Chemistry 231 – Elementary Organic Chemistry
Problem Set – Conformational Analysis

1. Which of the following compounds would you expect to have the largest energy barrier to internal rotation for the bond indicated? Explain your reasoning
   a. (CH₃)₃C—C(CH₃)₃ or (CH₃)₃Si—Si(CH₃)₃
   b. CH₃CH₂—CH₃ or CH₃CH₂—OH
   c. CH₃CH₂—CH₂CH₃ or CH₃CH₂—OCH₃

2. Consider the two isomers (cis/trans) of 1,4-dimethylcyclohexane. For each case, draw the most stable conformation. Indicate which of the two isomers is cis or trans and which you would expect to be the more stable (lower energy) of the two.

3. Draw the two limiting conformations (chair v. boat) of 1,4-di-tert-butylcyclohexane. Be sure to include the orientations and full carbon skeletons of the tert-butyl groups. Based on your knowledge of conformational energies, explain why the lowest energy conformation of this trans isomer is the boat and not the chair.

4. Dibromoethane (C₂H₄Br₂) exists as one of two constitutional isomers, 1,1-dibromoethane or 1,2-dibromoethane. Using a Newman projection, draw the lowest energy conformation of 1,2-dibromoethane along the C-C bond axis.

5. Bromopropane (C₃H₇Br) exists as one of two constitutional isomers, 1-bromopropane or 2-bromopropane.
   a. Draw a line structure corresponding to each of these isomers according to their IUPAC name.
   b. Using a Newman projection, draw the highest energy conformation of 1-bromopropane along the C₁-C₂ bond axis.
   c. Of the two isomers of bromopropane (1-bromopropane or 2-bromopropane), indicate which would you expect to have the higher boiling point. Explain your reasoning.

6. The (1R,3R)-1,3-dibromocyclohexane is a chiral compound. Using an unambiguous notation, draw the lowest energy conformation of this compound.

7. One of the many monoterpenes found in naturally occurring essential oils and flavors has the trivial name menthol. It finds utility in the manufacture of cough drops, shaving cream, and cigarettes. Its structure is given below. Using an unambiguous notation, draw the lowest energy conformation of Menthol.

![Menthol Structure](image)

Menthol 

\[ \alpha = -50^\circ \] at 18 °C
8. Using any unambiguous notation, suggest a steric and/or electronic argument for the following observed conformational phenomena. Support your argument with specific structural evidence (experimental bond lengths, angles, dihedrals, etc.)

   a. The rotational barrier in methanol is lower than that for ethane.
   b. The C_2-C_3 rotational barrier in 2,2-dimethylbutane is higher than that for ethyltrimethylsilane ((CH_3)_3Si—CH_2CH_3).

9. Myo-inositol, the most prominent naturally-occurring form of inositols, is a carboxyclic polyol that plays an important role as the structural basis for a number of secondary messengers in eukaryotic cells. It is generated in vivo from the aldol cyclization of glucose-6-phosphate to myo-inositol-1-phosphate (eq. 1).

   \[
   \begin{align*}
   \alpha\text{-D-glucose-6-phosphate} & \quad \text{myo-inositol-1-phosphate synthase} \quad \text{myo-inositol-1-phosphate} \\
   & \quad (1)
   \end{align*}
   \]

   Using an unambiguous notation, draw the lowest energy conformation of myo-inositol-1-phosphate.

10. Draw all of the limiting conformations (staggered and eclipsed) of the naturally occurring amino acid L-Valine. Based on your knowledge of conformational energies, explain (a) why the staggered conformations of this molecule are lower in energy than any corresponding eclipsed conformation and (b) which of the staggered conformations represents the lowest energy conformation of this compound overall.

11. Squaric acid (C_4H_2O_4) is a synthetic organic molecule that consists of four carbon atoms arranged at the corners of a square, with one oxygen atom attached to each carbon molecule. It was first prepared in 1962 by the team of Park, Cohen, and Lacher at the University of Colorado, Boulder (see J. Am. Chem. Soc. 1962, 84(15), 2919). Portions of their classic synthesis of this molecule are shown below with four intermediates (compounds 1 through 4) being highlighted.

   It has been shown experimentally that squaric acid stores a great deal of energy in its carbon-carbon double bond (when compared to other compounds containing carbon-carbon double bonds). Using your knowledge of organic structure, explain this observation. Be specific.