*Using PC Model, answer the questions below. If you have questions/issues working on this Problem Set, do please consider using Piazza to address them.*

1.   In the AMBER and MMFF94 force fields, what are the parameters for the harmonic force constants and equilibrium bond lengths for the bond between an alkyl carbon and a sulfide sulfur? How closely do the two sets of constants agree?

Optimize dimethyl sulfide using the AMBER force field. What is the C–S bond distance and what is the total bond stretching strain? Now, fix one C–S bond to a *different* bond length and compute the bond stretching strain. Is it equal to the expected value? Explain how you carry out this calculation and how you compute the "expected value".

Stretch one C–S bond by the same amount with MMFF94. Is the increase in bond stretch strain for MMFF94 consistent with the AMBER value and the relative force constants for the two force fields? If not, why not?

2.   In Kobayashi, S.; Pitet, L. M.; Hillmyer, M. A. "Regio- and Stereoselective Ring-Opening Metathesis Polymerization of 3-Substituted Cyclooctenes" *J. Am. Chem. Soc.* **2011**, *133*, 5794-5797, the Hillmyer group reported the regio- and stereoselective polymerization of 3-substituted cyclooctenes, which process leads to precision linear low density polyethylene.

3RCOE   regio- /stereoregular   precision LLDPE
R = Me, Et, Hex, Ph   polyoctenamer
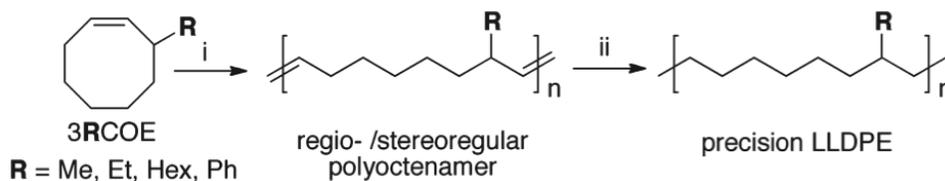
The ring-opening metathesis polymerization mechanism involves a [2+2] cycloaddition of the *Z*-cyclooctene with a ruthenium carbene that is the terminus of the growing polymer chain. The observed stereoselectivity implies strong preference for a trans-relation of the polymer chain and the cyclooctyl ring on the formed metallocyclobutane, and also a proximal relationship of the 3-substituent with the growing polymer chain, as illustrated on the next page.

**Most favorable
and fit with *trans*-/head to tail
polymer structure**
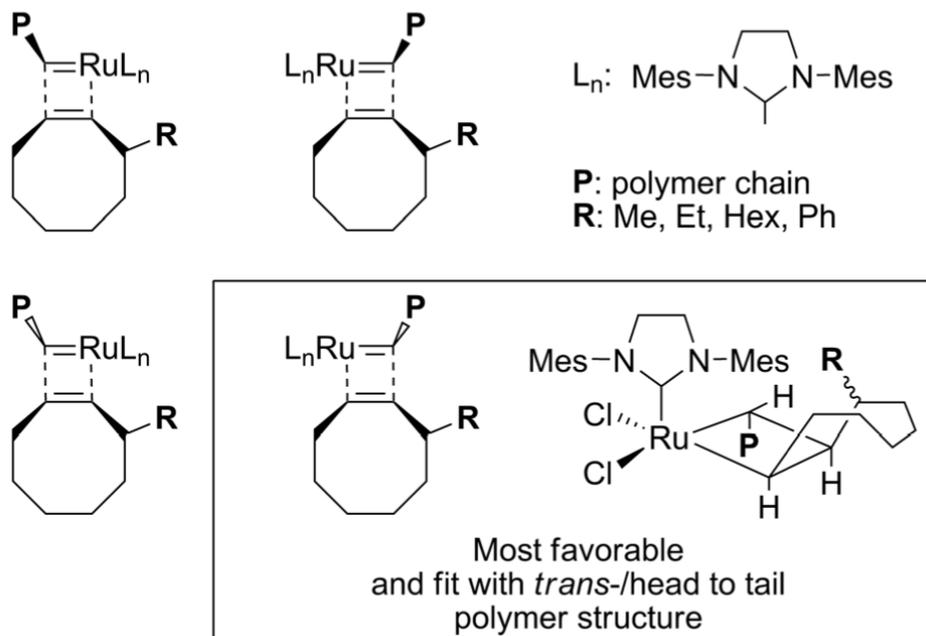
While molecular mechanics is poorly suited to predicting transition-state energetics, in general, it is certainly true that possible transition states will include within them the strain associated with a given conformation of a 3-substituted cyclooctene, above and beyond additional strain associated with non-bonded interactions as the cyclooctene approaches the Grubbs catalyst.

Thus, using the MM3 force field, which should be particularly good for hydrocarbons, carry out a careful search for all possible conformers of *Z*-cyclooctene within 10 kcal/mol of the global minimum (note that enantiomers are not conformers). Report their structures (a picture is fine) and relative energies. Next, carry out a full conformational analysis for 3-methyl-*Z*-cyclooctene. Note that there is a brute force approach that is probably easiest, or there is a systematic approach that is probably more informative and satisfying as a chemist. Let's assume that we're only likely to be interested in conformers within 3 kcal/mol of the global minimum (as otherwise they won't contribute to reactivity in any case)—try to report results from the rational approach, as opposed to the thoughtless brute force approach. Structures and relative energies. Discuss any clear trends that catch your attention.

Now, we can't really model even the metallacyclobutane with the force fields available to us in PC Model, but, if you had to use the program to make some estimate of these energies of the four competing TS structures above, describe what you might do. You don't have *actually* to do it—just describe it.

For the above problem, graphics credits go to S. Kobayashi.

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 $^3J_{HH} = 4.0$ 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 some 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 2.5 ppm with the doublet coupling $^3J_{HH} = 7.4$ Hz.
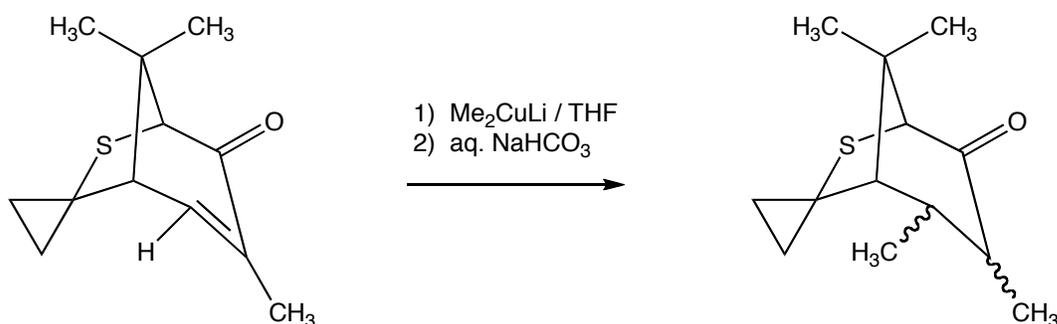
What do you predict to be the integration ratio of the doublet of quartets at 2.3 ppm to that at 2.5 ppm at 298 K? Explain how you arrived at your answer using the MMFF force field.