Chemistry 5021/8021 **Computational Chemistry** 3/4 Credits

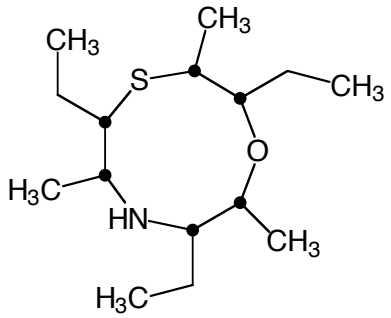
Spring Semester 2004

(Due 2 / 23 / 04)

Using PC Model, answer the three questions below.

1. How many different carbon atomic types are there in each of the MM3, MMX, MMFF94, and Amber force fields? Which force field has the least number, and why do you think that is?

2. Chemical degradation studies indicate a recent fungal extract having anticancer properties to have the chemical structure indicated below. Using the MMX force field with default settings, find 3 distinct structures for this molecule (make sure you get the stereochemistry right!—the bold black dots in the structure represent H atoms coming toward you from the plane of the paper) Print the structures and record their energies. Prior to completing the rest of the problem, express your confidence level (on a scale from 0 to 100%) that you have found the global minimum energy structure.



Now, use the GMMX utility to stochastically search for the global minimum. You will need to add the ring and rotatable bonds to the search criteria using the appropriate buttons in the GMMX dialog box. In addition, to save some time, open the Options dialog box and set the minimum number of optimizations to 100 and the maximum number to 200 (the bottom two boxes). It will take a few minutes for the process to complete once you have told it to begin.

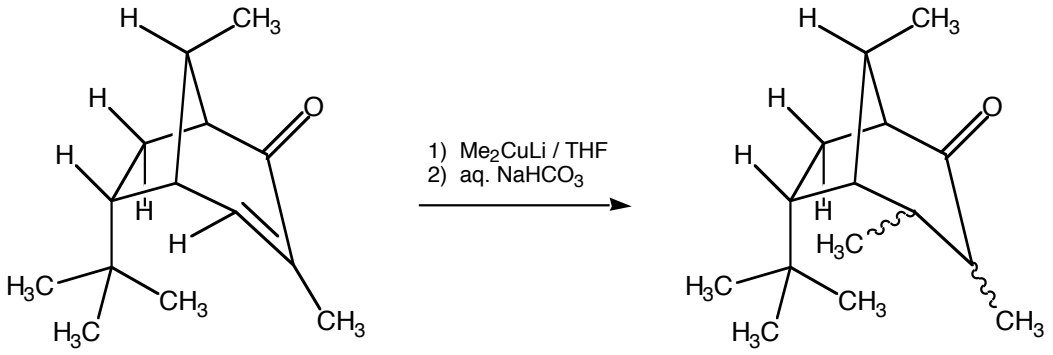
Print the structure and report the MMX energy and all of its components (Str, Bnd, etc.) for the global minimum that was found. Which individual component contributes most to the strain? Does any component contribute in a favorable (i.e., negative) way? If so, what particular interaction seems to be involved? What is the predicted heat of formation? What is the predicted dipole moment? How do

you think this was computed? What is the predicted XLogP? What is XLogP and how is it computed?

Did your final structure match one of the three you found originally? Having finished this exercise, express your confidence level (on a scale from 0 to 100%) that you have found the global minimum energy structure. If not 100%, what else might you do to raise your confidence level?

Finally, of all of the structures found in your search, what percentage of the population does the global minimum comprise at 300 K? (You'll need to look for an output file to answer that question and open it with a text editor.)

3. The unsaturated ketone below reacts with lithium dimethyl cuprate in two steps. In the first step, the nucleophilic methyl anion adds in a Michael fashion to the β position of the double bond. In the second step, the intermediate enolate anion is protonated by the work-up buffer solution to generate the final product. Gas chromatographic (GC) analysis indicates a single product, presumably stereochemically pure. In the nuclear magnetic resonance (NMR) spectrum, the non-bridgehead proton that is α to the carbonyl group is readily apparent at 2.3 ppm. It appears as a doublet of quartets with the doublet coupling $^3J_{HH}$ = 5.3 Hz. When this product compound is dissolved in methanol containing a trace of NaOMe, left overnight at room temperature, and re-isolated, GC indicates it to be a mixture of a small portion of the original product and one new substance. In the NMR, in addition to weak peaks corresponding to the original spectrum, there is now a doublet of quartets at 2.4 ppm with the doublet coupling $^3J_{HH}$ = 7.3 Hz.



What is the integration ratio of the doublet of quartets at 2.3 ppm to that at 2.4 ppm at 298 K? Explain how you arrived at your answer using the MMFF force field; in your explanation, emphasize mechanistic analysis.