Homework problems – Chapter 5

1. In your textbook (Organic Chemistry by Maitland Jones, Jr): 5.35-5.41, 5.45 and 5.48. – see your solutions manual.

2. Assume that you have a variety of cyclohexanes substituted in the positions indicated. Identify the substituents as either axial or equatorial. For example, a 1,2-\textit{cis} relationship means that one substituent must be axial and one equatorial, whereas a 1,2-\textit{trans} relationship means that both substituents are axial or both are equatorial.

(a) 1,3-trans disubstituted
(b) 1,4-cis disubstituted
(c) 1,5-trans disubstituted
(d) 1,3-cis disubstituted
(e) 1,5-cis disubstituted
(f) 1,6-trans disubstituted

Remember,

All circled groups are \textit{cis}.
All uncircled groups are \textit{cis}.
All circled groups are \textit{trans} to all uncircled groups.

Thus,

\begin{equation}
\text{rotate counterclockwise } 120^\circ \rightarrow\text{flip } 180^\circ \rightarrow
\end{equation}

1,3-trans disubstituted
3. Draw the two chair conformations of 1,1,3-trimethylcyclohexane and estimate the amount of strain energy in each. Which conformation is favored?
Conformer A contains two Me/H 1,3-diaxial interactions and one Me/Me 1,3-diaxial interaction (3.7 kcal/mol) while conformer B contains two Me/H 1,3-diaxial interactions only. Each Me/H 1,3-diaxial interaction adds 0.9 kcal/mol in strain energy to the overall energy of the molecule while a Me/Me 1,3-diaxial interaction adds 3.7 kcal/mol in strain energy. Thus, the difference in energy between A and B = [(2 x 0.9) + 3.7] - (2 x 0.9) = 3.7 kcal/mol.

In other words, the strain energy in A = 5.5 kcal/mol while the strain energy in B = 1.8 kcal/mol; and hence conformer B is favored.

4. We will see later that alkyl halides undergo an elimination reaction to yield alkenes on treatment with strong base. For example, chlorocyclohexane gives cyclohexene on reaction with NaNH₂.

\[
\text{Cl} \quad \text{NaNH}_2 \quad \xrightarrow{\text{NaCl + NH}_3} \quad \text{Cl}
\]

If axial chlorocyclohexanes are generally more reactive than their equatorial isomers, which do you think will react faster, cis-1-tert-butyl-2-chlorocyclohexane or trans-1-tert-butyl-2-chlorocyclohexane? Explain why!

The four possible conformers for 1-tert-butyl-2-chlorocyclohexane are shown above. Conformers B and C are much higher in energy than conformers A and D since both B and C contain two Buᵗ/H 1,3-diaxial interactions (each costing...
2.7 kcal/mol). Conformers A has two Cl/H 1,3-diaxial interactions and one gauche C(Me)₃/Cl gauche interaction while conformer D contains only one C(Me)₃/Cl gauche interaction. Thus, A is higher in energy and will react faster. Hence *cis*-1-tert-butyl-2-chlorocyclohexane will react faster.

5. One of the two chair structures of *cis*-1-chloro-3-methylcyclohexane is more stable than the other by 3.7 kcal/mol. Which is it? What is the energy cost of a 1,3-diaxial interaction between a chloride and a methyl group?

Conformer A contains one Me/H 1,3-diaxial interaction, one Cl/H 1,3-diaxial interaction, and one Me/Cl 1,3-diaxial interaction. On the other hand, conformer B has no 1,3-diaxial interactions and no gauche interactions. Thus, conformer B with equatorial methyl and chloride groups is more stable (by 3.7 kcal/mol).

The strain energy of conformer A (3.7 kcal/mol) is due to the three 1,3-diaxial interactions mentioned above. Thus, the energy costs of a Me/Cl 1,3-diaxial interaction = [Total strain energy – (Me/H 1,3-diaxial interaction + Cl/H 1,3-diaxial interaction)]

3.7 – (0.9 + 0.25) = 2.55 kcal/mol
6. Draw *trans*-1,4-dimethylcyclohexane in its two chair conformations, and determine whether the two chairs are identical, conformational enantiomers, or conformational diastereomers. Then do the same for the *cis* isomer.

The chair conformers of *trans*-1,4-dimethylcyclohexane are conformational diastereomers since they are not mirror images and hence have different internal dimensions (e.g. different distances between the Me groups). Also note that the axial, axial conformer has four Me/H 1,3-diaxial interactions whereas the equatorial, equatorial conformer has no Me/H 1,3-diaxial interactions.

In contrast, the chair conformers of *cis*-1,4-dimethylcyclohexane are identical since they are superimposable mirror images (rotate one of them in the plane of the paper by 180°). Also note that they both have two Me/H 1,3-diaxial interactions and hence are equal in energy.
7. Given that one 1,3-diaxial interaction of isopropyl and hydrogen costs 1.1 kcal/mol in energy, calculate the ratio of axial to equatorial isopropylcyclohexane that is present at room temperature.

The axial isomer of isopropylcyclohexane contains two 1,3-diaxial interactions between isopropyl and hydrogen whereas the equatorial isomer of isopropylcyclohexane contains none. Thus, the axial isomer is (2 x 1.1) 2.2 kcal/mol higher in energy and the equatorial isomer is favored. In other words, the $\Delta G^\circ$ for conversion of axial to equatorial isomer is -2.2 kcal/mol.

$\Delta G^\circ = -RT \ln K$ hence $K = e^{(-\Delta G / RT)}$ where $R$ is the universal gas constant (1.987 cal/mol·K) and $T$ is the temperature at which the measurement is being made (295 K (room temperature) in this case).

The axial- to equatorial isopropylcyclohexane equilibrium constant ($K$) is obtained as follows:

$$K = e^{\left(\frac{2200 \text{ cal/mol}}{1.987 \text{ cal/mol} \cdot K \times 295 \text{ K}}\right)} = 0.023$$

To get to whole number ratio,

$$\frac{0.023}{0.023} : \frac{1}{0.023} = 1 : 42.6$$

Alternately, the equatorial- to axial isopropylcyclohexane equilibrium constant ($K$) can be directly obtained as follows:

$$K = e^{\left(\frac{-2200 \text{ cal/mol}}{1.987 \text{ cal/mol} \cdot K \times 295 \text{ K}}\right)} = 42.6$$

Thus, the ratio of axial to equatorial isopropylcyclohexane that is present at room temperature is $\sim 1:43$. 