

Beginning with Maestro

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Document Conventions

In addition to the use of italics for names of documents, the font conventions that are used in this document are summarized in the table below.

Font	Example	Use
Sans serif	Project Table	Names of GUI features, such as panels, menus, menu items, buttons, and labels
Monospace	<code>\$SCHRODINGER/maestro</code>	File names, directory names, commands, environment variables, command input and output
Italic	<i>filename</i>	Text that the user must replace with a value
Sans serif uppercase	CTRL+H	Keyboard keys

Links to other locations in the current document or to other PDF documents are colored like this: [Document Conventions](#).

In descriptions of command syntax, the following UNIX conventions are used: braces { } enclose a choice of required items, square brackets [] enclose optional items, and the bar symbol | separates items in a list from which one item must be chosen. Lines of command syntax that wrap should be interpreted as a single command.

File name, path, and environment variable syntax is generally given with the UNIX conventions. To obtain the Windows conventions, replace the forward slash / with the backslash \ in path or directory names, and replace the \$ at the beginning of an environment variable with a % at each end. For example, `$SCHRODINGER/maestro` becomes `%SCHRODINGER%\maestro`.

Keyboard references are given in the Windows convention by default, with Mac equivalents in parentheses, for example CTRL+H (⌘H). Where Mac equivalents are not given, COMMAND should be read in place of CTRL. The convention CTRL-H is not used.

In this document, to *type* text means to type the required text in the specified location, and to *enter* text means to type the required text, then press the ENTER key.

References to literature sources are given in square brackets, like this: [10].

About This Document

This document is designed to show you how to use the basic capabilities of Maestro, in easy steps. In the early parts of the book, we will explain everything in great detail—what to do with the mouse, where to click, where buttons are, and so on—so you aren't missing any part of the procedure. At the same time, we'll provide a more compact notation for explaining what to do. Later in the book, we'll use the compact notation, with references back to the explanation, and still later, we'll just use the compact notation. By that time, you'll have learnt what it means and how to perform the actions, and won't need the detailed explanation. But it'll always be there to refer back to.

This tutorial is designed for you to work through from the beginning, but you can start at any of the chapters if you so desire. However, the explanations in the later chapter are more compact, so you might have to go back to the earlier chapters to find out how to perform an action.

If you are reading this book online, you may notice that there are words that are marked in an indigo color, like this: [Contents](#). These are links to other parts of the book. If you click on the word in your PDF reader, it takes you to the other part of the book. To go back to the place you came from, click the Back button in your PDF reader. Try it with the word [Contents](#), above. It will take you to the table of contents for this book.

There are also indigo-colored links to various sections of the *Maestro User Manual*. These links are provided so you can read more about the feature you are working with, if you are interested. Clicking on these links takes you to the section referred to. Try clicking the words *Maestro User Manual* in the first sentence of this paragraph, then click the Back button.

Starting Maestro and Viewing Molecules

Maestro is a freely available, full-featured molecular visualization environment that also serves as the interface to all of Schrödinger's computational chemistry software. When coupled with Schrödinger software such as Glide, Prime, or Phase, Maestro is a powerful tool for interpreting, managing, and sharing the results of computational experiments. As a standalone program, Maestro is an easy-to-use tool for building, visualizing, and sharing 3-dimensional chemical models. In this tutorial, you'll learn how to perform these simple tasks using Maestro's intuitively designed interface. Working through the exercises in this chapter, you'll start Maestro, import structure files, and learn how to view them in the Maestro Workspace.

Maestro is designed to run on Linux, Windows, and Mac machines. It's always best to display Maestro on your local machine, but if you have to, you can run Maestro on a remote machine and display it over the network to your local machine.

2.1 Starting Maestro

Starting the program is done in the normal way on each platform. If this is the first time you've used Maestro, you'll see some panels open after the interface opens, asking you to make a choice of "profile" and giving you a chance to see some information about Maestro.

To start Maestro under Windows:

1. Double-click the Maestro icon on your desktop.

A splash screen shows up first, then the Choose Profile dialog box opens, asking you to choose a profile. Profiles are different customizations of the Maestro interface. We will use the Maestro profile, which is highlighted in yellow, and has a star in the Default column.

If you want to use the Maestro profile by default, and don't want to choose it each time, you can clear the check box labeled Show this dialog box at startup.

2. Click Start.

After a while the Maestro interface appears, and a Welcome dialog box opens, giving you some options for information about Maestro. If you don't want to see this dialog box again, clear the check box labeled Do not show this dialog again.

3. Click OK.

To start Maestro under Mac OS X:

1. Double-click the Maestro icon on the dock.

If the Maestro icon isn't on the dock, you can drag it there: go to Applications, and look in the Schrodinger folder.

A splash screen shows up first, then the Choose Profile dialog box opens, asking you to choose a profile. Profiles are different customizations of the Maestro interface. We will use the Maestro profile, which is highlighted in yellow, and has a star in the Default column.

If you want to use the Maestro profile by default, and don't want to choose it each time, you can clear the check box labeled Show this dialog box at startup.

2. Click Start.

After a while the Maestro interface appears, and a Welcome dialog box opens, giving you some options for information about Maestro. If you don't want to see this dialog box again, clear the check box labeled Do not show this dialog again.

3. Click OK.

To start Maestro under UNIX:

1. Open a terminal window so that you have a command-line prompt.

The steps to open a terminal window vary slightly between operating systems, but it is generally possible to right-click in your desktop and select an option from the menu that appears. Usually it will have an icon that looks like a computer monitor.

2. Next, set the SCHRODINGER environment variable.

This environment variable contains the path to your installation of Maestro. How you set the SCHRODINGER environment variable depends on the "shell" used in the terminal window. If you are using either the bash or ksh shell, enter the following command:

```
export SCHRODINGER=installation-directory
```

If you are using either the csh or the tcsh shell, enter the following command:

```
setenv SCHRODINGER installation-directory
```

In the commands above, *installation-directory* should be replaced with the path to the directory where Maestro is installed. If you're not sure which shell you're using you can type the command `which $SHELL`, which will return the location and name of the shell that you're using.

3. If you need to, change to a directory for which you have write permission.

```
cd my-directory
```

4. Start Maestro by entering the following command:

```
$SCHRODINGER/maestro &
```

The “&” at the end of the line means that Maestro is run in the “background”, and you can continue to use the terminal window. Without it, you would have to wait until Maestro has finished running to type any other commands. (This has no effect on how well Maestro runs.)

From here on, the terminal and the command line are no longer used—all tasks can be performed within the Maestro interface.

A splash screen shows up first, then the Choose Profile dialog box opens, asking you to choose a profile. Profiles are different customizations of the Maestro interface. We will use the Maestro profile, which is highlighted in yellow, and has a star in the Default column.

If you want to use the Maestro profile by default, and don’t want to choose it each time, you can clear the check box labeled Show this dialog box at startup.

5. Click Start.

After a while the Maestro interface appears, and a Welcome dialog box opens, giving you some options for information about Maestro. If you don’t want to see this dialog box again, clear the check box labeled Do not show this dialog again.

6. Click OK.

2.2 Copying the Files You Need To Run this Tutorial

To perform the exercises in this tutorial, you’ll need to have the structures easily accessible. These structures can be copied from the installation to your own directory.

1. In Maestro, choose Help → Tutorials.

The Tutorials panel opens. This panel gives you access to all the available tutorials. You can organize the list and filter it to show only what you’re interested in. To start, the panel shows tutorials listed by product.

2. Click the table row that contains Beginning with Maestro in the Tutorial column.

Now that you have selected a tutorial, you can copy its files. You can copy the files to the default location, which is shown in the Copy to text box, or you can copy them to a location of your choice. If you want them in your own location, follow the next few instructions.

3. Click the **Browse** button, which is to the right of the Copy to text box.
4. Go to a suitable folder (directory).
5. If you want to create a new folder, type the folder name into the Directory box.
6. Click **Choose**.

OK, you have a location to put the tutorial files. The last step is to copy them.

7. Click **Copy**.

You might see a progress box displayed briefly as the files are copied. You can also open the tutorial instructions by clicking **View**, but since you are already reading them now, you don't need to do this.

8. Close the Tutorial panel.

2.3 Features of the Maestro Main Window

Once you've started Maestro, you'll want to take note of various features in the Maestro main window, as shown in [Figure 2.1](#).

- At the center of the interface is the Maestro Workspace, which remains empty until you import structures, build molecules, or open a "project".
- At the top of the Maestro interface is the Maestro menu bar, which gives you access to all kinds of options, features, and programs.
- Below the menu bar is the Project toolbar, which you can use to do tasks on your project.
- Below this toolbar is the Manager toolbar, which has buttons that you can use to show or hide all the other toolbars. When a toolbar is shown, the button is highlighted.
- The status bar near the bottom of the window gives information about the number of atoms and molecules in the Workspace, and also displays more specific structural information when you pause the pointer over an atom in the Workspace.
- The job monitor button shows how many jobs you are running. If you click it, the Monitor panel opens, showing details of the jobs.
- At the bottom of the window is the Auto-Help area. This area automatically displays a hint about the task you're doing.

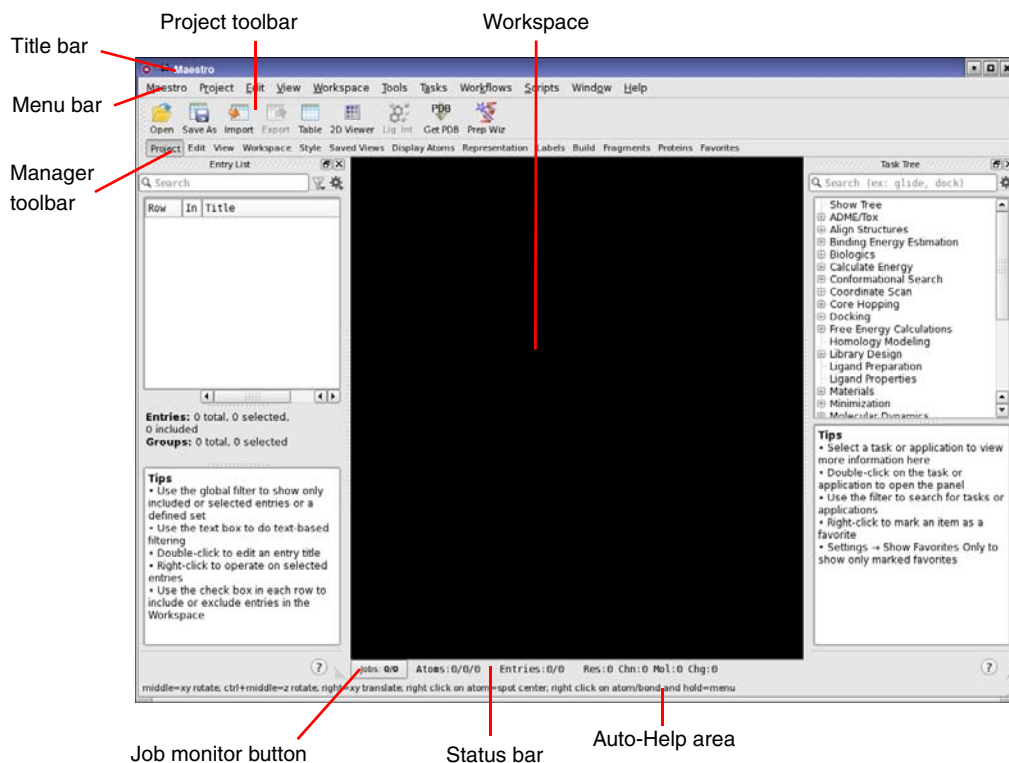


Figure 2.1. The Maestro main window.

The main window also has two panels “docked” into it: the Entry List panel on the left, and the Task Tree panel on the right. The Entry List panel shows a list of all the entries (structures) in your project. It’s empty because the project hasn’t got any structures in it yet. The Task Tree panel shows all the tasks you can do with various applications, and allows you to find different tasks. We won’t be using the applications in this tutorial, so you can close this panel.

1. Click the close button in the title bar of the Task Tree panel.

What this button looks like will depend on whether you are running Maestro on a Mac, Windows, or Linux.

There are other features that can be added to the main window, which aren’t displayed by default. You can display these features using the Window menu. For more information, see [Section 2.2](#) of the *Maestro User Manual*.

In this tutorial, you'll be using the toolbars a lot, so it's useful to know a bit about them beforehand. Notice that in [Figure 2.1](#), the Export button on the Project toolbar is dimmed, which means it can't be used. That's because there's nothing in the project to export. To see other features, you'll need to display some of the toolbars.

2. Click the View button on the Manager toolbar.

The View toolbar appears on the left side of the main window.

Notice that the buttons on this toolbar don't have the button names underneath them, like the buttons on the Project toolbar. If you want to see the button names, you can change the toolbar appearance from its shortcut menu. Just right-click on the toolbar and choose *Style*, then choose the style of the button that you want, like *Text Under Icon*.

Some of the toolbar buttons have a little triangle in the lower right corner—we'll discuss those shortly. The ones that don't are buttons that perform a simple action, like opening a panel or changing the view of what's in the Workspace. All you need to do is click the button to perform the action.

The buttons that have little triangles in the lower right corner are *menu buttons*. If you click and hold on any of these buttons, a menu appears to the lower right. This menu is called a *button menu*. You can choose an item on the menu by continuing to hold the mouse button down, moving the mouse until the item you want is highlighted, then releasing the mouse button. The menu disappears and the item you highlighted is selected. We'll call this action "choosing an item from a button menu". It's just like choosing an item from any other menu. If you accidentally click on the wrong button, just move the pointer out of the menu and release the mouse button.

If you chose an item that represents a group of atoms or a structural feature—Atoms, Bonds, Molecules, Residues, and so on—the toolbar button is indented after you release the mouse button. This indicates that the button's action will be applied to the group of atoms you pick. When you move the pointer into the Workspace, it turns into a small square with a letter beside it. The letter tells you what you chose on the menu. The button indentation and the appearance of the pointer tells you that Maestro expects you to click on an atom ("pick" an atom) or bond in the Workspace to select some atoms. The action represented by the button is then performed on these atoms. To get out of this "picking" mode, just click on the button again. The button is no longer indented, and the pointer has its normal appearance in the Workspace. When you display the button menu again, you'll see that the item you chose has a black circle beside it.

Other items on the button menus can be groups of atoms to which the action is applied immediately, options that are set, or properties that can be applied to structures. Some items open dialog boxes in which you can perform an action or select atoms to apply the button's action to. Some examples of button menus are shown in [Figure 2.2](#).

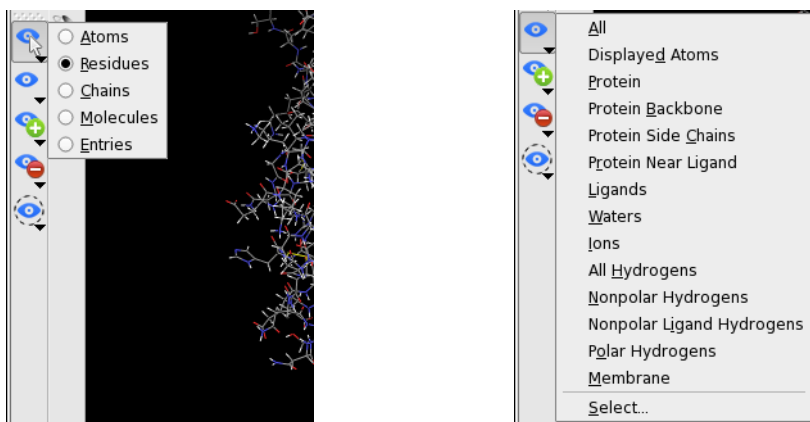


Figure 2.2. Display Sel and Display Only button menus.

One of the useful features of the Maestro interface is the availability of help features. In addition to the Auto-Help text area, you'll see a Help menu that can be used to find information about Maestro features. You may have also noticed that when you pause the pointer over one of the buttons in the toolbar, a pop-up "tooltip" appears, with text that describes the function of the button. (When you move the mouse again, it disappears.) All Maestro windows, called *panels*, have a Help button at the bottom that can be used to display relevant information. If you can't find the information you need, you can also e-mail help@schrodinger.com to get an answer to your questions.

2.4 Importing a Maestro File

The most common operation within Maestro is the simple manipulation of structures in the Workspace—they can be rotated, translated, and made to appear larger or smaller. But before you can experiment with these manipulations, you'll need to import some structures. To do so:

1. Open the Import panel by clicking the Import button on the Project toolbar. (You can also open the panel with the keyboard shortcut CTRL+I.)



Take a moment to study the layout of the Import panel. At the top is the Look in option menu, which displays the location of the directory that you'll be importing structures from. By default, the path is first set to your current working directory. To the left are buttons to quickly change directory to either your Home Directory, a Custom Directory, or the Working Directory. At the center of the Import panel is a list that displays all of the files in

the selected directory of the format selected in the Files of type option menu. If you correctly copied the tutorial structure files to your current working directory, you should see the file `small_molecule.mae` in the list.

If you type in the name, note that as you start to type name in the File name text box, Maestro auto-completes the file name with the first matching name. If it's not the right file, just keep typing until you get the right name.

2. To import the file `small_molecule.mae`, either double-click on the file name, or click the file name, and click **Open**.

The Import panel closes and a structure appears in the Workspace. A line also appears in the Entry List panel, checked to indicate that the structure is in the Workspace.

Take a moment to observe the color scheme used. Carbon atoms are colored gray, nitrogen atoms are colored blue, oxygen atoms are colored red, and hydrogen atoms are colored white. This commonly used color scheme makes it easy to identify the elements in the Workspace.

If you're curious about the Options button in the Import panel, click it to see the options that are available. To find out about these options, you can either click on the Help button in the Import panel, or see [Section 3.1](#) of the *Maestro User Manual*.

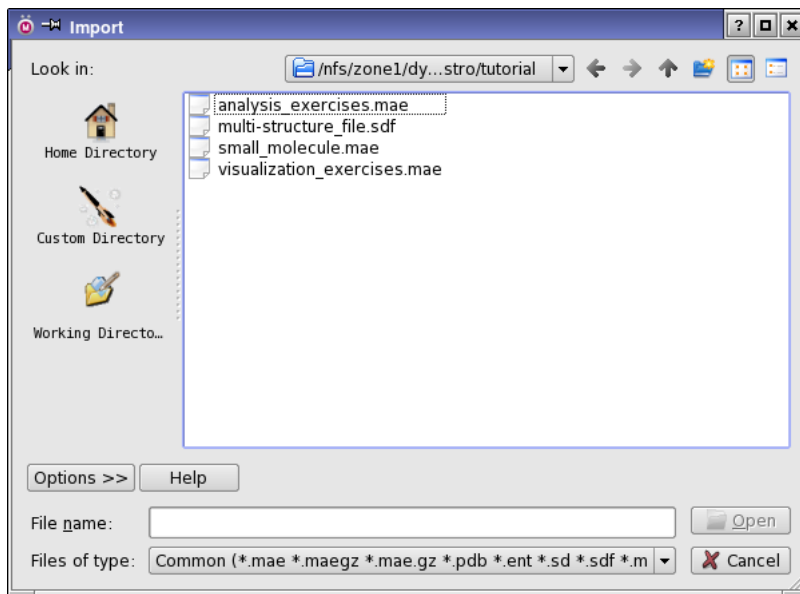


Figure 2.3. The Import panel.

2.5 Viewing a Structure in the Workspace

After importing a molecule into Maestro, you're ready to manipulate the structure in the Workspace. In this exercise, you'll learn how to translate, rotate, and zoom in or out on a molecule. You'll also want to note that these manipulations require the use of a three-button mouse. If you don't have a three-button mouse (or a two-button mouse capable of three-button emulation), you may want to consider obtaining one.

But first, a word about the axis system used by Maestro. The x axis is the horizontal axis, and the y axis is the vertical axis. The z axis is the axis coming out of the screen towards you (this is the positive z direction).

Now, let's try some manipulations. And, by the way, when you do these manipulations, you aren't really changing the position of the molecule. It's as if you were operating a video camera, and you are changing the camera angle to get a different view of the molecule.

Rotating the molecule:

- To rotate the molecule left or right (around the y axis), place the pointer anywhere in the Workspace, hold down the middle mouse button, and move the mouse to the left or right.

The pointer changes to an arrow going around in a circle, with the letters xy above it, to show that you are rotating around the x (horizontal) or y (vertical) axis.

- To rotate the molecule up or down, (around the x axis) repeat the above step, but move the mouse up or down.

You can rotate in both directions simultaneously by moving the mouse diagonally. If you want to make sure you rotate only in the x direction or the y direction, hold down the SHIFT key along with the middle mouse button.

- To rotate the molecule in the plane of the screen (around the z axis), place the pointer anywhere in the Workspace, hold down the CTRL key and the middle mouse button, and move the mouse to the left or right.

The pointer changes to an arrow going around in a circle, with the letter z above it, to show that you are rotating around the z axis (the one perpendicular to the screen).

Translating the molecule:

- To translate the molecule in the Workspace (change its position in the Workspace), place the pointer anywhere in the Workspace, hold down the right mouse button, and move the mouse left, right, up, or down.

The pointer changes to a pair of double-headed arrows perpendicular to each other, to show that you are translating the Workspace structure.

Zooming in or out:

- To zoom in on the structure, place the pointer anywhere in the Workspace, hold down the middle and right mouse buttons, and move the mouse to the right. If your mouse has a scroll wheel for a middle button, you can also use it to zoom in and out.

The pointer changes to a magnifying glass, to indicate that you are zooming.

- To zoom out on the structure, repeat the above step, but move the mouse to the left instead of to the right.
- It's also possible to automatically "fit" the structure to the Workspace, so that it fills the screen. To do so, simply click the Fit button on the View toolbar.



Saving the view:

You can also save the orientation of the Workspace, and return to it later. Here's an example.

1. First, click the Saved Views button on the Manager toolbar.

The Saved Views toolbar is displayed at the bottom of the Workspace.

2. Click the Save button on the Saved Views toolbar.



The Save View dialog box opens, with a default name for the view in the Name text box. We'll use the default name in this exercise.

3. Click OK.

Notice that the Previous and Next buttons are now available, and the first of the numbers is no longer dimmed.

4. Next, rotate the structure toward you by clicking on the Rotate X button.



5. Click the Rotate Y button to rotate 90 degrees to the right.



6. Click on the 1 button on the Saved Views toolbar to return to the view that you saved in Step 2.

Congratulations, you're now manipulating structures in the Workspace. Feel free to practise these operations until you are familiar with them. You can always restore the original view of the molecule by clicking the Reset button:



This button is part of the View toolbar, but isn't displayed by default. To display it, right-click in the View toolbar, and choose Customize. The Customize Toolbars panel opens with the View menu selected. In the Available buttons list, under Workspace view changes, you'll see the Reset button. Select it and click the arrow in the middle to move it to the Toolbar items list, and then close the panel. The Reset button is now displayed.

2.6 Including and Excluding Entries in the Workspace

Now that you know how to manipulate structures in the Workspace, you're ready to learn how to include and exclude structures from the Workspace. Maestro has two places that list the structures that you've imported: the Entry List and the Project Table. The Entry List just shows the title for each structure and a check box for whether it's shown in the Workspace or not. The Project Table shows the structures, but it has a lot more features: it can also be used to manage the results of computations, and store structure-associated data. For now, we'll use the Entry List to control which molecules are displayed in the Workspace. For more information about the Project Table, see [Chapter 9](#) of the *Maestro User Manual*.

1. Open the Import panel by clicking the Import button on the Project toolbar.



2. From the Files of type option menu, choose MDL SD.

All files in SD format (with the extension `.sdf` and other variations) appear on the list. There are many file formats used to store molecular structures, and Maestro can read a most of them. The common ones are available on this option menu as the type Common. For the less common types, you'll need to choose the type from this option menu. SD files are one of the common types, but here we chose the menu item for practice.

3. Double-click on `multi-structure_file.sdf` to import it.

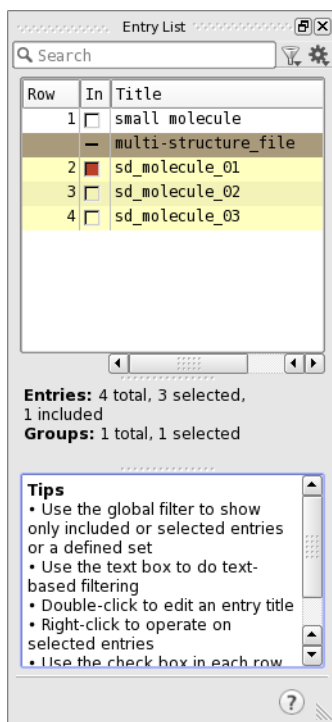


Figure 2.4. The Entry List Panel.

In the Entry List, you'll notice that several "entries", represented by various rows with text in them, are highlighted in yellow. These highlighted entries are the structures that you just imported. You'll also notice a tan row with a "-" in the In column. This is the label row for an *entry group*. When you imported the structures, they were added as a group, named after the file they came from. You can open and close the group by clicking the - which turns to a + when it's closed.

You can include the structures in the Workspace, or exclude them from the Workspace, by clicking the check box to the left of the title text. There is no limit to the number of entries that can be included in the Workspace. A checked box (red or black) indicates that the structure is currently included in the Workspace. By default, only the first new entry (in this case `sd_molecule_01`) is included in the Workspace when you import multiple structures. (A red check box marks the "target" entry, for which special actions can be taken, like showing text in the Workspace.)

4. Include `sd_molecule_02` in the Workspace by checking the box next to its title.

(Later on, we'll just say "Include *entry* in the Workspace".)

When you click, the molecule that was originally in the Workspace, `sd_molecule_01`, is excluded from the Workspace, and `sd_molecule_02` is included in the Workspace. This is the normal behavior: including one entry in the Workspace excludes all others.

5. To include both `sd_molecule_02` and `sd_molecule_03` in the Workspace, control-click the square next to the entry for `sd_molecule_03`.

Holding down the Control key when including an entry just affects that entry: other included entries remain included.

6. To clear the Workspace, control-click the square next to `sd_molecule_02`, and then control-click the square next to `sd_molecule_03`.

Control-clicking the square for an entry that is already included in the Workspace excludes it from the Workspace. This only affects whether or not the structure appears in the Workspace—no atoms are deleted when excluding an entry.

7. To include `sd_molecule_01`, `sd_molecule_02`, and `sd_molecule_03` in the Workspace, click the square next to `sd_molecule_01`, then shift-click the square next to `sd_molecule_03`.

Shift-clicking includes all entries between the two most recently clicked entries in the Workspace.

To remove all these structures from the Workspace, you could control-click their columns, but there's a quicker way. First, you'll need to display the Workspace toolbar.

8. Click the Workspace button on the Manager toolbar to display the Workspace toolbar.
9. Clear the Workspace by clicking the Clear button on this toolbar.



This automatically excludes all entries from the Workspace. (Later on, we'll just say "Clear the Workspace".)

2.7 Saving the Maestro Project

Maestro "projects" are collections of structures and data that you can save in a designated location and then return to later on. Because structures that you work with in Maestro are copies that are saved to disk in a designated directory, structural changes that you make in Maestro will not affect the actual files that you imported. If you've saved your Maestro project, these copies are saved in the project directory that you specified. Otherwise, the copies are saved in a temporary directory. In this exercise, you'll save your project so that you can return to it later.

1. Click the Save As button on the Project toolbar.



The Save Project dialog box appears.

2. In the File name text box, type a name for your project, such as `tutorial`.
3. Click the Save button.

Changes you make in the project are automatically saved, so there's no need to save the project again later.

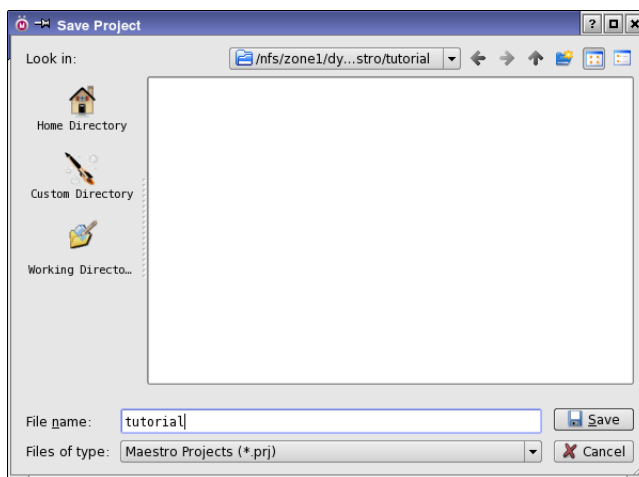


Figure 2.5. The Save As Project dialog box.

If you quit Maestro and want to re-open this project later, click the Open button on the Project toolbar. This opens a project selector so you can select a project.



Building Structures

Once you've mastered the process of starting Maestro and importing structures, you're ready to begin building structures of your own. Maestro's Build panel supports a wide variety of 3D building operations that can be used to easily create any reasonably sized chemical structure that you're interested in. You can even build polypeptides and DNA sequences, although experimentally resolved structures of proteins and other macromolecules are freely available online at <http://www.rcsb.org/>. (For protein sequences without experimentally resolved structures, Schrödinger's Prime program can be used to predict the naturally occurring low-energy protein structure.)

In this chapter, you'll work through the process of creating three familiar analgesic drugs— aspirin, tylenol, and ibuprofen—using Maestro's structure-building tools. For a full description of the Build toolbar and the Build panel with all its various features, see [Chapter 5](#) of the *Maestro User Manual*. If you'd like to learn about using Schrödinger software to prepare experimentally resolved protein structures for calculations, see the *Protein Preparation Guide*.

Building 3D structures is a multi-step process, and for any given structure there are many different ways to create it. This tutorial suggests just one way of building these structures, and is designed to introduce most of the useful facets of the Build panel rather than demonstrate the quickest possible way to build this particular molecule. After you complete the exercises in this chapter, feel free to rebuild these molecules without the aid of the tutorial, and see how the process can differ.

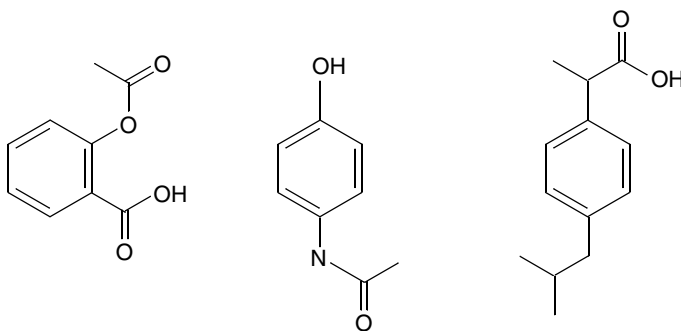


Figure 3.1. Aspirin, tylenol, and ibuprofen.

If you make an error while working through the exercises in this chapter, keep in mind that you can always undo your last action by clicking on the Undo button on the Edit toolbar:



3.1 Displaying the Tools for Building

To begin the exercises in this chapter, we'll display several toolbars we'll need: the Build, Edit, Label, and Fragment toolbars. Then we'll open the Build panel and survey its contents.

1. Click the Edit button on the Manager toolbar.

The Edit toolbar is displayed below the Project toolbar.

2. Click the Workspace button on the Manager toolbar.

The Workspace toolbar is displayed to the right of the Project toolbar.

3. Click the Labels button on the Manager toolbar.

The Labels toolbar is displayed at the top of the Workspace below the Edit toolbar. If the Workspace is getting too small, click and hold on the bottom edge of the panel and drag it down, to make the main window bigger.

4. Click the Build button on the Manager toolbar.

The Build toolbar is displayed on the right of the Workspace.

5. Click the Fragments button on the Manager toolbar.

A toolbar with chemical structures is displayed to the right of the Build toolbar. These structures can be used to build molecules—but you can also build molecules with a much larger variety of fragments in the Build panel, which we'll now open.

6. Choose Edit → Build → Fragments in the main window.

You'll see the Build panel open. It contains the tools you need to perform the first part of the structure-building exercises in this chapter.

The Build panel has three tabs, Fragments, Atom Properties, and Residue Properties. The Fragments tab allows you to build structures with common, predefined substructures in the Workspace with one click—anything from simple organic fragments to more complicated heterocycles. The Atom Properties tab allows you to set element types, formal charges, and so on, although much of this behavior can be performed using the toolbar. The Residue Properties tab can be useful when building polypeptides or refining protein structures, but is generally not needed when building small molecules.

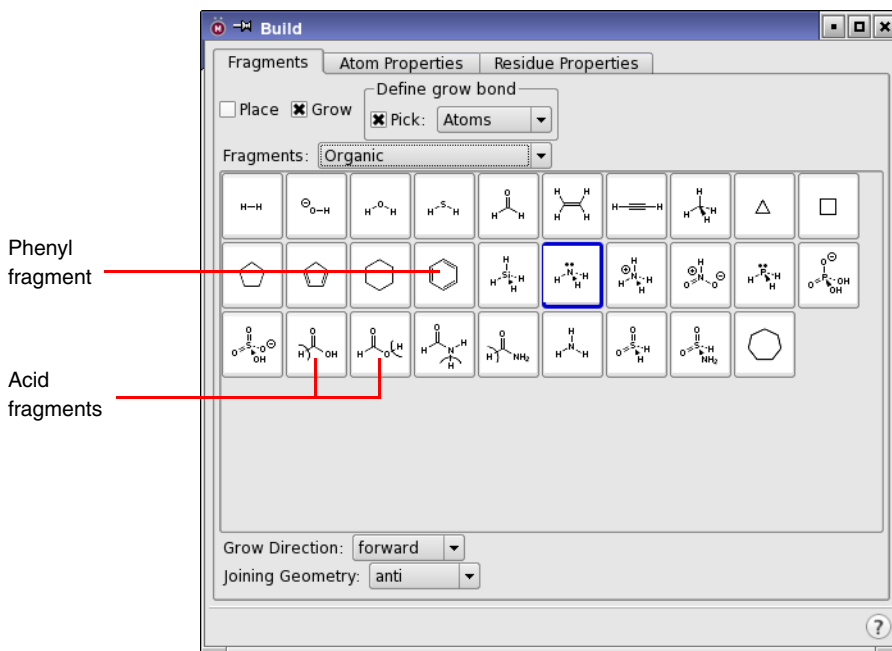


Figure 3.2. The Build panel.

3.2 Clearing the Workspace and Building with Fragments

Now that you've opened the Build panel, you can begin building the structure using Maestro's fragment libraries. These pre-defined groups of substructures and functional groups can be placed in the Workspace or attached to existing structures, eliminating the need to manually add every individual atom in a structure.

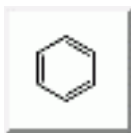
1. Begin by clicking the Clear button on the Workspace toolbar.



This simply “excludes” any structures that may currently be in the Workspace—no atoms or molecules in existing structures are deleted. This button is dimmed if there's nothing in the Workspace, so you don't need to click it.

If you were looking at the other tabs in the Build panel, you'll need to return to the Fragments tab.

2. Click on the Fragments tab.
3. Choose Organic from the menu labeled Fragments (if it isn't already selected).
4. Click on the phenyl fragment in the library in the center of the panel (see [Figure 3.2](#)).

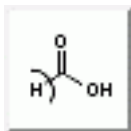


5. To place the fragment, click near the center of the Workspace.

You'll see the complete phenyl ring appear in "wire frame" representation. Carbon atoms are colored gray, and hydrogen atoms are colored white. If you look at the Entry List, you'll see that a new entry has been added. We'll rename it later.

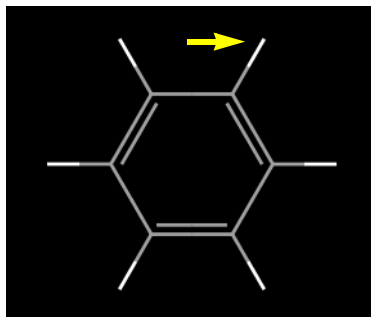
Next, we'll add an acid group to the ring. There are two acid fragments in the Organic fragment library, one for adding at the C–H bond, and the other for adding at the O–H bond. The bond that is replaced is indicated by a curved line.

6. Click on the carboxylic acid fragment whose C–H bond is divided by a curved line.



7. To place this fragment, click on the white hydrogen atom attached to the benzene ring as shown in the figure to the right. (You could click on any hydrogen atom, but using this one will help you follow the diagrams in the rest of the exercise.)

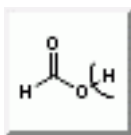
When you move the pointer into the Workspace, it turns into a yellow square with an "A" beside it. The square is the "target area"—when an atom is inside the square and you click, that atom is selected for the operation you are doing.



Once you click, the hydrogen atom is replaced with a carboxylic acid group. Now you have a benzoic acid molecule in the Workspace.

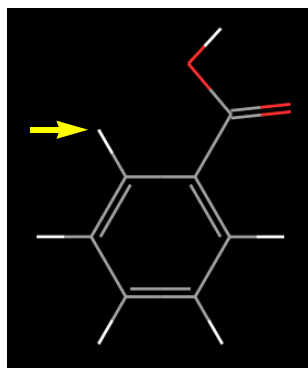
To complete the structure of aspirin, we need to add an acetate group. We can do this by adding the other carboxylic acid group and a methyl group, in two steps.

8. Click on the other carboxylic acid fragment, whose OH bond is divided by a curved line.

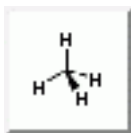


9. Click on the ring hydrogen atom nearest to the OH of the acid group, as shown in the figure to the right.

The acid is added to form an ester, but it is a formate ester, not an acetate ester. The last step is to add a methyl group in place of the formate hydrogen.



10. Click on the methyl fragment.



11. Now click on the hydrogen of the formate group, as shown in the figure to the right.
12. The formate group is converted into acetate. You should now have a structure that looks like the one in [Figure 3.3](#), below.

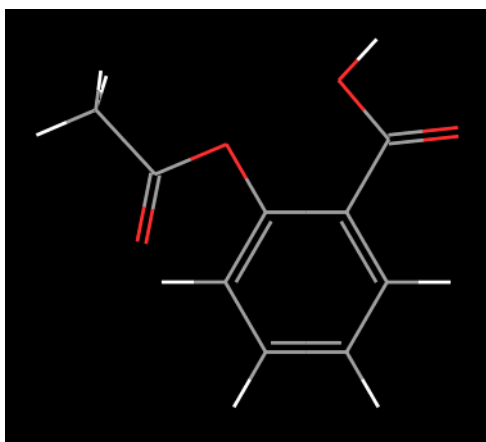
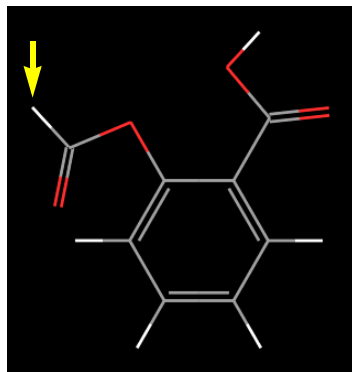


Figure 3.3. The completed aspirin structure.

Congratulations! You've just successfully built aspirin (acetylsalicylic acid) in a few easy steps using Maestro's fragment library. In the following exercises, you'll see how to adjust the positions of the atoms in a molecule and transform this structure into other molecules.

3.3 Adjusting Angles

Some of the angles in the structure you've just built don't look quite right. In this exercise, we'll adjust the C–O–C angle of the ester to make the structure look a bit better.

1. Click and hold on the Adjust button on the Edit toolbar, and choose Angle from the menu that appears.



(If you don't remember how to do this, see the explanation on [page 8](#).)

Notice that the pointer changes to a yellow square with an "A" beside it, to indicate that you are picking atoms, in this case to define the angle.

2. Click on the carbon atom in the ring, then the oxygen atom, then the carbon atom of the carboxylate (see [Figure 3.4](#)).

At each click, a purple box appears around the atom. When you have clicked the third atom, the boxes disappear and the angle is marked with a line over the bonds and an orange arrow, with the value of the angle next to it (see [Figure 3.4](#)).

3. Hold down the left mouse button and move the mouse left or right until the angle is about 120° (this is called "dragging horizontally with the left mouse button").

You'll see the angle and its value change as you move the mouse. The atoms that move are the ones attached to the last atom you picked in [Step 2](#). You can also use the mouse wheel to change the angle.



Figure 3.4. Selecting an angle.

- Click and hold on the Adjust button on the Edit toolbar, and choose Delete Adjustments from the button's menu.



The lines and the arrow that marked the angles disappear from the Workspace. Deleting the adjustment just means to remove the markers, not undo the adjustment itself.

- Finally, click the Adjust button (click and release immediately, not click and hold) to leave adjustment mode.

3.4 Deleting and Labeling Atoms and Adjusting Formal Charge

Acetylsalicylic acid is partially ionized in solution. In this exercise, you'll delete the acidic hydrogen, label atoms with structural information, and adjust the formal charge of an atom.

- Choose Atoms from the Delete button menu on the Edit toolbar.



(If you don't remember how to do this, see the explanation on [page 8](#).)

When you move the pointer into the Workspace, it turns into a square with an "A" beside it, to show that you are picking atoms, which will be deleted.

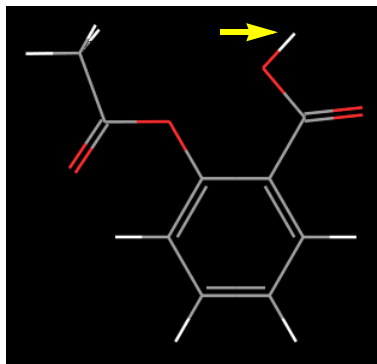
- Click on the acidic hydrogen atom in the Workspace.

The hydrogen atom is removed. If you make a mistake when you delete an atom, you can always click the Undo button to restore it.

- Next, choose Formal charge from the Label All button menu on the Labels toolbar.



You'll notice that no new information appears in the Workspace—that's because the formal charge of all the atoms is still zero. The oxygen atom of the acidic group needs to have a formal charge of -1 for a carboxylate anion.



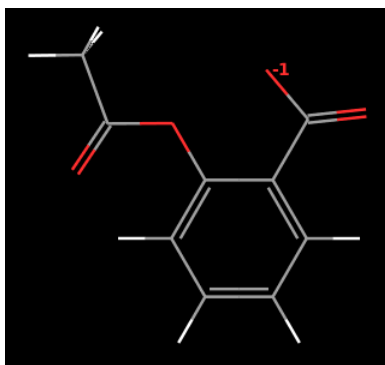


Figure 3.5. The ionized aspirin structure showing the formal charge.

4. Click the Decrement formal charge button on the Build toolbar.



The button is indented. When you move the pointer into the Workspace, it turns into a square with an “A” beside it, to show that you are picking atoms, which will have their formal charge decremented.

5. Click on the oxygen atom that the hydrogen atom was attached to.

You’ll see that the atom is then labeled with formal charge information (see [Figure 3.5](#)).

6. To undisplay the atom labels, choose Delete Labels from the Label All button menu.

Congratulations, you’ve just adjusted the geometry and formal charge of a structure. In the next exercise, you’ll place the structure in the Maestro Project Table.

3.5 Saving Your Structure to the Project

Now that you’ve finished your structure, it’s time to give it a real title. Saving your structure in the project allows you to include and exclude the structure from the Workspace, save it to a structure file, copy it, and add properties to it.

1. Click the title of the Structure2 entry in the Entry List panel.

This is the structure you just created, and it should be in the second row. The title is highlighted, to indicate that the text is selected, and you can edit it.

2. Type “ionized aspirin”, and press ENTER.

The title is changed to the text you typed in.

You might see an information box when you press ENTER. It tells you about applying a value to multiple entries. You can select Do not show this dialog box again, and click OK. The cursor disappears and the background goes back to yellow. The title is now changed.

3.6 Copying and Renaming a Project Entry

For the next few exercises, you'll need a copy of the aspirin structure that you just created. We'll create a copy by duplicating the aspirin entry and renaming it.

1. If the aspirin entry is not selected, click on its title in the Entry List.

The entry should be highlighted in yellow, as in [Figure 3.6](#), to show that it is selected.

2. Right-click on the aspirin entry and choose Duplicate → In Place.

Another row appears in the Entry List, with the same title. This isn't a problem for Maestro, because the entry also has an "entry ID" which is unique, and is used to identify the entry. If you use the Project Table instead of the Entry List, you can duplicate an entry in place with CTRL+D.

Now we'll change the title, so we can tell which entry is which.

3. Click in the Title column of the third row of the Entry List.

The cell background turns white, and the text is highlighted in blue. A cursor appears where you clicked in the text, to indicate that you can edit the contents of the table cell.

4. Change the title to "tylenol" and press ENTER.

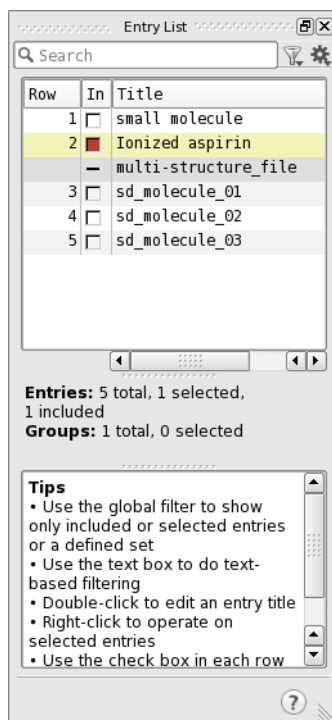


Figure 3.6. The Entry List Panel with the aspirin entry.

3.7 Deleting Bonds and Reattaching Fragments

Now that you have duplicated and renamed the aspirin entry, you can modify the new entry to create another molecule. This process can be useful when you want to make a series of molecules that have a similar core structure but with different groups attached.

In this exercise, you'll move the acetate group from the ortho position to the para position. The new entry should already be in the Workspace, because when you duplicate a single entry, it is automatically included. If the check box beside the tylenol entry is not filled, click on it. Now you're ready to continue.

1. Choose Bonds from the Delete button menu on the Edit toolbar.



(If you don't remember how to do this, see the explanation on [page 8](#).) When you move the pointer into the Workspace, it turns into a square with an "B" beside it, to show that you are picking bonds, which will be deleted.

2. Click on the bond between the ring and the acetate oxygen (see [Figure 3.7](#)).

The bond disappears, and there are two fragments in the Workspace.

3. Click the Delete toolbar button again to exit Delete mode.

Next, we want to move the acetate fragment. Normally, when you move something in the Workspace, everything moves. To move this fragment and leave everything else where it is, we must perform a "local transformation".

4. Choose Molecules from the Transform button menu on the Edit toolbar.



Note that the button is indented, to show that we are doing a local transformation.

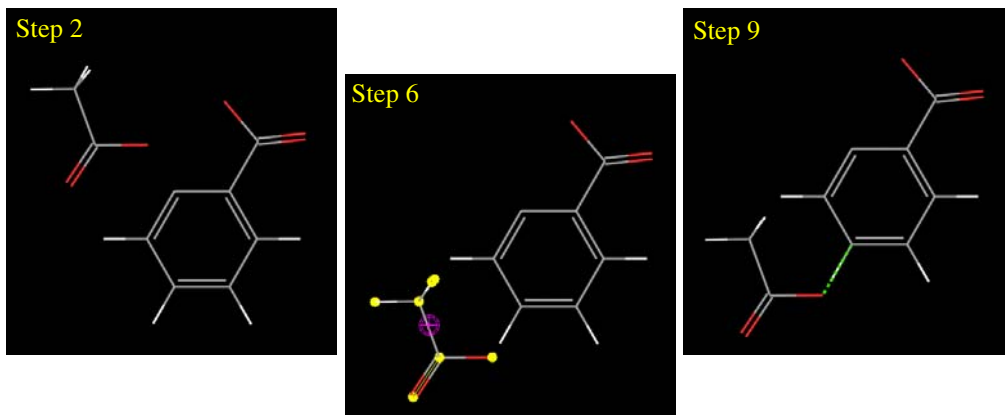


Figure 3.7. Detaching, moving and reattaching the acetate fragment.

5. Click an atom in the acetate fragment.

This selects the acetate molecule for a local transformation. You can now move the fragment without moving the rest of the structure. It's marked in yellow with a magenta circle with crossed lines in it. This circle marks the center around which you can rotate the fragment, if you want. If you don't want to see these markers, deselect Show Markers on the Local transformation button menu. For now we are only going to translate the fragment.

6. Drag the fragment with the right mouse button so that the oxygen atom that was attached to the ring is near the para hydrogen of the ring (see [Figure 3.7](#)).

If you see a menu appear in the Workspace, it means that you were a bit too slow in dragging the fragment. Just release the right mouse button and press it again to drag. If you pressed it while the pointer was over an atom, a yellow dot appears on the atom. To get rid of the dot, click the Select atoms toolbar button, then click in the Workspace; if you didn't finish moving the fragment, click again on the Transform button. These menus are shortcuts to various commands that you can apply to the Workspace or to the selected atoms. We won't be using them, but feel free to explore them.

Now we'll reconnect the acetate fragment to the ring.

7. Choose Edit → Connect and Fuse.

The Connect and Fuse panel opens, docked into the Workspace. If you want to move it out, click the button at the top right that has two rectangles in it. You can then move it to where you want it. To put it back in the Workspace, click the docking button again.

Note that the markers disappear and the Transform button is no longer indented—the mode has been turned off by this panel.

8. Make sure that Pick to define atom pairs and Show markers are both selected.

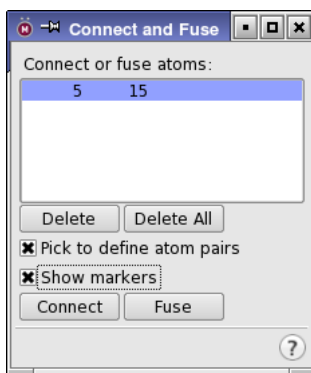


Figure 3.8. The Connect & Fuse panel.

9. Click on the ring carbon atom in the para (or 4) position, then on the singly-bonded oxygen atom of the acetate fragment (see [Figure 3.7](#)).

A purple box appears around the carbon atom on the first click. On the second click, a green dotted line appears between the two atoms (see [Figure 3.7](#)). In the Connect or fuse atoms list in the Connect & Fuse panel, the atom numbers of the two atoms are displayed.

10. Click Connect.

A bond appears between the acetate oxygen and the ring carbon, and the hydrogen that was attached to the ring is deleted. The methyl group of the acetate is very close to the ring. We will adjust the structure later.

11. Close the Connect and Fuse panel.

If you want to connect two molecules with more than one bond, you can select more atom pairs. When you click Connect, a bond is created for each atom pair.

3.8 Adding Hydrogen Atoms to a Structure

Now that the acetate group is joined back on, we need to add a hydrogen atom to the place where it was removed. Although you can add hydrogen atoms one-by-one to a structure, this is unnecessarily tedious. Maestro allows you to automatically add hydrogen atoms wherever they're needed with just a few clicks of the mouse. In this exercise, we'll add the missing hydrogen atom to the ring, where we cut off the acetate group.

Missing hydrogen atoms can be added to any structure in the Workspace by double-clicking the Add H button on the Edit toolbar.

- Double-click the Add H button to build the necessary hydrogen atoms.



The ring carbon atom now has a hydrogen atom attached to it. For more information on the Add Hydrogens feature, see [Section 5.10](#) of the *Maestro User Manual*.

3.9 Substituting Functional Groups in Place Mode

When you built the aspirin structure, you added functional groups by clicking on hydrogen atoms. The new group replaced the hydrogen atom. You can also substitute functional groups in the middle of a molecule, provided they have similar sorts of connections. For example, you can convert a hydrocarbon into an ether by replacing a $\text{-CH}_2\text{-}$ group with an -O- group. In this exercise, you'll convert the acetate group into an acetamide group. This time, you'll use the fragment on the Fragments toolbar. These fragments can be placed in Place mode.

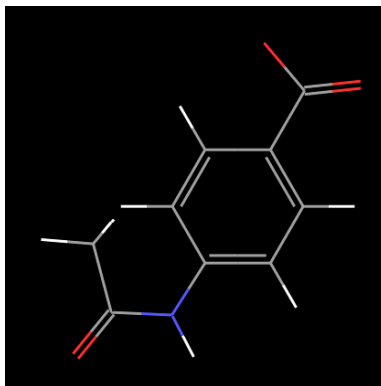


Figure 3.9. The structure after conversion of acetate to acetamide.

1. On the Fragments toolbar, click on the amine fragment.



2. Click on the oxygen atom that connects the acetate group to the ring.

The oxygen atom is replaced with an NH group: the acetate group is now an acetamide group.

3.10 Replacing Functional Groups in Grow Mode

Maestro has two modes for adding or replacing fragments in a molecule, “Place” mode and “Grow” mode. So far, you have been using Place mode, in which you click to place a fragment in the desired location. In Grow mode, the location of the fragment is determined by the “grow bond”, which is displayed in the Workspace as a green arrow. This mode is very useful for rapidly adding fragments to a molecule. All you need to do is to click on the fragment you want to add next, and it’s added to the structure. You can also use Grow mode to replace fragments, which is what you’ll do in this exercise.

1. In the Build panel, select Grow.

A green arrow appears on the C–H bond next to the carboxylate group (see [Figure 3.10](#)). This isn’t the place we want to add a fragment, so we’ll move the grow bond. (It’s possible that the green arrow might be somewhere else, but it doesn’t matter if it is.)

2. Make sure that Pick is selected in the Define grow bond section, and that Atoms is selected on the Pick menu.

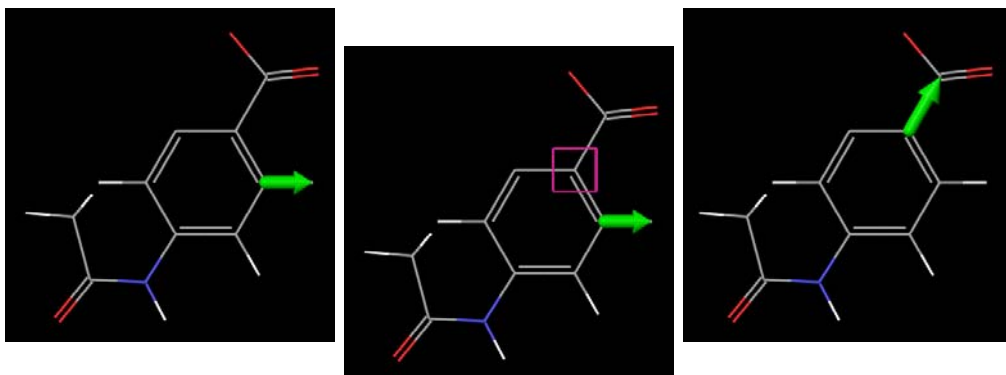
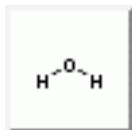


Figure 3.10. Moving the grow bond.

3. Click on the ring carbon that's attached to the carboxylate group, then on the carboxylate carbon (see Figure 3.10).

The green arrow moves to the bond you just picked, and is pointing towards the carboxylate. If you had picked the atoms in the other order, the bond would be pointing in the opposite direction. The atom that the arrow head points to is the one that is replaced.

4. Click on the hydroxyl fragment in the Build panel.



The carboxylate is replaced with a hydroxyl group.

5. Deselect Grow in the Build panel.

3.11 Adjusting a Dihedral Angle

Finally, the acetyl group needs to be rotated around the C–N bond because the methyl group is too close to the ring hydrogen. We'll change a dihedral angle to do this.

1. Choose Dihedral from the Adjust button menu on the Edit toolbar.



2. Click on the carbon atom in the ring that the nitrogen atom is attached to, then the nitrogen atom, then the carbonyl carbon atom, and finally, the oxygen atom (see Figure 3.11).

At each click, a purple box appears around the atom. When you have clicked the fourth atom, the boxes disappear and the angle is marked with a red line over the bonds and a turquoise arrow, with the value of the angle next to it. The angle should be about 180° (it might be plus or minus).

3. Hold down the left mouse button and move the mouse horizontally until the angle is about 0° (or use the scroll wheel on the mouse).

You should see the acetyl group rotate around the C–N bond as you move the mouse.

4. Choose Delete Adjustments from the Adjust button menu on the Edit toolbar.



The lines and the arrow that marked the angles disappear from the Workspace.

5. Finally, click the button again to leave adjustment mode.

Congratulations! You have just turned aspirin into tylenol. You've also learned how to use Grow mode, replace functional groups in both Grow and Place modes, and detach and reattach fragments.

In the remaining exercises, you'll convert tylenol into ibuprofen.

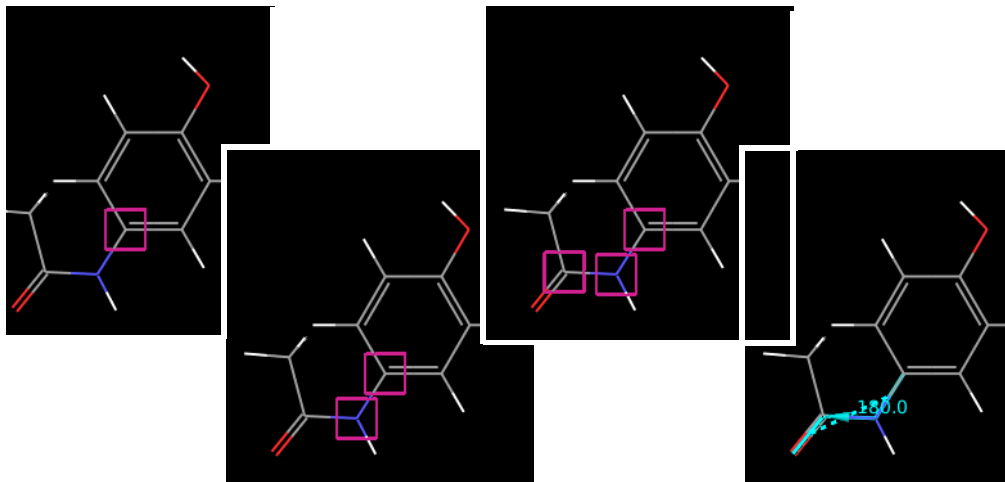


Figure 3.11. Selecting a dihedral angle.

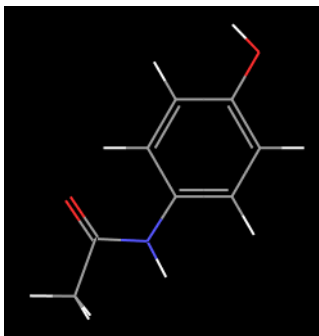


Figure 3.12. The completed tylenol structure.

3.12 Duplicating a Project Entry

Before we go ahead with the structural changes, we need to duplicate the tylenol entry and rename it. This time we'll use the keyboard shortcut for duplication.

1. Make sure the tylenol entry is selected in the Entry List. If not, click on its row number.

The entry should be highlighted in yellow.

2. Right-click on the tylenol entry and choose Duplicate → In Place.

Another row appears in the Entry List, with the same Title. Notice that this row is selected, and the check box in the In column is red, to indicate that this new entry is in the Workspace.

3. Now change the title to "ibuprofen". If you aren't sure how to do this, see [Section 3.6 on page 25](#).

We now have a new entry, and we will convert the structure in it to ibuprofen.

3.13 Changing Bond Orders

So far, we haven't had to change any of the bond orders. The functional groups we added already had the correct bond orders. In this exercise, the first thing to do is to change some bond orders. Maestro has a very easy way of changing bond orders. We're going to experiment with adjusting bond orders while we prepare the structure for the next step.

1. On the Build toolbar, click the - Bond Order toolbar button.



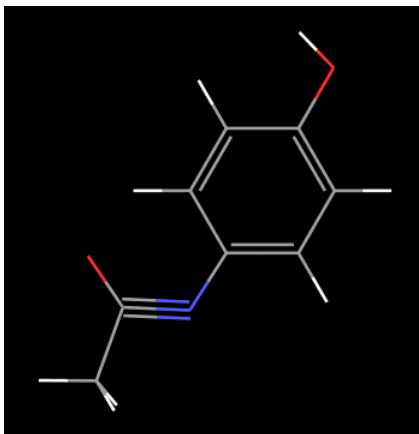


Figure 3.13. The incremented C–N bond showing the valence violation.

- In the Workspace, click on the carbonyl C=O bond.

The double bond turns into a single bond.

- On the Build toolbar, click the + Bond Order toolbar button.



- In the Workspace, click on the C–N bond between the carbonyl carbon and the nitrogen.

You'll see the bond order increase, and the number of hydrogen atoms is automatically adjusted.

- Click again on the carbon-nitrogen bond.

The bond is now a triple bond, but the bonds to the other atoms aren't changed. Maestro lets you violate the valences of atoms when adjusting bonds, because it's sometimes more convenient to increase the bond order of one bond before decreasing the bond order of other bonds. Before you finish changing bond orders, don't forget to make sure that the valences are correct. Now we'll set the bond orders the way they need to be.

- On the Build toolbar, click the - Bond Order button.



- In the Workspace, click twice on the carbon-nitrogen bond.

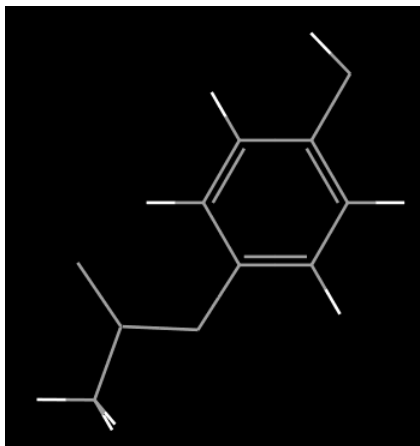


Figure 3.14. The structure after conversion of N and O to C.

The triple bond turns back into a single bond. The hydrogen atoms aren't added back again, so the nitrogen is missing a hydrogen atom. We'll add hydrogens later, when we have finished changing the rest of the structure.

3.14 Changing Elements

Once you've built a molecule, it's possible to change the atoms in the molecule to atoms of a different element without deleting and then rebuilding a substructure. In this exercise, you'll see how to change elements using the Build toolbar. This is the next step in converting tylenol to ibuprofen.

1. Choose C from the Set element button menu on the Build toolbar.



2. Click on the nitrogen atom, then on the two oxygen atoms.

The blue nitrogen atom and the red oxygen atoms are replaced with gray carbon atoms, changing the side chains into hydrocarbon chains. No hydrogen atoms were added to the carbons—we'll add these in a later exercise.

For less commonly modeled elements that aren't available from the toolbar, you can choose Other from the Set element button menu, and then select an element in the periodic table that is displayed, by clicking on it. Clicking on an atom in the Workspace then changes it to the selected element.

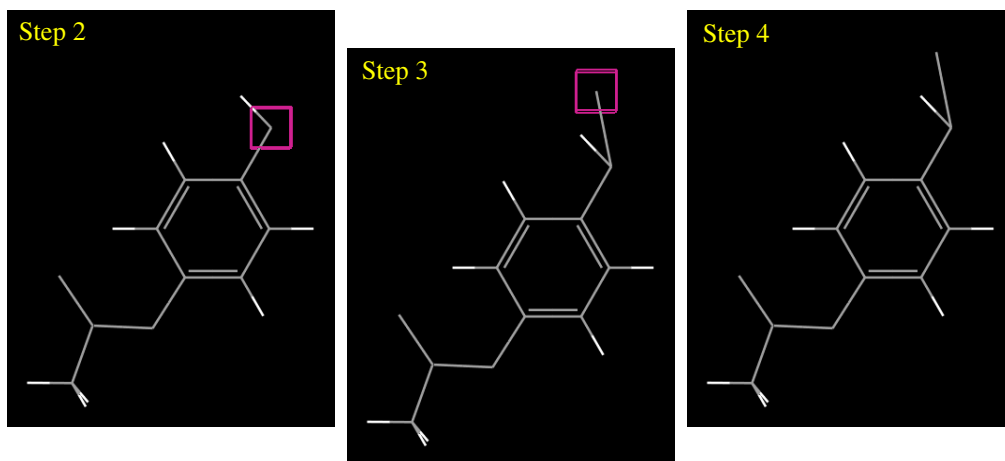


Figure 3.15. Adding a carbon atom by drawing.

3.15 Adding Atoms by Freehand Drawing

Although the Build panel contains a variety of common fragments that can be combined to form complex molecules, it is sometimes useful to build parts of your structure manually. In freehand drawing mode, Maestro allows you to do just that. This exercise will introduce you to the freehand drawing tool as you continue to convert tylenol to ibuprofen. For more information on freehand drawing in Maestro, see [Section 5.4](#) of the *Maestro User Manual*.

1. Click and hold the Draw button on the Build toolbar, and choose C from the menu.



This action sets the element type to carbon. The menu allows you to choose from a variety of common elements, including hydrogen, oxygen, nitrogen, sulfur, and phosphorous.

2. Click on the carbon atom attached to the ring, that only has a hydrogen attached to it (see [Figure 3.15](#)).

A purple box appears around the atom, indicating that you've selected this atom (the "active" atom) as the starting point for the next drawing operation.

3. Click near the hydrogen atom to place a new carbon atom (see [Figure 3.15](#)).

You'll see that a new carbon atom is placed and bonded to the first carbon atom. It's only a carbon atom—it doesn't have any hydrogens attached to it. We'll add those later.

4. Click again on the new carbon atom.

The purple box disappears, to show that you've finished drawing at this location.

We need to add a carboxylic acid group to the carbon atom. We could do this with the fragments, but this time we'll do it by drawing.

5. Click on the same carbon atom as you clicked on in Step 2 (see Figure 3.16).

The purple box around the atom reappears.

6. Click near this carbon atom, but away from the carbon and hydrogen atoms (see Figure 3.16), and click again in the same place to stop drawing.

Another new carbon atom is placed and bonded to the first carbon atom.

Now, we'll change the element we're drawing with to oxygen, so we can draw the acid group.

7. Choose O from the Draw structures button menu on the Build toolbar.



8. Click on the carbon atom you just placed, then click nearby (see Figure 3.16).

A red oxygen atom appears, bonded to the carbon atom, but the bond is only a single bond. We could use the toolbar buttons to increment the bond, but this time we'll draw in the second bond.

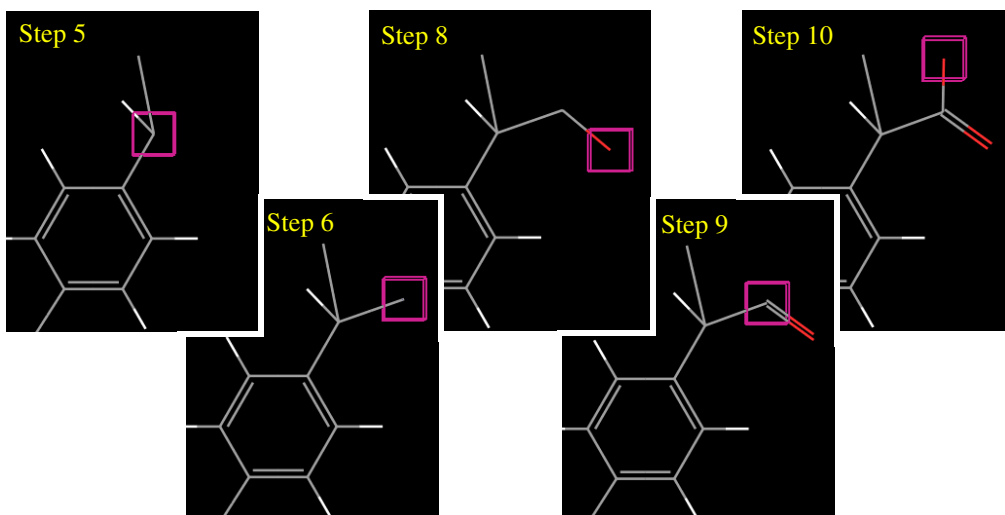


Figure 3.16. Completing the carboxylate group by drawing.

9. Click back on the carbon atom that's bonded to the oxygen (see [Figure 3.16](#)).

The bond changes from a single bond to a double bond, and the carbon atom becomes the active atom. Notice that, even though we are drawing with oxygen, the carbon atom didn't turn into an oxygen atom. If you click on an atom that's already there, it doesn't change to a different element. That's very useful for drawing in multiple bonds—you don't have to worry about which element you have selected.

10. Click again near the active carbon atom, away from the other atoms (see [Figure 3.16](#)).

Another oxygen atom is placed. New atoms are always atoms of the selected element; old atoms keep their elemental identity.

You can also join one atom to another in Draw mode. We'll do this, and then undo the operation.

11. Click on the carbon atom you placed first.

A bond is created, to form a 4-membered ring.

12. Click the Undo button on the Edit toolbar.



The bond disappears, and the purple cube is now on the oxygen atom.

13. Click the active oxygen atom to finish drawing.

Finally, we need to add hydrogen atoms. We could draw in the hydrogen atoms on this structure (and feel free to do so if you like), but as we saw in [Section 3.8](#), Maestro provides a convenient way of automatically adding hydrogen atoms wherever they're needed.

14. Double-click the Add H button to add the necessary hydrogen atoms.



Hydrogen atoms are added to all the carbon atoms that are missing them, and to the singly bonded oxygen in the carboxylate group.

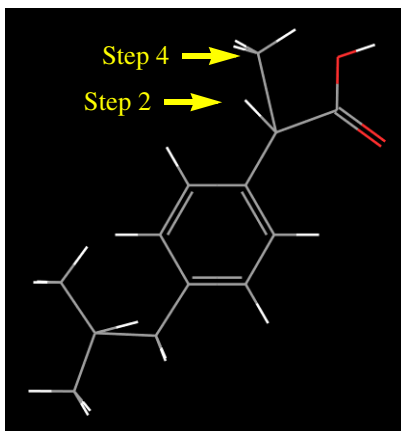


Figure 3.17. The hydrogen and carbon atoms to move.

3.16 Moving Atoms

When you've been drawing atoms, it's usually the case that they aren't in the optimum location—the bond lengths and angles can be far from what they are in the real structure. Also, when you are drawing atoms, they are always placed in the same plane. If you want to place atoms in a different plane, you can rotate the structure and start placing them again, but if they are already in place, you might want to move them. The Build panel provides a tool for moving atoms that have already been placed.

In this exercise, you'll move some of the atoms so that they are in a more realistic location. In the next exercise, you'll use another tool to get much better structures.

First, let's move one of the CH hydrogens out of the plane.

1. Choose $-Z$ from the Move button menu on the Build toolbar.



2. Click on the CH hydrogen atom in the $-\text{CH}(\text{CH}_3)\text{COOH}$ group (see Figure 3.17).

Although it looks like nothing happened, the hydrogen moved 0.5 \AA away from you (in the $-z$ direction) each click. You can rotate the structure to see what happened. Click the Reset button when you have finished looking at the rotated structure.

Next, we'll move one of the methyl groups out of the plane.

- Choose +Z from the Move button menu on the Build toolbar.



- Click twice on the methyl carbon atom in the $-\text{CH}(\text{CH}_3)\text{COOH}$ group.
- Now rotate the structure (middle mouse button) to see what happened.

Notice that the methyl hydrogens moved with the carbon atoms. Groups that are attached to an atom move with the atom.

- Click the Reset button after you have looked at the rotated structure.



Finally, we'll move one of the CH hydrogen atoms in plane.

- Choose XY from the Move button menu on the Build toolbar.



- Click on the CH hydrogen atom in the $-\text{CH}_2\text{CH}(\text{CH}_3)_2$ group (see [Figure 3.18](#)).

A purple cube appears around the atom, to show that it has been selected for movement in the xy plane.

- Click somewhere between the two methyl groups.

The hydrogen atom moves to the new location.

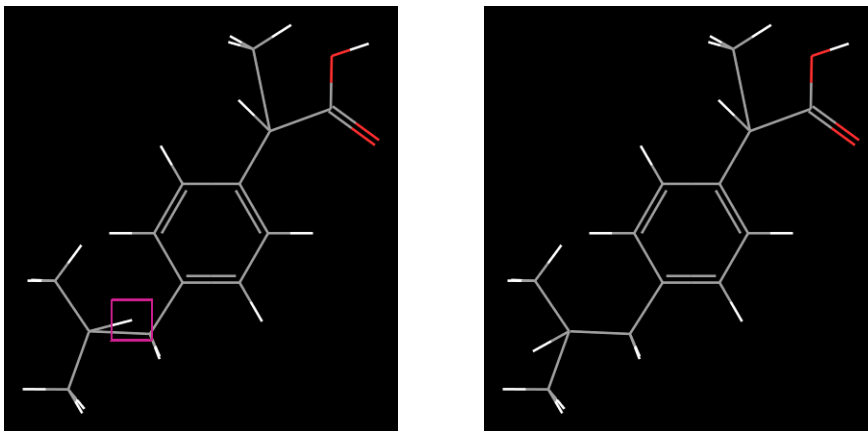


Figure 3.18. Moving the CH hydrogen in the xy plane.

Moving atoms with these tools is useful when you are drawing a structure, so that you get approximately the right geometry, but it doesn't give structures that are close to the "real" structure. In the next exercise, you'll see how to improve the structure.

3.17 Cleaning Up Structures

Maestro's fragment libraries allow you to build molecules out of fragments with optimized geometries, and the structures you create usually have reasonable geometries. When you have been using Draw mode, the structures usually need cleaning up. The Build panel allows you to "clean up" the structure by minimizing its energy using a force field.

- Click the Clean Up button on the Build toolbar.



As the structure is refined, a dialog box appears that says "Cleanup in progress", and you can see the structure changing in the Workspace. When cleanup is finished, notice how the functional groups have moved (see [Figure 3.19](#)).

The cleanup only works for elements in the OPLS force fields. You can use the UFF force field instead by setting a preference in the Preferences panel. This force field is suitable for refining manually built structures, but it offers less accuracy and flexibility than the minimizers and force fields present in software such as MacroModel, and it sometimes doesn't give good geometries for groups that should be planar. Always check your structures after using the UFF force field.

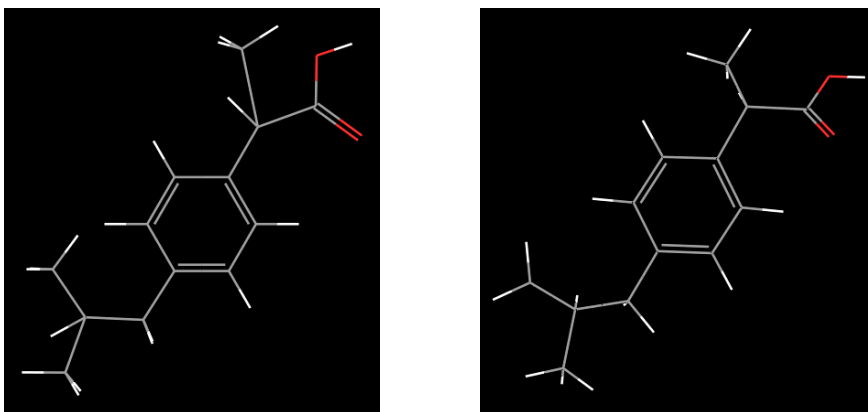


Figure 3.19. The ibuprofen structure before (left) and after (right) cleanup.

3.18 Changing the Chirality

Ibuprofen is a chiral molecule. The configuration at the chiral atom of the actual molecule (the CH carbon atom in the $-\text{CH}(\text{CH}_3)\text{COOH}$ group) is S. We need to check the chirality of this atom, and change it if it isn't correct. First, we'll label the atoms with their chirality labels.

1. Choose Chirality from the Label All button menu on the Labels toolbar.



A label appears on the chiral atom. For the structure that you built, it should be R. If you can't see the label clearly, rotate the molecule.

Now we'll change the chirality from R to S.

2. Click the Invert Chirality button on the Build toolbar.



3. Click on the chiral carbon atom.

The hydrogen and the carboxylate groups are swapped. If you want more control over which groups are swapped, you can choose Chirality from the Adjust button menu on the Build toolbar. Then you pick the chiral atom, followed by the two groups that you want to stay in the same place. On the third pick, the groups are moved.

Congratulations! You have completed the transformation of aspirin to tylenol to ibuprofen, and have learnt how to use most of the tools in the Build panel. In the next few chapters, you'll see how to use some of the other capabilities of Maestro.

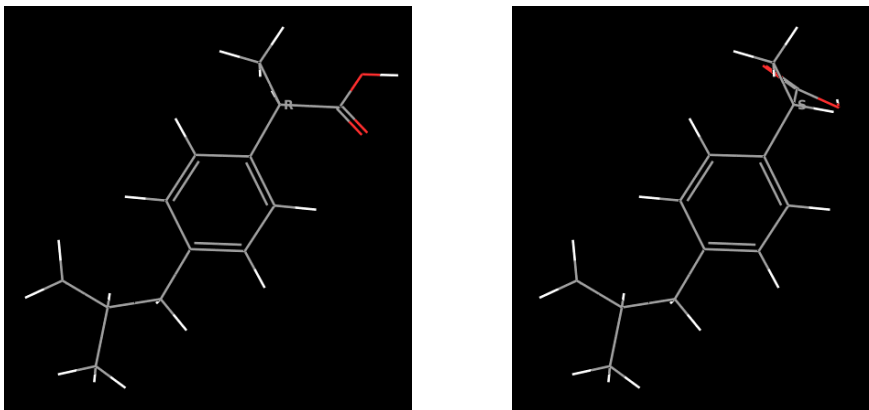


Figure 3.20. Changing the configuration of ibuprofen from R to S.

3.19 Exporting Structures to a File

Now that you've created these three molecules, you can share them by exporting them to a disk file. SD format is used by a number of other programs, so we'll export them in this format.

1. In the Entry List, click the aspirin entry, then shift-click the ibuprofen entry.

The three structures should be highlighted in yellow, which means they are selected.

2. Click the Export Structures button on the Project toolbar to open the Export dialog box.



You can also open this dialog box by choosing Table → Export → Structures in the Project Table panel or by choosing Project → Export Structures in the main window.

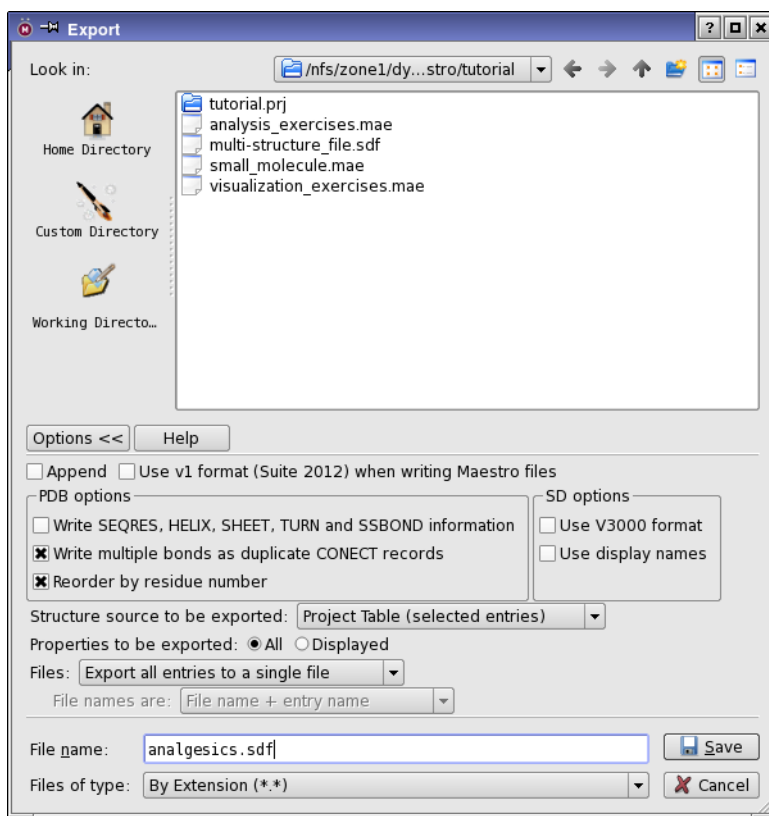


Figure 3.21. The Export dialog box.

Notice that the Files of type option menu setting is By Extension. This means that Maestro will use the extension of the file name (the part after the dot) to determine what kind of file to write. It can recognize many of the common formats. If you want to be sure that it's the right type, you can always make a choice from this option menu.

3. If you want to save the file in place other than your tutorial directory, navigate to the place you want to save the structure.
4. Choose Project Table (selected entries) from the Structure source to be exported option menu.
5. Enter the name `analgesics.sdf` in the File name text box.

The `.sdf` extension tells Maestro that you want to save the file in MDL SD format.

6. Click Save.

The Export dialog box closes and the file should now be saved to disk.

To learn more about exporting your structures, see [Section 3.2](#) of the *Maestro User Manual*.

Changing the Appearance of Structures

Now that you know how to import and build structures using Maestro, you're ready to change the way structures appear in the Workspace. Using Maestro's visualization tools, you can color atoms, change the three-dimensional representation of atoms and bonds, and view molecular surfaces. This section of the tutorial will demonstrate how to make such changes, allowing you to draw attention to important structural features and create presentation-quality graphics.

4.1 Getting Ready for the Exercises in this Chapter

To perform the exercises in this chapter, you'll need to import the structure file `visualization_exercises.mae`. This file includes a protein-ligand complex originally taken from the PDB (Protein Data Bank) and "prepared" using Schrödinger's *Protein Preparation Guide*.¹ This protein-ligand complex contains a protein structure, a ligand, and several active site water molecules. If you haven't already copied this file from the installation subdirectory `maestro-vversion/tutorial`, copy it now from this directory to your working directory.

To import the file into Maestro:

1. Click the Import toolbar button to open the Import panel.



2. Ensure that the file format is set to Common (or to Maestro).
3. Select the file `visualization_exercises.mae` from the Files list.
4. Click Open to import the multi-structure Maestro file.
5. Click the Representation button on the Manager toolbar.
6. Click the Display Atoms button on the Manager toolbar.

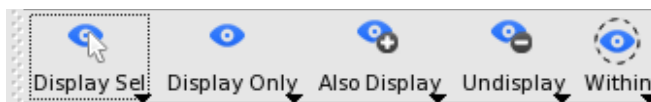
You're now ready to begin the exercises in this chapter.

1. PDB structures are experimental protein structures. The data in these structures can be incomplete: missing hydrogen atoms, formal charges, and so on. The protein preparation process ensures that all atoms are present and have the correct charges and bonding patterns, and can also do other tasks to "clean up" the structures.

4.2 Displaying and Undisplaying Atoms

One of the most common changes you might want to make to the molecular representation is to display or undisplay structural features. In order to draw attention to certain parts of a molecular structure, it is often helpful to display only a portion of the entire structure. Rather than doing so by deleting other parts of the structure, this can be done using Maestro's "undisplay" and "display" tools. These tools allow you to make visible parts of the structure invisible, and to make invisible parts of the structure visible again.

The Display Atoms toolbar includes several buttons for displaying and undisplaying atoms, shown below. This isn't how it looks normally: for this image the style was changed to Text Under Icon and the toolbar was dragged to the bottom of the Workspace. You can even drag a toolbar right out of the Workspace—just grab it by its handle (the dotted part) and drag.



This section of the tutorial will demonstrate how to use these tools. You will use them again in a later part of this chapter.

4.2.1 Using the "Display Only" Buttons

There are two buttons in the toolbar that allow you to display only a subset of the atoms in the Workspace. These buttons are the Display Sel button, which allows you to select individual groups of atoms for display, and the Display Only button, which allows you to choose predefined structural feature types for display.

This exercise demonstrates how to use these toolbar buttons.

When you imported the file in the previous exercise, it should have been automatically included in the Workspace. If it wasn't, open the Project Table panel and include the entry Protein-ligand complex. See [Section 2.6 on page 13](#) for more information on including and excluding entries.

1. Choose Atoms from the Display Sel button menu (see the figure above).



(If you don't remember how to do this, see the explanation on [page 8](#).) When you move the pointer into the Workspace, you should see a yellow square with the letter "A" next to it, indicating that you can select atoms in the Workspace.

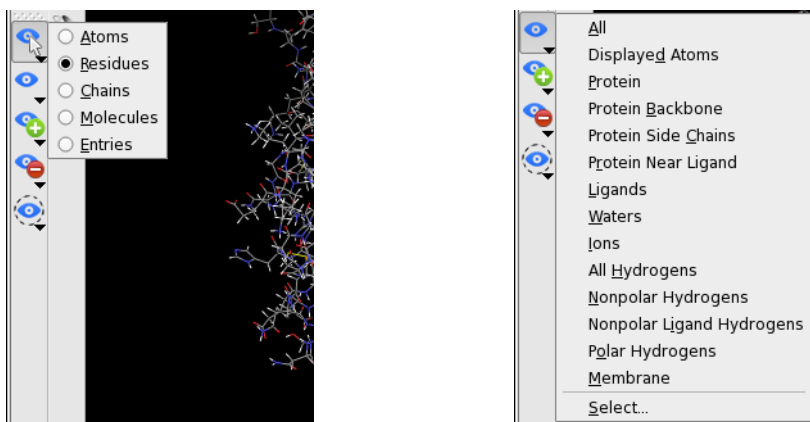


Figure 4.1. Display Sel and Display Only button menus.

2. Hold down the left mouse button, drag the pointer over any set of atoms in the Workspace (creating a dotted yellow box), and let go of the left mouse button.

The atoms that were not within the yellow box are undisplayed—only the atoms that you selected remain visible.

3. Choose All from the Display Only button menu (see the figure on [page 46](#)).



All atoms in the Workspace are displayed again.

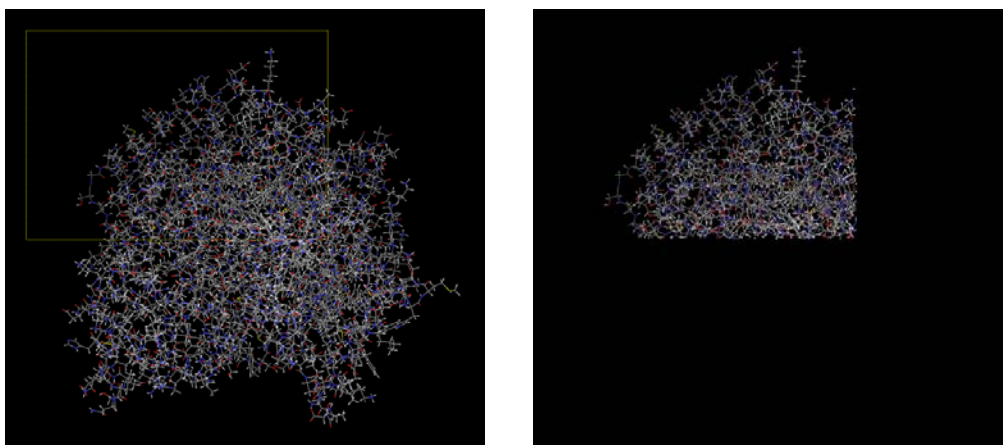


Figure 4.2. Atoms selected for display (left) and the result (right)

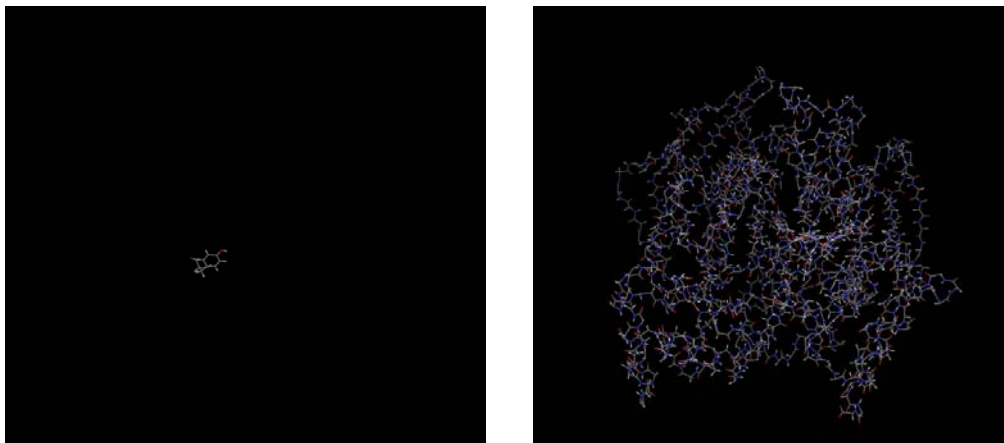


Figure 4.3. Residue displayed (left) and protein backbone displayed (right).

4. Choose Residues from the Display Sel button menu.

In a protein, a “residue” typically refers to a single amino acid subunit, a ligand, a water molecule, or a cofactor. When you move the pointer into the Workspace, you should see a yellow square with the letter “R” next to it, indicating that you can select residues in the Workspace.

5. Click on any one atom in the Workspace.

Maestro displays only the residue that contains the atom you clicked on. All other atoms are undisplayed.

6. Choose Protein Backbone from the Display Only button menu.

Now only the protein backbone is visible, and all other atoms are invisible.

7. Choose All from the Display Only button menu, to redisplay all atoms.

The toolbar buttons behave similarly when other modes are selected from the button menus. For example, if you choose Molecules from the Display only selected atoms button menu, you can click on any molecule in the Workspace, and all other molecules will be undisplayed.

4.2.2 Using the Other Display Buttons

In the previous section we saw how to display only a certain set of atoms in a single operation. However, Maestro also allows you to display subsets of invisible atoms without undisplaying any currently visible atoms, and to selectively undisplay a subset of currently visible atoms. These actions can be performed using the Also Display and Undisplay toolbar buttons.

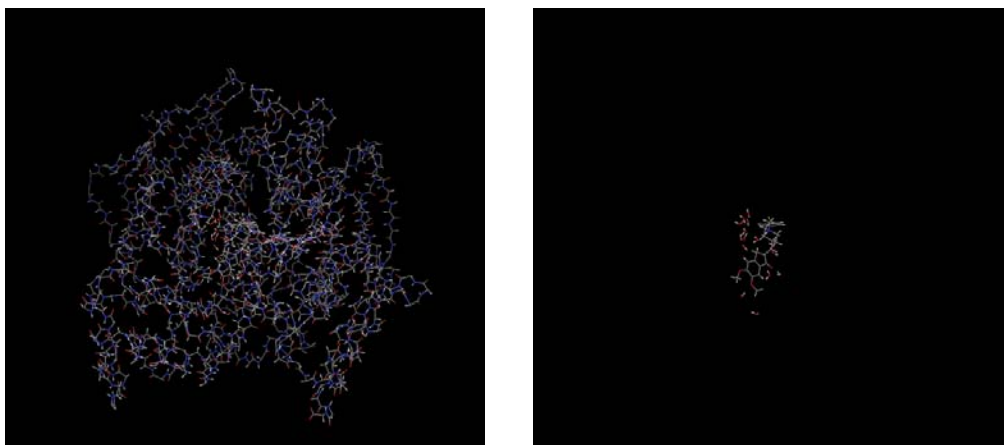


Figure 4.4. Protein side chains undisplayed (left) and entire protein undisplayed (right).

Maestro also allows you to display atoms within a given distance of any currently displayed atoms. This can be done using the Within toolbar button.

This exercise demonstrates how the Also Display, Undisplay, and Within toolbar buttons can be used to selectively display the structural features that you are interested in.

1. Choose All from the Also Display button menu.



This is to make sure that all atoms are displayed. Note that this operation will have no apparent effect if you displayed all atoms at the end of the previous step.

2. Choose Protein Side Chains from the Undisplay button menu.



Observe that the protein backbone, ligand, and water molecules are now visible, but the side chains have disappeared.

3. Choose Protein Backbone from the Undisplay button menu.

The protein backbone has disappeared, and only the water molecules and the ligand remain visible in the Workspace.

4. Choose Waters from the Undisplay button menu, to undisplay the water molecules.

Only the ligand remains visible in the Workspace.



Figure 4.5. Ligand only (left) and ligand with residues within 4Å (right).

Now that the ligand is the only molecule displayed in the Workspace, we can use the Within toolbar button to display the active site features.

5. Choose +4 Å from the Within button menu



Residues that have any atoms within 4 Å of the currently displayed ligand are now visible. These residues are all part of the active site, and include some water molecules.

6. To display the remaining water molecules without undisplaying any of the currently visible atoms, choose Waters from the Also Display button menu.

Observe that the ligand, active site residues, and waters are all visible. If you want to enlarge the view of the structure, click the Fit button.



7. To display the protein backbone without undisplaying any of the currently visible atoms, choose Protein Backbone from the Also Display button menu.

Observe that the protein backbone, ligand, active site residues, and water molecules are all visible. To view the entire structure, click the Fit button again.

Now that you know how to operate the various tools that control atom visibility, you can apply the same basic steps when working with structures of your own. Keep in mind that there may

be more than one way to display or undisplay any given set of atoms—feel free to use whatever method works best for you. We’ll be using many of these controls again in a later exercise.

You may have noticed that most of the menus for the toolbar buttons described in the above exercises all had an option called **Select**. When you choose this option, Maestro opens the **Atom Selection** dialog box. This tool allows you to select combinations of atoms that are a bit more complicated than those in the tutorial examples. To learn more about the **Atom Selection** dialog box, see [Section 6.5](#) of the *Maestro User Manual*.

4.3 Changing the Atom Coloring Scheme

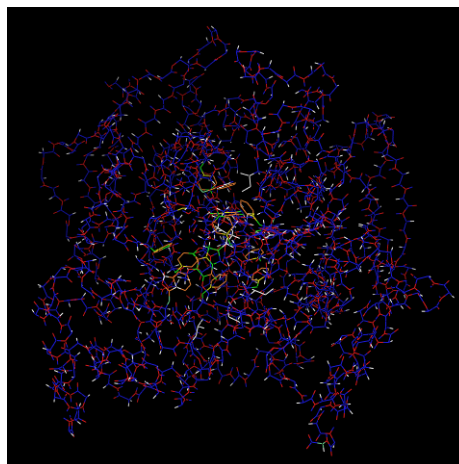
When working in a three-dimensional modeling environment, you can use color to show information about a structure. In most cases, Maestro uses an element-based coloring scheme by default. In this exercise, we’ll use atom coloring schemes to visualize information about our protein structure. Right now, the color scheme represents the elements in the Workspace structure, but it can also tell you about calculated and experimental structural properties.

1. Choose **Atom Partial Charge** from the **Color Scheme** button menu on the **Representation** toolbar.



The atoms are colored by their partial charge. The correspondence of the colors to the partial charges is shown in the table below. The partial charge is an estimate of the “real” charge on an atom, as opposed to the “formal” charge, which is always an integer and is derived from valency rules. These partial charges came from a MacroModel calculation.

Color	Charge Range
blue	$\geq +0.25$
aquamarine	+0.15 to +0.25
green	+0.05 to +0.15
white	-0.05 to +0.05
yellow	-0.15 to -0.05
orange	-0.25 to -0.15
red	≤ -0.25



Another property that can be visualized using color is the “*B* factor” that was experimentally determined when the protein structure was resolved. The *B* factor is a measure of how mobile a particular region of a protein is. Side chains and loops, for example, tend to have higher *B* factors while the relatively rigid helix and sheet regions of the protein backbone tend to have lower *B* factors.

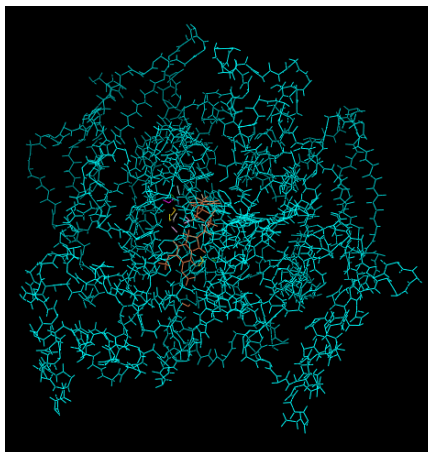
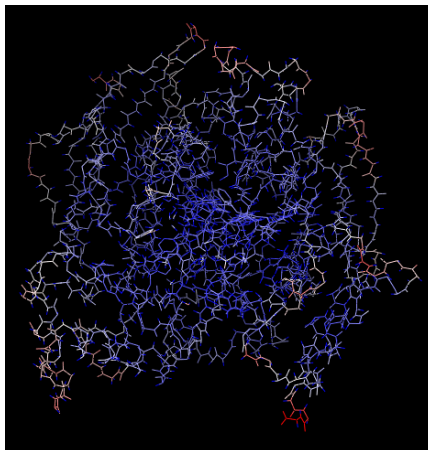
2. To view the *B* factors, choose Atom PDB B Factor (Temperature Factor) from the Color Scheme button menu.

The color scheme used by Maestro ranges from blue for low values through white at values in the mid 30s, to red for high values, above about 60.

Color schemes can be useful for identifying parts of the displayed structure. In a big molecule like this protein-ligand complex, it's hard to tell what's the protein, what's the ligand, and what's something else. Each of these pieces is usually a separate molecule, so you can color them by molecule number to tell which is which.

3. Choose Molecule Number from the Color Scheme button menu.
4. To return to the element-based coloring scheme, choose Element from the Color Scheme button menu.

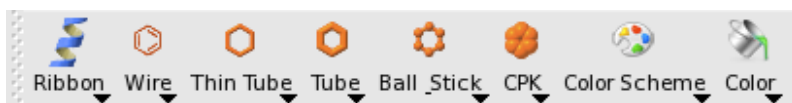
Using the Atom and Bond Coloring panel, it's possible to apply custom color schemes to structures. For more information on using the Atom Coloring panel, see [Section 7.2](#) of the *Maestro User Manual*.



4.4 Changing the Appearance of Atoms and Bonds

Prior to this section, the tutorial operations were all performed using a simple “wire frame” representation for molecular structures. In this section, you’ll learn how to represent atoms and bonds as spheres and tubes. Not only can you make it easier to view the structure by changing the way that atoms and bonds appear, but you can also use various representation modes to differentiate substructures in the Maestro Workspace.

The Representation toolbar (shown below) includes several buttons used to control the representation of atoms and bonds in the Workspace. Structures can be represented as wires, space-filling CPK atoms, balls and sticks, or tubes.



To begin this exercise, you will need to ensure that you can see the ligand and the water molecules clearly. Follow the instructions below to set up the Workspace for this exercise.

1. Zoom in on the ligand until it occupies a large part of the Workspace. (Use the mouse wheel, or drag horizontally with the middle and right mouse buttons.)
2. Right-click on an atom in the middle of the ligand, to center the ligand in the Workspace.

Now we’ll start changing the representation. First, we’ll display the structure in Ball & Stick representation instead of wire frame, and then convert the protein back to wire frame.

3. Double-click the Ball & Stick button menu (page 54, upper left).

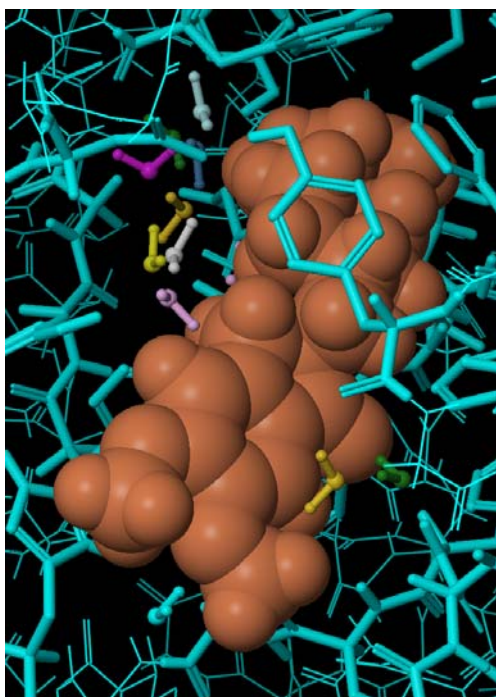
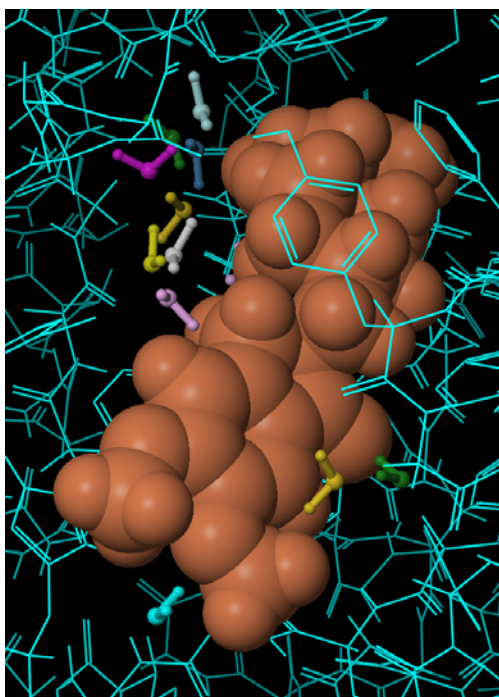
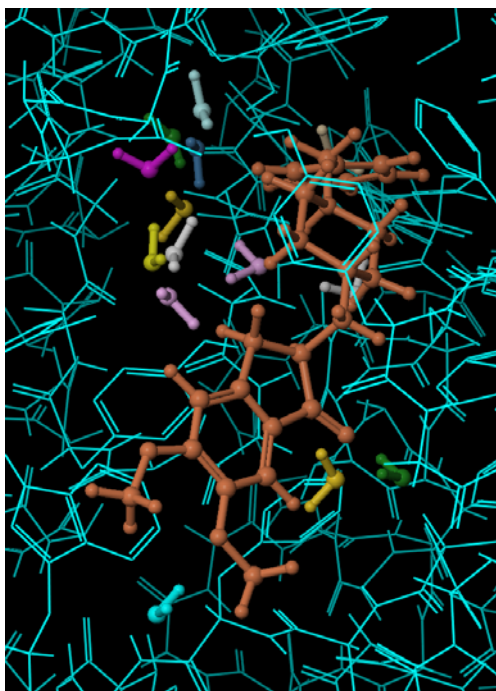
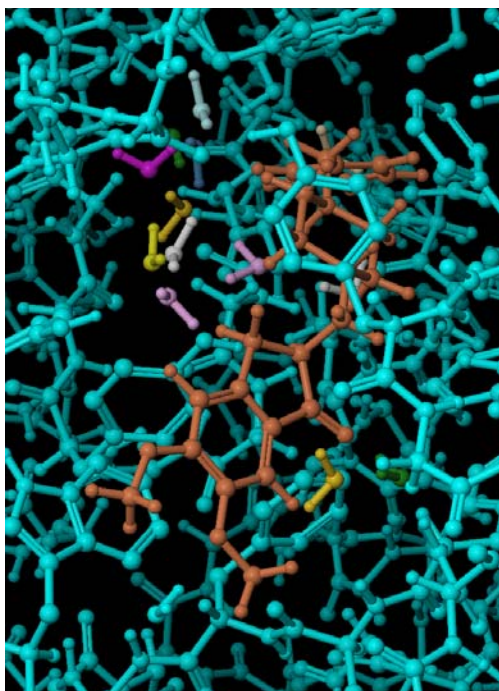
Double-clicking applies the action of the button to all atoms in the Workspace. You can use a double-click for all four representation buttons.

4. Choose Protein from the Wire button menu.

Observe that both the protein backbone and active site residues are displayed as wires, but the ligand and the water molecule remain unchanged (page 54, upper right). The ligand and water molecules are now much easier to distinguish from the protein.

Next, we’ll change the representation of the ligand and the residues in the active site.

5. To represent the ligand using space-filling CPK atoms, choose Molecules from the CPK button menu, and click on any atom in the ligand (page 54, lower left).
6. To represent active site residues as tubes, choose Protein Near Ligand from the Tube button menu (page 54, lower right).



Beyond the options on the Representation toolbar, it is also possible to customize settings such as the width of tubes, the size of spheres, and so on. For more information on changing these settings, refer to [Section 7.3](#) of the *Maestro User Manual*. In addition, the Style toolbar can be used to automatically apply molecular representations or styles to the Workspace (see [Section 7.6](#) of the *Maestro User Manual*).

4.5 Displaying the Protein Backbone as a Ribbon

In addition to representing atoms and bonds using 3D features, Maestro can also represent protein backbones using three-dimensional “ribbons”. Ribbons can be turned on or off using the Ribbon button on the Representation toolbar:



In this exercise, you’ll represent the protein backbone using a ribbon.

1. Click the Fit toolbar button, so you can see all of the protein.



2. From the Ribbon button menu, choose Show Ribbons for All Residues.

The protein is now represented by ribbons that trace the protein backbone. The ligand and the water molecules remain in their previous representation.

Color schemes
for ribbons

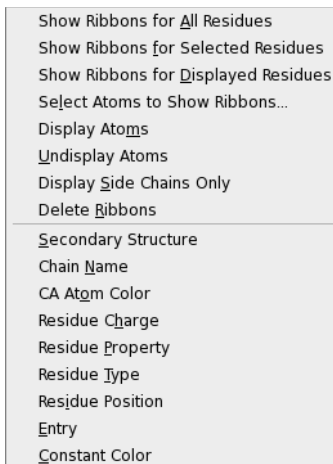


Figure 4.6. Ribbon button menu.

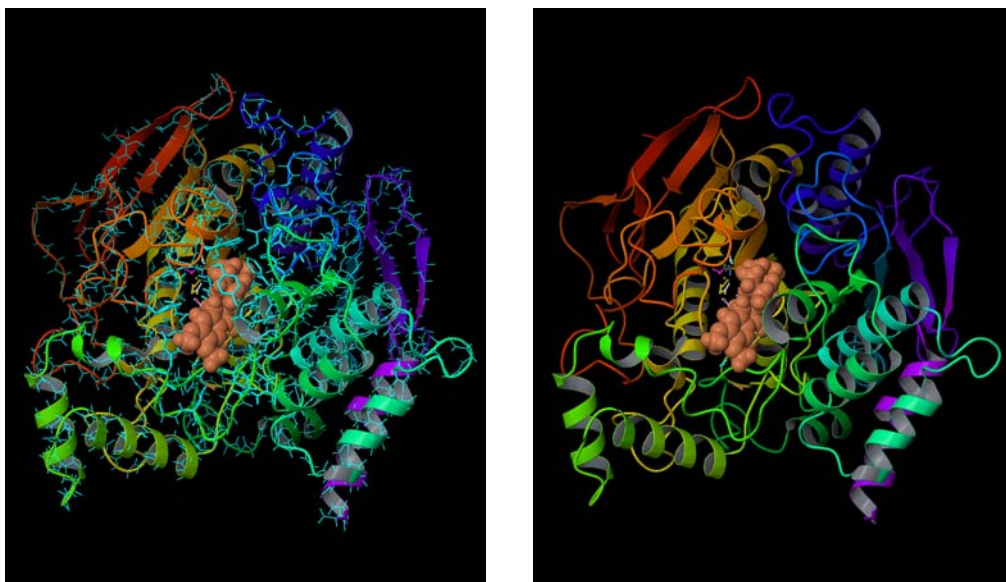


Figure 4.7. Ribbon representation of protein with atoms (left) and without (right).

3. Choose Undisplay Atoms from the Ribbon button menu.

The protein atoms are hidden, and only the ribbons are displayed. Observe that the ribbon follows the protein backbone.

4. Choose Display Atoms from the Ribbon button menu.

5. Choose Delete Ribbons from the Ribbon button menu.

The ribbons disappear, leaving the atoms on display.

The default coloring scheme for ribbons is to color according to residue position. As you follow the ribbon along, you'll see the colors progress through the spectrum as the residue number increases. The menu on the ribbons button includes alternate coloring schemes that you can select.

Once you have experience with Maestro's ribbon rendering options, you may wish to further customize the look and feel of protein ribbons. For more information on doing so, see [Section 7.3.2](#) of the *Maestro User Manual*.

4.6 Creating and Displaying a Molecular Surface

In addition to custom rendering for higher-level structural features like protein backbones, Maestro can also represent the “surfaces” that are created by groups of molecules. Surfaces can represent the volume of a molecule as approximated by van der Waals radii. Surfaces can also display properties such as the electron density created by programs like Jaguar. In this example, we’ll create and visualize a “molecular surface,” which is a smooth, contiguous surface that represents the solvent-accessible area presented by a structure. We’ll use the protein from the previous exercise, so leave the structure in the Workspace.

1. Choose Workspace → Surface → Molecular Surface in the main window.

The Molecular Surface panel opens, docked into the Workspace.

The area at the top titled Atoms for surface display is used to define the structure for which Maestro creates a surface. For this exercise we’ll select the protein structure only:

2. Choose Molecules from the Pick option menu.
3. Click on any atom in the protein to select the entire protein.

The wire bonds in the protein are temporarily colored a purple color, to show that they have been selected for the surface. Note that the text in the text box is automatically filled in when you click on the protein. The text describes the atoms you selected, in “Atom Specification Language”. If you want to be more selective in the atoms you choose, you can click the “plus” button, which offers a range of predefined atom groups, and can also be used to open the Atom Selection dialog box. For more information, see [Section 6.5](#) of the *Maestro User Manual*.

The rest of the settings can be left at their default values. For large molecules such as proteins, the default image quality setting of Low is usually appropriate. For small molecules, higher quality settings may be useful.

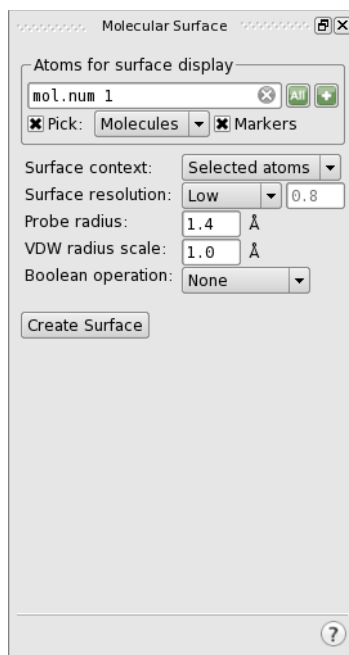


Figure 4.8. The Molecular Surface panel.

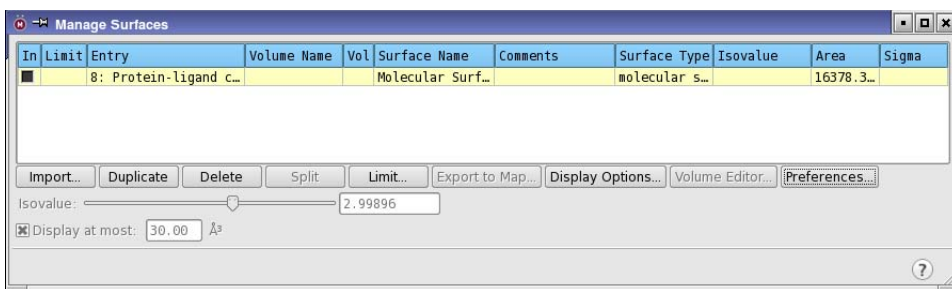


Figure 4.9. The Manage Surfaces panel.

4. Click Create Surface to generate the molecular surface.

Notice that you can still see where the ligand atoms are. This is because the surface doesn't cover these atoms: we chose to put a surface on only the protein.

5. Click Close to close the Molecular Surface panel.

Next, we'll experiment with the color and transparency of this surface. To do this, we need to open the Manage Surfaces panel.

6. Choose Workspace → Surface → Manage Surfaces in the main window.

The Manage Surfaces panel opens. It lists the surfaces associated with the current entry. The properties of the surface can be changed in the Display Options dialog box.

7. Click the Display Options button near the bottom of the Manage Surfaces panel.

The Surface Display Options dialog box opens.

8. Select Green from the Color option menu, and click Apply.

The surface is colored green. The dialog box remains open so you can make more changes.

9. Use the Transparency slider to set the transparency to 25 (twenty-five percent transparent).

10. Select Light Blue from the Color option menu.

11. Click OK to accept and view the changes (see [Figure 4.10](#)).

The dialog box closes and the changes are applied. If you want to experiment more with the display options, click Apply instead. The dialog box remains open, and you can make whatever other changes you would like to make.

Once you've viewed the surface, control-click the square in the leftmost column of the Manage Surfaces panel to undisplay the surface.

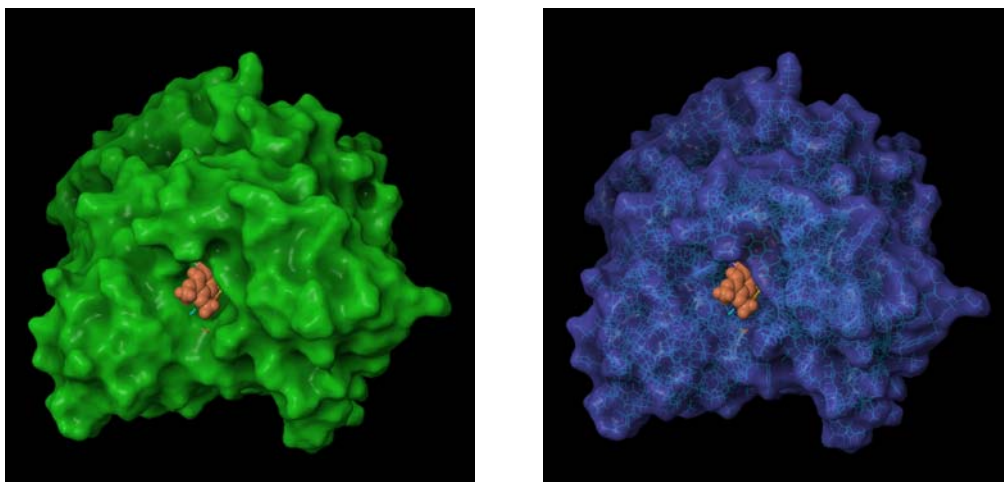


Figure 4.10. Molecular surface, green at 0% transparency (left) and light blue at 25% transparency (right).



Figure 4.11. The Surface Display Options dialog box.

12. Close the Manage Surfaces panel (click the close button on the title bar).

Maestro is also capable of generating several other surface types. The interfaces used to create these surfaces are generally similar to the Molecular Surfaces panel, and all settings for the generated surfaces are controlled via the Manage Surfaces panel. For more information on creating and viewing surfaces using Maestro, see [Chapter 12](#) of the *Maestro User Manual*.

Measuring, Analyzing, and Superimposing Structures

Once you're satisfied with the way that your structures appear in the Workspace, you can go on to examine the structures and their properties. For example, you can examine the geometric differences between two conformations of a molecule by superimposing them, or you can have Maestro display the hydrogen-bonding interactions between a ligand and a receptor. In this chapter, we'll start with basic operations like measuring distances and angles before performing more complicated structural analyses.

For more information on the full extent of Maestro's analysis capabilities, see [Chapter 10](#) of the *Maestro User Manual*.

5.1 Getting Ready for the Exercises in this Chapter

To perform the exercises in this chapter, you'll need to import the structure file `analysis_exercises.mae`. This is a multi-structure file that includes several small molecules, a set of conformations created by MacroModel, and a ligand that has been docked to a protein structure using Glide.

To import the file into Maestro:

1. Click the Import toolbar button to open the Import panel.



2. Ensure that the file format is set to Maestro.
3. Select the file `analysis_exercises.mae` from the list.
4. Click Open to import the multi-structure Maestro file.
5. Open the Project Table panel by clicking the Table toolbar button.



In this exercise, you'll use the Project Table panel rather than the Entry List panel. The Project Table has an easy-to-use set of controls that allow you to record structure-related properties, present the results of calculations, and include and exclude entries in the Workspace. The exercises in this chapter will walk you through any necessary Project Table manipulations, but for more information on the Project Table, see [Chapter 9](#) of the *Maestro User Manual*.

Row	In	Stars	Title	Entry ID	PDB ID	QM Method	QM Basis	Potential Energy-MMFF94s
4	<input type="checkbox"/>	☆☆☆☆	ibuprofen	7				
5	<input type="checkbox"/>	☆☆☆☆	Protein-ligand complex	8	1EVE			
1 - multi-structure_file [3]								
6	<input type="checkbox"/>	☆☆☆☆	sd_molecule_01	2				
7	<input type="checkbox"/>	☆☆☆☆	sd_molecule_02	3				
8	<input type="checkbox"/>	☆☆☆☆	sd_molecule_03	4				
2 - analysis_exercises [4]								
9	<input checked="" type="checkbox"/>	☆☆☆☆	Small Molecule 01	13		HF	6-31g**	
10	<input type="checkbox"/>	☆☆☆☆	n-propanol anti	14				-26.95
11	<input type="checkbox"/>	☆☆☆☆	n-propanol staggered	15				-23.02
12	<input type="checkbox"/>	☆☆☆☆	Protein with Glide-docked ligand	16				-23.02

Figure 5.1. The Project Table panel with the new entries.

We'll be using the Project Table quite a bit in these exercises, so we're going to leave it open. If it gets in the way, you can move it, or you can close it and reopen it when you need to use it again. To close the Project Table panel, click the Table button on the Project toolbar (it should be indented), or use the close button on the title bar of the panel.

You're now ready to begin the exercises in this chapter.

5.2 Measuring Distances

One simple analysis task is to determine the distance between two atoms. These can be any two atoms, bonded or non-bonded. In this example, we'll use the Measure button on the Labels toolbar to determine bonded and non-bonded interatomic distances on a structure that has been optimized using Jaguar.

To begin, we'll make sure that the appropriate Project Table entry is included in the Workspace.

1. In the Project Table, find the entry named Small Molecule 01.
2. If the check box in the In column for this entry isn't filled in, click it to include this entry in the Workspace and exclude all others.

You might find that the molecule is included but it's not very big. If the molecule doesn't fill most of the screen, click the Fit to Workspace button to make sure it's big enough.



3. Choose Distance from the Measure button menu on the Labels toolbar.



(If you don't remember how to do this or are starting with this chapter, see the explanation of how to use button menus on [page 8](#). If the Labels toolbar isn't displayed, click the Labels button on the Manager toolbar.)

4. Click on any atom in the Workspace.

A purple cube appears over the atom, to indicate that you have selected it as the starting point for your measurement.

5. Click on an atom that is bonded to the atom you've just selected.

A dashed marker appears between the atoms, and the interatomic distance (measured in angstroms) is displayed over the marker. If you rotate the molecule in the Workspace (by holding down the middle mouse button and moving the mouse), you'll see that the measurement marker moves with the structure.

Next, we'll measure a distance between two non-bonded atoms. Because the measurements tool is still active (the Measure button is indented to show this), with Distance selected, you don't need to repeat the process of selecting Distance from the toolbar button menu.

6. Click on the same atom that you clicked on in [Step 4](#).

Note that the purple box appears again, indicating that you've selected this atom as the starting point for your measurement.

7. Now click on any atom in the Workspace that's not bonded to the atom that you clicked on in the previous step.

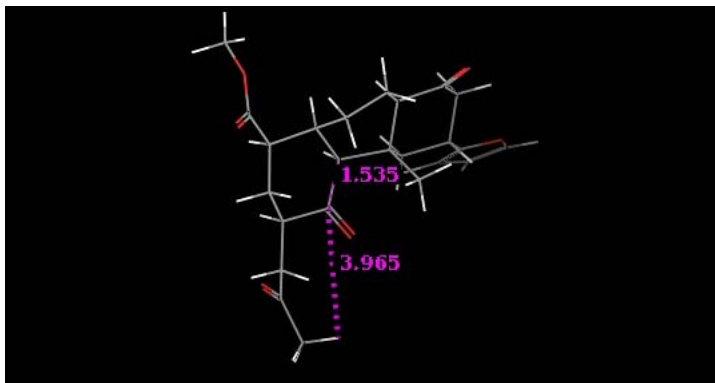


Figure 5.2. Distance measurements.

You'll see that a new distance marker appears between the two atoms that you just clicked on. You may also have noticed that the width of the original measurement marker decreased when you made the new measurement. This is because the wide dashed lines simply indicate that this is the most recently measured distance.

Finally, after measuring the distances, we can remove the markers from the Workspace.

8. Choose Delete Measurements from the Measure button menu.

The structure remains in the Workspace unchanged, and the distance markers disappear.

5.3 Measuring Angles

Another easily performed analysis task is angle measurement. In this example, we'll use the structure from the previous exercise to see that angles can be measured in much the same way that distances can be measured.

1. Choose Angle from the Measure button menu.



2. Click the oxygen of the carbonyl near the middle of the molecule.

You'll notice that a purple cube appears to indicate that you've selected an atom to begin an angle measurement.

3. Click the carbonyl carbon atom.

You'll see a second purple cube appear, indicating that you've selected the clicked atom to be part of your angle measurement. This second atom clicked will always be the vertex of the angle that is measured.

4. Finally, click on a carbon atom that is bonded to the atom you picked in the last step.

After you click on the third atom, the purple cubes vanish, and a green angle marker appears.

If you like, you can define several other angle measurements on the structure. Just like distance measurements, multiple angle measurements can appear in the Workspace at any given time, and you can measure angles between non-bonded atoms.

5. Finally, delete the angle markers from the Workspace by choosing Delete Measurements from the Measure button menu.

The angle markers disappear, and the structure remains unchanged in the Workspace.

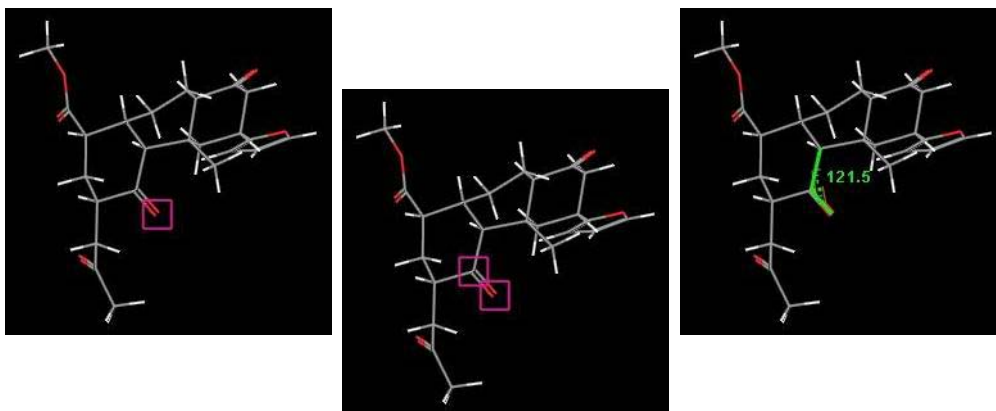


Figure 5.3. Measuring an angle.

5.4 Measuring Dihedrals

Once you know how to measure distances and angles, it's a simple matter to measure a dihedral angle, the torsion defined by any four atoms. For this example, we'll measure the dihedral angles in two different conformations of n-propanol. We'll begin this exercise by placing one of the n-propanol structures in the Workspace.

1. Locate the entry n-propanol anti in the Project Table.
2. Include this entry in the Workspace.
3. Choose Dihedral from the Measure button menu.
4. Click on the carbon atom of the terminal methyl group.

A purple cube appears, indicating that you've selected this atom to be used as part of the dihedral measurement.

5. Next, click on the carbon atom that is bonded to the one you clicked on in the previous step.

After doing so, another purple cube appears.

6. Click on the one remaining carbon atom in the structure.

A third purple cube appears.

7. Finally, click on the red oxygen atom.

A marker is superimposed over the structure, and the measurement (180°) is displayed over the marker. (It might be -180° instead of 180° .)

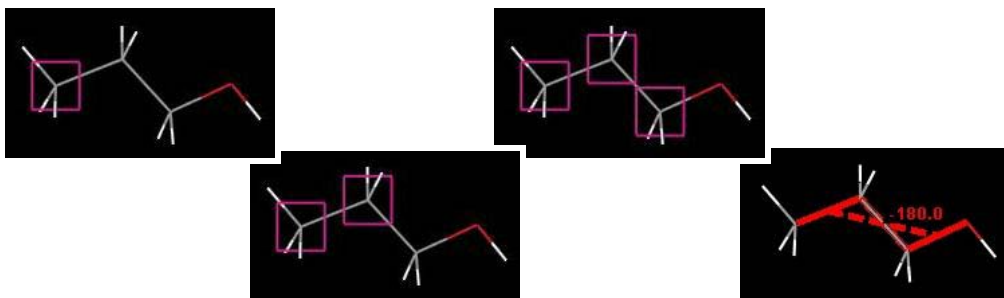


Figure 5.4. Measuring a dihedral angle.

After measuring the dihedral angle of the “anti” conformation, we’ll include the “staggered” conformation in the Workspace and measure the corresponding dihedral angle.

8. Locate the entry n-propanol staggered in the Project Table.
9. Control-click (click while holding down the CTRL key) the check box next to the title to include this entry in the Workspace.

You’ll notice that control-clicking makes the “staggered” entry appear in the Workspace next to the “anti” entry rather than replacing it. This is because control-clicking has no effect on the inclusion of other entries: it only affects the entry you are working with.

Because the measurement tool is still active (indicated by the indented appearance of the Measure distances, angles, dihedrals or coupling button in the toolbar), with Dihedral selected, you don’t need to click the button again to measure another dihedral angle.

To measure the dihedral, you click on four atoms, just as for the “anti” conformation.

10. Click the carbon atom in the terminal methyl group of the entry that you just added to in the Workspace, then on the carbon atom that’s bonded to it, then on the remaining carbon atom, and finally on the oxygen atom.

A purple cube appears for each of the first three atoms. When you click on the fourth atom, the purple cubes vanish, and a dihedral marker appears. The dihedral measurement (-63.9°) is visible near the marker.

11. After you’ve examined both dihedral measurements, delete the dihedral markers from the Workspace by choosing Delete Measurements from the Measure button menu.

As you saw, it’s possible to view measurements on multiple Project Table entries at the same time. You can display as many different measurements at the same time as you like, and include angle and distance measurements along with dihedral measurements. For more measurement options within Maestro choose Tools → Measurements in the main window.

5.5 Superimposing Multiple Structures

Since we've already placed two conformations of a molecule in the Workspace, we're ready to superimpose the two structures. Maestro's Superposition panel allows you to easily align two or more structures and calculate the root-mean-square deviation (RMSD) between atom pairs. This can be useful when examining the results of MacroModel conformation searches, comparing computational results to experimentally determined structures, or any other time you might want to gauge geometric differences between multiple structures. In this exercise, we'll open the Superposition panel and then go on to align the conformations used in the previous exercise.

1. If the two Project Table entries used in the previous exercise are not present in the Workspace, locate the entries in the project table, click on the check box for n-propanol staggered, and then control-click on the check box for n-propanol anti.
2. Open the Superposition panel by choosing Tools → Superposition in the main window.

When the Superposition panel appears (docked in the Workspace), you'll see that it has a number of tabs that have controls for defining molecules and substructures that you can align. We'll use the ASL tab in this example.

3. Select the Create RMSD property option.
4. Click on the ASL tab.
5. Click All to perform the RMSD calculation for all atoms.

You'll notice that one of the conformations is aligned on top of the other, and the RMSD value is printed in the table at the bottom of the panel.

If you scroll the Project Table to the right, you'll see that a property has been added that contains the RMSD value for the staggered conformation.

6. Close the Superposition panel.

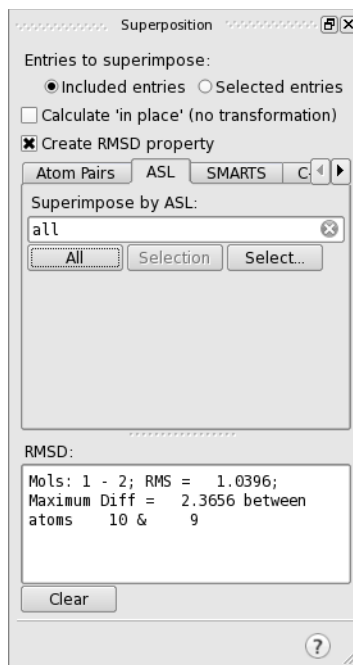


Figure 5.5. The Superposition panel.

Row	In	Stars	Title	Energy-MMFF94s	Relative Potential Energy-MMFF94s	RMSD 14
4	<input type="checkbox"/>	☆☆☆☆	10uprotren			
5	<input type="checkbox"/>	☆☆☆☆	Protein-ligand complex			
1 - multi-structure_file [3]						
6	<input type="checkbox"/>	☆☆☆☆	sd_molecule_01			
7	<input type="checkbox"/>	☆☆☆☆	sd_molecule_02			
8	<input type="checkbox"/>	☆☆☆☆	sd_molecule_03			
2 - analysis_exercises [4]						
9	<input checked="" type="checkbox"/>	☆☆☆☆	Small Molecule 01			
10	<input type="checkbox"/>	☆☆☆☆	n-propanol anti	-26.957	0.000	0.000
11	<input type="checkbox"/>	☆☆☆☆	n-propanol staggered	-23.022	3.935	1.040
12	<input type="checkbox"/>	☆☆☆☆	Protein with Glide-docked ligand			

Entries: 12 total, 12 shown, 4 selected, 1 included Groups: 2 total, 1 selected

Figure 5.7. The Project Table panel with the RMSD property added.

Maestro can also calculate a root-mean-square deviation (RMSD) for structures without aligning them. This capability is useful when you want to compare two structures in the context of another structure, such as two ligands docked to a receptor. To calculate the RMSD without aligning the structures, select the Calculate ‘in place’ (no transformation) option.

In addition to the abovementioned tools for superimposing using atom pairs, you may have noticed that the Superposition panel contained a button labeled Select. This button opens the Atom Selection dialog box, an interface that allows you to select groups of atoms that can be used as input for most Maestro operations. For more information on the Atom Selection dialog box, see [Section 6.5](#) of the *Maestro User Manual*. For a more thorough description of the Superposition panel, see [Section 10.3](#) of the *Maestro User Manual*.

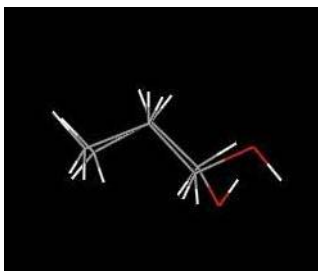


Figure 5.6. The superimposed propanol conformers.

5.6 Displaying Hydrogen Bonds

In this exercise, we'll use the results of a Glide docking job to demonstrate one of Maestro's useful analysis tools, the ability to display hydrogen bonding interactions. By displaying hydrogen bonding interactions, it's possible to visualize the interactions that make ligand binding energetically favorable. We'll begin this exercise by including the protein-ligand complex in the Maestro Workspace, and then use the toolbar to display and undisplay hydrogen bonding interactions.

1. Clear the Workspace. (Click the Clear Workspace toolbar button.)



2. In the Project Table, click on the square next to the entry named Protein with Glide-docked ligand.

The protein complex appears in the Workspace. The protein is colored blue and the ligand is colored orange. You might want to zoom in on the ligand and center the ligand in the Workspace. To do this, drag horizontally with the middle and right mouse buttons or use the mouse wheel, then right-click on a ligand atom.

3. To display hydrogen-bonding interactions between the ligand and the receptor, choose Inter H-bonds from the Hbonds button menu.



4. Click on any atom in the ligand (colored orange), to display intermolecular hydrogen bonds between that molecule and all other molecules in the Workspace.

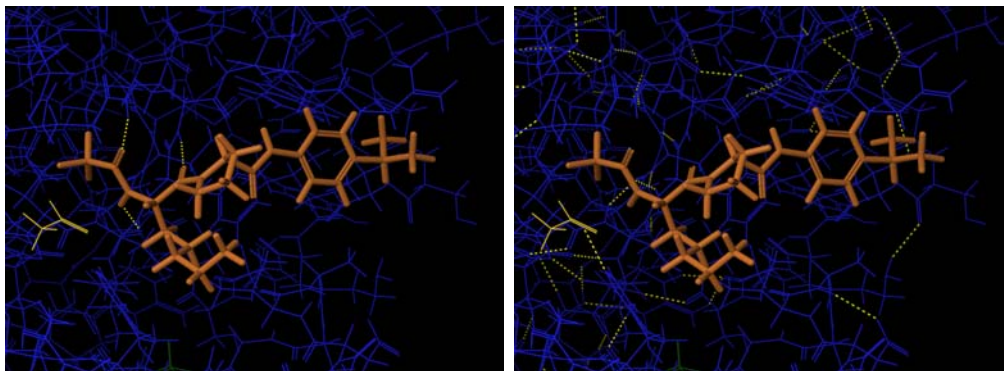


Figure 5.8. Protein-ligand complex showing hydrogen bonds between the ligand and the protein (left) and internal protein hydrogen bonds (right).

You'll see that hydrogen-bonding interactions are marked with dashed yellow lines. Now we'll look at hydrogen bonds within the protein.

5. Choose Intra H-bonds from the Hbonds button menu.
6. Click on any atom in the protein structure (colored blue) to visualize intramolecular hydrogen bonds.

You'll see many dashed yellow markers appear—among these are the hydrogen-bonding interactions that form helices and sheets, resulting in the overall structure of the protein.

7. Undisplay the hydrogen bonds by choosing Delete H-bonds from the Display H-bonds button menu.
8. Finally, close the Project Table by clicking the Table button in the toolbar (it should be indented), or by clicking the close button on the title bar of the panel.

Congratulations, you've just completed a quick survey of Maestro's analysis capabilities. In addition to the analysis tasks covered in this chapter, Maestro can also display intermolecular steric contacts, add H-bond counts to the project table, and align protein structures. For more information on Maestro's analysis tasks, see [Chapter 10](#) of the *Maestro User Manual*.

In the next chapter, you'll see an overview of some of Maestro's more advanced visualization and analysis capabilities, and a brief description of other Schrödinger products.

Beyond the Basics

6.1 Advanced Maestro Features

Beyond the Maestro operations surveyed in the previous chapters, there are other advanced tasks that Maestro can perform. This section offers an overview of a few such tasks, explaining when they might come in handy and where to go for more information.

- **Plotting Data:** Using Maestro's plotting tools, it's possible to examine relationships between structure-related data that's saved in the Project Table. For more information on Maestro's plotting tools, see [Chapter 11](#) of the *Maestro User Manual*. For more advanced statistical analysis, the program Strike is integrated into Maestro—see the *Strike User Manual* for details.
- **Viewing vibration animations:** Both Jaguar and MacroModel allow chemists to visualize vibrational modes using Maestro. For more information on calculations, see [Section 3.9](#) of the *Jaguar User Manual*. For information on viewing MacroModel vibration animations, see [Section 17.4](#) of the *MacroModel User Manual*.
- **Viewing electronic structure:** Beyond the molecular structure representations described in this tutorial, Maestro also allows chemists to view the electronic structure of a molecule, as determined by Jaguar, using surfaces. For more information on viewing electronic structure information, see [Section 3.10](#) of the *Jaguar User Manual* and [Section 12.3](#) of the *Maestro User Manual*.
- **Visualizing active site properties:** In addition to the shape-based volumetric surfaces that Maestro can calculate, Maestro can also map regions of space that correspond to active site properties such as hydrophobicity. For more information on mapping active sites with Maestro, see [Section 12.2](#) of the *Maestro User Manual*.
- **Command Scripting:** You can automate repetitive tasks using Maestro's command scripting tools. Because all actions in the Maestro interface are automatically logged by the Command Script Editor, there's no need to learn the actual commands themselves—just perform the desired actions using the Maestro interface, and save the command log for future use. For more information, see [Section 15.4](#) of the *Maestro User Manual*.
- **Python Scripting:** Maestro's support for Python scripting gives users even more power than command scripting. Using Python, it's possible to connect discrete steps in the research pipeline and to create new interfaces that are suited to your needs. For information on Python scripting with Maestro, see [Section 15.2](#) of the *Maestro User Manual*.

6.2 Programs Accessible from Maestro

As described in the introduction to the first chapter, Maestro is more than a molecular visualization environment—it's also the interface to all of Schrödinger's chemical simulation software. The interfaces to these products, available from the Applications menu on the main Maestro toolbar, include:

- **BioLuminate:** A comprehensive modeling package for biologics. BioLuminate combines superior scientific modeling algorithms with a brand-new, intuitive user interface that is specifically designed for examining biologics and protein systems.
- **CombiGlide:** Combinatorial technology for lead discovery and optimization. CombiGlide combines accurate ligand-receptor scoring and clever combinatorial docking algorithms to design focused libraries and identify new scaffolds. These technologies greatly facilitate lead discovery and optimization efforts.
- **ConfGen:** Accurate and efficient bioactive conformational searching for computer-aided drug design. Reproducing bioactive ligand geometries in minimally sized conformer sets, accurate results from high-performance ConfGen calculations save time and effort in downstream applications.
- **Core Hopping:** Comprehensive ligand- and receptor-based scaffold exploration for lead optimization. In addition to more conventional ligand-based methods, Core Hopping offers receptor-based scaffold hopping, exploiting information about the active site and known binding poses to guide the search for novel cores.
- **Desmond:** High-performance molecular dynamics simulations for biomolecular systems. Desmond's combined speed and accuracy make possible longer time-scale simulations of events of great biological and pharmaceutical importance. Seamlessly integrated with Maestro, Desmond provides a comprehensive set of analysis tools.
- **Epik:** Rapid and robust pK_a predictions. Combining the proven reliability of Hammett and Taft methods with powerful tautomerization tools, Epik is a capable tool for adjusting ligand protonation states.
- **Glide:** Designed to offer the full of range of performance from extremely high throughput to extremely high accuracy, Glide is Schrödinger's ligand docking program. Through the Maestro interface, it's possible to screen millions of compounds against a target receptor, and retrieve and evaluate likely hits.
- **Jaguar:** Emphasizing speed and accuracy, Jaguar is Schrödinger's widely used software for ab initio quantum mechanical (QM) calculations. The Maestro interface to Jaguar allows users to easily set up calculations based on the desired task and level of theory.

- **Liaison:** The Maestro interface for Liaison facilitates the setup and applications of linear interaction (LIA) calculations to predict the binding energies of lead candidates.
- **LigPrep:** Versatile generation of accurate 3D molecular models. LigPrep goes far beyond simple 2D to 3D structure conversions by including tautomeric, stereochemical, and ionization variations, as well as energy minimization and flexible filters to generate fully customized ligand libraries that are optimized for further computational analyses.
- **MacroModel:** A general purpose molecular modeling (MM) program, MacroModel is equipped with a full range of proven computational methodologies. Using the Maestro interface, it's possible to set up and run anything from simple molecular minimizations to active site conformational searches.
- **MCPRO⁺:** MCPRO⁺ is a highly configurable, general purpose Monte Carlo simulation package for biomolecules with an easy-to-use interface to accommodate both novice and advanced users. Relative binding affinities for protein-ligand complexes can be predicted via multiple approaches.
- **Phase:** Phase is Schrödinger's full-featured tool for ligand-based drug design, and includes a step-by-step wizard-like interface that intuitively guides researchers through the process of creating a pharmacophore model, creating a 3D database, and screening databases for matches to the pharmacophore model.
- **Prime:** An accurate program for protein structure prediction, Prime boasts an intuitive, easily mastered step-by-step Maestro interface that leads researchers from sequence data to finished protein models.
- **PrimeX:** PrimeX uses the OPLS-AA force field along with state-of-the-art technologies to refine protein crystal structures for computational drug discovery.
- **QikProp:** The Maestro QikProp panel allows researchers to perform extremely rapid ADME property predictions, for hundreds of thousands of compounds per hour.
- **QSite:** Using the Maestro interface for QSite, researchers can easily set up and interpret the results of QM/MM calculations, where reactive centers are modeled using Jaguar's accurate ab initio methodologies.
- **SiteMap:** SiteMap characterizes the regions near a protein binding site so that researchers can identify sites that are likely to be good targets for potential new drugs.
- **Strike:** Strike is closely integrated within Maestro, and affords researchers a chemically aware package of statistics tools, facilitating QSAR and statistical modeling.

Getting Help

Information about Schrödinger software is available in two main places:

- The `docs` folder (directory) of your software installation, which contains HTML and PDF documentation. Index pages are available in this folder.
- The Schrödinger web site, <http://www.schrodinger.com/>. In particular, you can use the Knowledge Base, <http://www.schrodinger.com/kb>, to find current information on a range of topics, and the Known Issues page, <http://www.schrodinger.com/knownissues>, to find information on software issues.

Finding Information in Maestro

Maestro provides access to nearly all the information available on Schrödinger software.

To get information:

- Pause the pointer over a GUI feature (button, menu item, menu, ...). In the main window, information is displayed in the Auto-Help text box, which is located at the foot of the main window, or in a tooltip. In other panels, information is displayed in a tooltip.

If the tooltip does not appear within a second, check that Show tooltips is selected under General → Appearance in the Preferences panel, which you can open with CTRL+, (⌘,). Not all features have tooltips.

- Click the Help button in the lower right corner of a panel or press F1, for information about a panel or the tab that is displayed in a panel. The help topic is displayed in the Help panel. The button may have text or an icon:



- Choose Help → Online Help or press CTRL+H (⌘H) to open the default help topic.
- When help is displayed in the Help panel, use the navigation links in the help topic or search the help.
- Choose Help → Manuals Index, to open a page that has links to all the PDF documents. Click a link to open the document.
- Choose Help → Search Manuals to search the manuals. The search tab in Adobe Reader

opens, and you can search across all the PDF documents. You must have Adobe Reader installed to use this feature.

- Installation and licensing: see the *Installation Guide*.
- Running and managing jobs: see the *Job Control Guide*.
- Using Maestro: see the *Maestro User Manual*.
- Maestro commands: see the *Maestro Command Reference Manual*.

Contacting Technical Support

If you have questions that are not answered from any of the above sources, contact Schrödinger using the information below.

Web: <http://www.schrodinger.com/supportcenter>
E-mail: help@schrodinger.com
Mail: Schrödinger, 101 SW Main Street, Suite 1300, Portland, OR 97204
Phone: +1 503 299-1150 (USA, 9am – 5pm Pacific Time)
+49 621 438-55173 (Europe, 9am – 5pm Central European Time)
Fax: +1 503 299-4532 (USA, Portland office)
FTP: <ftp://ftp.schrodinger.com>

Generally, using the web form is best because you can add machine output and upload files, if necessary. You will need to include the following information:

- All relevant user input and machine output
- Maestro purchaser (company, research institution, or individual)
- Primary Maestro user
- Installation, licensing, and machine information as described below.

Gathering Information for Technical Support

The instructions below describe how to gather the required machine, licensing, and installation information, and any other job-related or failure-related information, to send to technical support. Where the instructions depend on the profile used for Maestro, the profile is indicated.

For general enquiries or problems:

1. Open the Diagnostics panel.
 - **Maestro:** Help → Diagnostics
 - **Windows:** Start → All Programs → Schrodinger-2014-3 → Diagnostics
 - **Mac:** Applications → Schrodinger2014-3 → Diagnostics

- **Command line:** \$SCHRODINGER/diagnostics

2. When the diagnostics have run, click Technical Support.

A dialog box opens, with instructions. You can highlight and copy the name of the file.

3. Attach the file specified in the dialog box to the web form.

If you have already submitted a support request, use the upload link in the email response from Schrödinger to upload the file. If you need to submit a new request, you can attach the file when you fill in the form.

If your job failed:

1. Open the Monitor panel, using the instructions for your profile as given below:

- **Maestro/Jaguar/Elements:** Tasks → Monitor Jobs
- **BioLuminate/MaterialsScience:** Tasks → Job Monitor

2. Select the failed job in the table, and click Postmortem.

The Postmortem panel opens.

3. If your data is not sensitive and you can send it, select Include structures and deselect Automatically obfuscate path names.

4. Click Create.

An archive file is created in your working directory, and an information dialog box with the name of the file opens. You can highlight and copy the name of the file.

5. Attach the file specified in the dialog box to the web form.

If you have already submitted a support request, use the upload link in the email response from Schrödinger to upload the file. If you need to submit a new request, you can attach the file when you fill in the form.

6. Copy and paste any log messages from the window used to start the interface or the job into the web form (or an e-mail message), or attach them as a file.

- **Windows:** Right-click in the window and choose Select All, then press ENTER to copy the text.
- **Mac:** Start the Console application (Applications → Utilities), filter on the application that you used to start the job (Maestro, BioLuminate, Elements), copy the text.

If Maestro failed:

1. Open the Diagnostics panel.

- **Windows:** Start → All Programs → Schrodinger-2014-3 → Diagnostics

- **Mac:** Applications → SchrodingerSuite2014-3 → Diagnostics
- **Linux/command line:** `$SCHRODINGER/diagnostics`

2. When the diagnostics have run, click Technical Support.

A dialog box opens, with instructions. You can highlight and copy the name of the file.

3. Attach the file specified in the dialog box to the web form.

If you have already submitted a support request, use the upload link in the e-mail response from Schrödinger to upload the file. If you need to submit a new request, you can attach the file when you fill in the form.

4. Attach the error files to the web form.

The files should be in the following location:

- **Windows:** `%LOCALAPPDATA%\Schrodinger\appcrash`
(Choose Start → Run and paste this location into the Open text box.)
Attach `maestro_error_pid.txt` and `maestro.exe_pid_timestamp.dmp`.
- **Mac:** `$HOME/Library/Logs/CrashReporter`
(Go → Home → Library → Logs → CrashReporter)
Attach `maestro_error_pid.txt` and `maestro_timestamp_machinename.crash`.
- **Linux:** `$HOME/.schrodinger/appcrash`
Attach `maestro_error_pid.txt` and `crash_report_timestamp_pid.txt`.

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