Calculating conformational energies in open chain compounds.

\[ \Delta H^o = \quad \Delta H^o = \quad \Delta H^o = \quad \Delta H^o = \]

Approximate Eclipsing Energy Values (kcal/mole)

<table>
<thead>
<tr>
<th></th>
<th>H</th>
<th>Me</th>
<th>Et</th>
<th>i-Pr</th>
<th>t-Bu</th>
<th>Ph</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>1.0</td>
<td>1.3</td>
<td>1.4</td>
<td>1.6</td>
<td>3.0</td>
<td>1.7</td>
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<tr>
<td>Me</td>
<td>1.3</td>
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<td>2.7</td>
<td>3.0</td>
<td>8.5</td>
<td>3.3</td>
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<tr>
<td>Et</td>
<td>1.4</td>
<td>2.7</td>
<td>3.3</td>
<td>4.5</td>
<td>10.0</td>
<td>3.8</td>
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<tr>
<td>i-Pr</td>
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<td>13.0</td>
<td>8.1</td>
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<tr>
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<td>13.0</td>
<td>23.0</td>
<td>13.5</td>
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<tr>
<td>Ph</td>
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<td>1.7</td>
<td>3.8</td>
<td>8.1</td>
<td>13.5</td>
<td>8.3</td>
</tr>
</tbody>
</table>

Approximate Gauche Energy Values (kcal/mole)

<table>
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<tr>
<th></th>
<th>H</th>
<th>Me</th>
<th>Et</th>
<th>i-Pr</th>
<th>t-Bu</th>
<th>Ph</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0.1</td>
<td>0.2</td>
<td>0.2</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Me</td>
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<td>0.9</td>
<td>1.1</td>
<td>1.4</td>
<td>2.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Et</td>
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<td>0.9</td>
<td>1.1</td>
<td>1.4</td>
<td>3.0</td>
<td>1.5</td>
</tr>
<tr>
<td>i-Pr</td>
<td>0.2</td>
<td>1.1</td>
<td>1.4</td>
<td>2.0</td>
<td>3.9</td>
<td>2.1</td>
</tr>
<tr>
<td>t-Bu</td>
<td>0.5</td>
<td>2.7</td>
<td>3.0</td>
<td>3.9</td>
<td>8.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Ph</td>
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<td>1.4</td>
<td>1.5</td>
<td>2.1</td>
<td>4.1</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Abbreviations for substituent groups in Newman projections.

- \( \text{H} \) hydrogen
- \( \text{Me} \) methyl = \( \text{Me} \)
- \( \text{Et} \) ethyl = \( \text{Et} \)
- \( \text{i-Pr} \) isopropyl = \( \text{i-Pr} \)
- \( \text{t-Bu} \) t-butyl = \( \text{t-Bu} \)
- \( \text{Ph} \) phenyl = \( \text{Ph} \)

Draw all of the Newman projections for rotations around each of the indicated bonds in the structures below and calculate the conformational energies for each conformation using the tables above. Start with the most stable conformation. You can use the above abbreviations in your structures. Calculate the ratios of the two lowest conformational energies and the two farthest apart energies.

2,4-dimethylhexane (use the C<sub>4</sub> C<sub>3</sub> bond)
Possible answer: Conformational energies of 2,4-dimethylhexane

front dot = C_4 = H, Me, Et
back circle = C_3 = H, H, i-Pr

1. most stable
2. 3. 4. 5. 6.

2,3,3-trimethyl-1-phenylhexane
(use the C_1 - C_2 bond)

You have to draw this.
3-methyl-2-phenylpentane
(use the C3 \(\rightarrow\) C2 bond)

You have to draw this.

2-phenyl-3-methylpentane
(use the C3 \(\rightarrow\) C2 bond)

enantiomers
\(A, C\) \(A, D\) \(B, C\) \(B, D\)

enantiomers
Calculating conformational energies in substituted cyclohexane rings.

Substituent \( \Delta G^0 \) (A value)

- \(-\text{H}\) 0.0
- \(-\text{CH}_3\) 1.7
- \(-\text{CH}_2\text{CH}_3\) 1.8
- \(-\text{CH} (\text{CH}_3)_2\) 2.1
- \(-\text{C}(\text{CH}_3)_3\) > 5.0
- \(-\text{F}\) 0.3
- \(-\text{Cl}\) 0.5
- \(-\text{Br}\) 0.5
- \(-\text{I}\) 0.5
- \(-\text{CH} = \text{CH}_2\) 1.7
- \(-\text{CH} = \text{C} = \text{CH}_2\) 1.5
- \(-\text{CCH}\) 0.2
- \(-\text{C}_2\text{H}_6\) (phenyl) 2.9
- \(-\text{CH}_2\text{C}_6\text{H}_5\) (benzyl) 1.7
- \(-\text{CO}_2\text{H}\) 0.6
- \(-\text{CO}_2\) 2.0
- \(-\text{CH} = \text{O}\) 0.7

Substituent \( \Delta G^0 \) (A value)

- \(-\text{CH}_3\text{OH}\) 1.8
- \(-\text{CH}_2\text{Br}\) 1.8
- \(-\text{CF}_3\) 2.4
- \(-\text{O}_2\text{CCH}_2\text{CH}_3\) 1.1
- \(-\text{OH}\) 0.9
- \(-\text{OCH}_3\) 0.6
- \(-\text{SH}\) 1.2
- \(-\text{SCH}_3\) 1.0
- \(-\text{SC}_5\text{H}_6\) 1.1
- \(-\text{SCH}_3\) 1.2
- \(-\text{SO}_2\text{CH}_3\) 2.5
- \(-\text{SeC}_5\text{H}_6\) 1.0
- \(-\text{TeC}_5\text{H}_6\) 0.9
- \(-\text{NH}_2\) 1.2(\(\text{C}_6\text{H}_5\text{CH}_3\)), 1.7(\(\text{H}_2\text{O}\))
- \(-\text{N(CH}_3)_2\) 1.5(\(\text{C}_6\text{H}_5\text{CH}_3\)), 2.1(\(\text{H}_2\text{O}\))
- \(-\text{NO}_2\) 1.1
- \(-\text{HgBr}\) 0.0
- \(-\text{HgCl}\) -0.2
- \(-\text{MgBr}\) 0.8

Trends to compare.

<table>
<thead>
<tr>
<th>Substituent</th>
<th>( \Delta G^0 ) (A value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-H</td>
<td>0.0</td>
</tr>
<tr>
<td>-CH</td>
<td>1.7</td>
</tr>
<tr>
<td>-CH_2_3</td>
<td>1.8</td>
</tr>
<tr>
<td>-CH_2_2</td>
<td>2.1</td>
</tr>
<tr>
<td>-C(CH_3)_3</td>
<td>&gt; 5.0</td>
</tr>
</tbody>
</table>

Use C\_1 \rightarrow C\_6 or Use C\_2 \rightarrow C\_1 C\_4 \rightarrow C\_3

Substituent \( \Delta G^0 \) (A value)

- \(-\text{CH} = \text{CH}_2\) 1.7
- \(-\text{CH} = \text{O}\) 0.7
- \(-\text{CCH}\) 0.5
- \(-\text{CN}\) 0.2

\(-\text{MgBr}\) 0.8

Substituent \( \Delta G^0 \) (A value)

- \(-\text{H}\) 0.0
- \(-\text{CH}_3\) 1.7
- \(-\text{CH}_2\text{CH}_3\) 1.8
- \(-\text{CH} (\text{CH}_3)_2\) 2.1
- \(-\text{C}(\text{CH}_3)_3\) > 5.0

Use C\_2 \rightarrow C\_1 or C\_4 \rightarrow C\_5
Disubstituted Cyclohexanes

Haworth Projections - rings are drawn flat and substituents are written in with straight lines on the top or bottom.

There are two chair conformations for each cyclohexane example above. One axial group increases the potential energy by an amount listed in the table for that substituent. If two axial substituents are on the same side (cis), add an additional 2 kcal/mole to the sum of their axial energies (arbitrary value for our course). If two substituents are 1,2 gauche increase the potential energy by an additional 0.8 kcal/mole (arbitrary value for our course). In some cases the two conformations are equivalent in energy if \( R_1 = R_2 \), (1,1, cis-1,2, trans-1,3 and cis-1,4), but in the other cases one conformation is preferred because it has lower potential energy.

We need a systematic method of analysis or we will quickly become hopelessly lost in the wilderness of flip-flopping cyclohexane rings. I recommend the following strategy for every cyclohexane analysis.

Possible systematic approach to Analyze Cyclohexane Conformations

1. Draw the cyclohexane ring framework as a bond-line formula (chair).
2. Add both axial and equatorial positions. Axial positions point straight up or down in alternating fashion (the ring points to the axial positions). Equatorials are off to the side (use the axial positions to guide you as to top and bottom positions). Both alternate on top or bottom of the face of the ring as you move around the ring. Use parallel bonds in the ring to guide you where to draw the equatorial bonds.
3. Add in the necessary substituents according to the name of the structure (fill in the blank). It is generally easier to visualize substituents drawn on the extreme left or extreme right carbon atoms of the ring because those bonds will be in the plane of the paper, so these are good places to draw your first substituent.
4. Draw the other conformation by flipping one side up and flip the other side down. All of the axial and equatorial positions will interchange, but the top will still be the top and the bottom will still be the bottom.
5. If required, draw Newman projections of any specified compounds according to the indicated perspective.
6. In addition to 1,3-diaxial interactions look for an extra gauche interactions when substituents are substituted 1,2 (vicinal substitution). We will use 0.8 kcal/mole for all gauche interactions of side groups, which is sometimes incorrect (or you can use the table of open chain ‘gauche’ values).
Evaluate which is the preferred conformation with the available energy values. Use the following equation to estimate the ratio between the two conformations.

\[
K = \frac{-\Delta G}{2.3RT}
\]

2.3RT = 1380 cal/mol
when R = 2 cal / (mol-K)
and T = 300 K.

1,1-disubstituted (If R₁ > R₂ then B is the preferred conformation.)

 cis-1,2-disubstituted (If R₁ > R₂ then B is the preferred conformation.)

 trans-1,2-disubstituted (B is always the preferred conformation.)

 cis-1,3-disubstituted (B is always the preferred conformation.)

 trans-1,3-disubstituted (If R₁ > R₂ then B is the preferred conformation.)

 cis-1,4-disubstituted (If R₁ > R₂ then B is the preferred conformation.)
trans-1,4-disubstituted  (B is always the preferred conformation.)

Use $C_1 \leftrightarrow C_6$  $C_3 \leftrightarrow C_4$ or Use $C_2 \leftrightarrow C_1$  $C_4 \leftrightarrow C_5$

Example: cis-1-isopropyl-2-methylcyclohexane

Use the gauche table for open chain conformations to calculate relative energy costs from each perspective and add them to find the total energy cost for each chair conformation.

3 perspectives for each ring's substituents (from all possible views)

more stable conformation

less stable conformation

Full Newman projection of more stable conformation.

Full Newman projection of more less stable conformation.

$\Delta G
K = 10$

2.3RT = 1380 cal/mol
when $R = 2$ cal / (mol-K)
and $T = 300$ K.