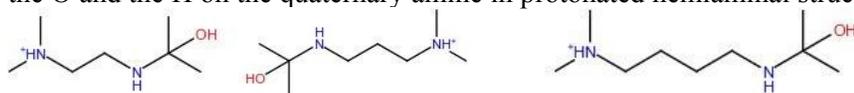


Introduction to Molecular Dynamics - Maestro Tutorial

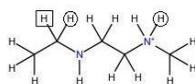
We are going to look at the percentage of conformers at room temperature which have an internal H-bond between the O and the H on the quaternary amine in protonated hemiaminal structures of this type:



Note that these have 2, 3 or 4 carbon linkers between the amines. These are flexible molecules and Molecular Dynamics is a good approach for sampling this conformational flexibility as a function of time.

Type **maestro** to start the program.

1. There are many ways to build the hemiaminal species. You can do it your own way or follow these steps. Under the **Edit** menu, select **Build** and then the **Fragments** option. That will open the **Build** window, **Fragments** Tab, with the **Fragments:** pulldown set to **Organic**. Click the box labeled “**Grow**” and then click the following icons in order: **methyl-methyl-amine-methyl-methyl-amonium-methyl**. So far you should have this structure:



One the **Build** window, check the box labeled “**Place**” and then click to select the **methyl** icon. Then click on the each of the circled H's to replace with methyl. One the **Build** window, click to select the **water** icon. Now click on the H in the rectangle to replace it and make the OH group. That should finish your first structure.

Hint: **Undo** under the **Edit** menu cancels the last action. The X icon on the left sidebar is the delete tool. If you double-click on the icon, the entire structure is deleted. Click/hold on the icon, to get a menu of choices.

Hint: Click **Close** on any Dialog Box to remove it from the screen.

2. In this section, you will save your structure. Under the **Project** menu, select **Save As**. Give it a simple one word name like “imines”. Click **Save**. Under the **Project** menu, select **Show Table**. Under the **Workspace** menu, select **Create Project Entry**. Again, give it a simple one word name like “c2”. Click **Create**. You should now see your entry listed in the Project Table. *You only have to save the “Project Table” once.* You can open and close it once you have saved it. However, *each time you build a new structure, you must **Create Project Entry** so the the new structure gets loaded into the table.*

3. In this section you will run a Conformational Search so that you are starting from a low energy structure for the next step. From the **Applications** menu, select **MacroModel** and then **Conformational Search** from the submenu. The **Conformational Search** window will open and has multiple tabs and the default settings are fine. Start the search by clicking **Start**. In the popup window, give the calculation a Name: **c2-csearch**. Note: There can be no spaces in the name. Use these characters only: a-Z or 0-9 or _ or -. Set the **Host:** pulldown to **macromodel_dino** and **Incorporate: Append New Entries as a Group**. After a few minutes, the data will either load automatically into the table or you may be prompted about incorporating it. The lowest energy structure should load into the workspace. If not, it is the entry at the top of the new set in the Project Table.

4. From the **Applications** menu, select **MacroModel** and then **Dynamics** from the submenu. The **Dynamics** window will open and has multiple tabs. Go to the **Monitor** tab and specify the **Number of Structures to Sample** as **1000**. Now click on the **H-Bonds** option to bring up the **Monitored H-Bonds** window. To define the hydrogen

bond correctly, you must click on 4 atoms in order: **N, H, O, C**. These are the protonated tertiary ammonium N, its H, then the O, and the C which bears the O.

Then go to the **Dynamics** tab and specify: **Simulation Time(ps) = 1000** and **SHAKE: Bonds to Hydrogens**. The **Method** is **Stochastic Dynamics**, **Temperature = 300**, **Equilibration Time(ps) = 1** and **Timestep(fs) = 1.5**.

Now start the dynamics by clicking **Start**. In the popup window, give the calculation a Name: **c2-moldyn**
Note: The same filename rules apply here as to the Conformational Search. Set the **Host**: pulldown to **macromodel_dino** and **Incorporate: Append New Entries as a Group**. After a few minutes, the data will either load automatically into the table or you may be prompted about incorporating it.

It will take about a few minutes to do this run. Progress data will be printed in the **Monitor** window. If you have closed the Monitor window, you can reopen it from the **Applications** menu. 1000 sampled structures will get loaded into the Project Table. If you scroll down the table and find the last entry and last column, this will tell you the average H-bonded population in your dynamics run. You can also display the dynamics run. In the **Project Table**, click on the line for the folder header, probably labelled c2-moldyn-out1. This will “select” (highlight in yellow) all of the 1000 sampled structures which are now individual entries in the table. Click on the  button at the top of the Project Table to play the simulation. Click on the  button when you are finished.

The data from this run is also stored in a series of files. The most useful is called c2-moldyn.log and c2-moldyn.mmo. You can open and view this files by using the **gedit** program. Type **gedit** in a terminal window and then use **File/Open** and Browse for the log file. Look for the line that shows “This H-bond was found in ___% of the samples”.

The length and angle limits of what constitutes a hydrogen bond was defined in the **Monitored H-Bonds** window when you setup the calculation. Your first run used the default definition but you may get better results if this definition is more expansive. Also, you could monitor the full range of O---H distances during the calculation in addition to monitoring it as an H-Bond. To do that, open **Applications - MacroModel - Dynamics** and go to the **Monitor** tab. Click on the **Distances** option to bring up the **Monitored Distances** window and then click on the two atoms whose distance you want to monitor. You can Monitor multiple Distances, Angles, H-Bonds, etc in a single calculation. Most of the data will be in the c2-moldyn.mmo file so be sure to view it using the **gedit** program. By default, only summary data is shown by Maestro so you must examine the c2-moldyn.mmo file to really see the data.

As you rerun this calculation, you may want to reconsider the **Number of Structures to Sample = 1000** setting. This causes 1000 structures to load into the project table for each run whereas a 1ns simulation with 1.5 fs sized steps generates about 7×10^8 structures in total! The 1000 structures is just a subset for you to visualize. The Monitor settings use the entire set of structures and not just this 1000 subset. You don't actually need to keep those 1000 structures in the project table unless you are analyzing them. You can delete them from the project table after each run. The 1000 structures are in the c2-moldyn-out.mae file if you want to later reread them into the project table. You can also simply never generate them in the first place by setting **Number of Structures to Sample = 0**.

This tutorial took you through the steps to analyze the system with a 2 carbon linker. Go back and build the 3, 4, and 5 carbon linker analogues, and repeat. Determine the percentage of H bonds in each.

Once you have completed the calculations and recorded the data, look up the original publication:
[Jack Hine, Michael S. Cholod, and Walter K. Chess](#) : (Journal of American Chemical Society Vol 95, Issue13, pp 4270 - 4276) Kinetics of the formation of imines from acetone and primary amines. Using data from that publication, plot the rate constant for imine formation vs percentage of H bonds corresponding to each molecule. Is there a correlation? Comment why or why not.