Chem 2312H **September 26, 2023**

Accessing and Navigating MacroModel (via Maestro) at MSI via Linux

You will need to access Maestro (using MacroModel, a module within Maestro) at Minnesota Supercomputing Institute (MSI) for doing the molecular mechanics minimization computation of the menthone isomers. Maestro may be accessed via the "Open On Demand" website.

Here are instructions for setting up access to MSI via Open OnDemand. You will need to be either on the campus network or connected via VPN in order to do this.

1. Make sure you have verified that you are "registered" with MSI by following the instructions in the email message that you should soon receive from MSI.

2. **i.** **On a 491 desktop computer:** "Open OnDemand" is already installed on the desktop computers on the right hand bench in the 491K computer room. Open Chrome and you will see the bookmark.

ii. **On your own computer/laptop** (you will first need to be connected to VPN if you are off-campus): Go to https://ood.msi.umn.edu/pun/sys/dashboard.

3. Create a session by

i. navigating to 'Interactive Apps'(in the top menu bar of the landing page and then to 'Desktop' in that dropdown menu.

ii. Under the 'Cluster' dropdown, select 'mesabi'

iii. Select 'Launch' at the bottom of the page

iv. Select 'Launch Desktop' from the new page that opens

v. Select the Terminal icon from the menu bar (looks like a computer screen)

vi. at the command prompt, type:

> module load schrodinger [return/enter]

> maestro [return/enter] – be patient here; it can take quite a bit of time to load the Maestro window

If you have difficulty with one or more of the above steps on your own computer/laptop, you can go to the MSI Help Desk (staffed from 9-4 weekdays), which is located on the 5th floor (587) of Walter Library (Digital Technology Center), the building just to the north of Smith Hall. Have your computer/laptop with you so they can help you past the hang-up. (https://www.msi.umn.edu/content/helpdesk)

4. Create an input geometry for menthone (the trans-diastereomer) and carry out a conformational search with molecular mechanics in MacroModel.

In the Maestro window, create a working directory:

Go to *File* → *Change Working Directory* (to open the file explorer) → *Create New Folder* (folder icon in right hand side of top menu bar)

Change the directory label to "menthonemaster_dir."

Open the menthone master directory and again click the "Create New Folder*"* button and change the directory label to 'menthonesub_dir.'

Select the ‘menthonesub_dir’ directory (single click to highlight, don’t double-click to open) and click “choose” (button at bottom right) to set the working directory for computational files associated with menthone.

Create an input structure and carry out a conformational search:

i. Go to *Edit* → *2D Sketcher*. Draw menthone in the right hand workspace; specify the relative configuration of the two stereocenters. Now change the title to ‘menthoneinitial_geometry’ and click “Save as new.” Close the 2D Sketcher window.

ii. Open the “Tasks” button (upper right on the menu bar) and browse/navigate to “conformational search.” A window will open that displays the possible options that can be modified for the conformational search.

iii. Select the “Force Field” tab, select MMFF, and select water as the solvation model (the closest solvent to methanol, the polar protic solvent in which you have measured the equilibrium ratio).

iv. Select the “CSearch” tab at the top. Change the method to Torsional Sampling (MCMM). Uncheck the Multiligand box and, then, the Perform Automatic Setup During Calculation box. Click the “Perform Automatic Setup” button. Change the torsional sampling options to Extended.

v. Delete the default job name and enter “menthone-csearch.” Do not use spaces, back-slashes or forward slashes in file names. Select “Run” to begin the conformational search. (You can close the “conformational search” window, if you like.)

vi. Click the *Jobs* → *Monitor* buttons (located to the left of tasks), and a monitor window will open that displays the progress of the conformational search. When finished, the status will read ‘incorporated’ (or ‘incorporated:completed’ in another Monitor window if you open it).

vii. View the structures of the family of unique conformers by selecting the Table icon in the upper right portion of the menu bar to display the Project Table window.

viii. Select *Show* → *All* to display all columns of information from the conformational search.

ix. Inspect the column named “Minimization Converged-(force field)” to ensure that each conformer has converged, as evidenced by a checked box for each conformer. Also, for each conformer reported in the Project Table, inspect the column named “Times Found-(force field)” to ensure that each conformer was found at least ten times.

x. Record the energies for each conformer found in the "Potential Energy" (not "Relative Potential Energy") into your Excel spreadsheet.

For additional help on performing the molecular mechanics computation using Maestro (the GUI for MacroModel), read “Operation 1” on p 646, Box 3 (p 647), and pp 649-651 in the following publication: A guide to small molecule structure assignment through computation of (^{1}H and ^{13}C) NMR chemical shifts. Willoughby, P. H.; Jansma M. J.; Hoye, T. R. *Nature Protocols* **2014**, *9*, 643–660. (You can link to this at https://www.nature.com/articles/nprot.2014.042 if you are connecting on a campus WiFi or internet or via VPN from off campus.)