
Thermodynamic properties,		V	
printing	184	Valence checking	160
requesting	182	Van der Waals radii	
Three key	18	use in space-filling models	141
Tool palette	12	Verbose output	195
Total charge	183	Vibrational frequencies	
Transition state geometry	76	displaying	201
Transition States; Search		units	246
menu, transition states	75,222	Vibrational frequencies, for	
Transition states, guessing	75,222	benzyne	42
Translation, of molecules		2-butyne	43
on screen	13,14	transition state for Diels-Alder	
Tube; Model menu, tube	24,140	cycloaddition of	
Tube model	24,140	cyclopentadiene and	
U		acrylonitrile	83
Undo; Edit menu, undo	22,133	transition state for	
Units	245	difluorocarbene addition	
Units, conversion factors	246	to ethylene	87
UV/vis spectra dialog	203	transition state for ene reaction	
		of 1-pentene	76
		transition state for ethylene	
		insertion into	
		<i>bis</i> (cyclopentadienyl)	
		(methyl) zirconium cation	117
		View; Build menu, view	23,169
		View	
		orthogonal	123
		perspective	123
		Volume	
		of CPK model	196



of graphical surface 198
partial 209
units 245

W

Wire; Model menu, wire 24,138
Wire model 24,138

X

XYZ file format 128,131

Z

Zooming 13,14

