Chem 633: Advanced Organic Chemistry 2016 · Midterm 1

Please answer the following questions *clearly and concisely*. In general, use pictures and less than 10 words in your answers.

Write your answers in the space provided.

Write your initials on each page you want graded.

There are 10 total pages to this exam. The last 2 pages were intentionally left blank and may be used for scratch paper. Please be sure your copy has 10 pages before you begin.

Molecular models are allowed.

Calculators are unnecessary and prohibited.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>_____/12</td>
</tr>
<tr>
<td>2</td>
<td>_____/18</td>
</tr>
<tr>
<td>3</td>
<td>_____/20</td>
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<tr>
<td>4</td>
<td>_____/15</td>
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<tr>
<td>5</td>
<td>_____/20</td>
</tr>
<tr>
<td>6</td>
<td>_____/15</td>
</tr>
<tr>
<td>TOTAL</td>
<td>_____/100</td>
</tr>
</tbody>
</table>
1. (12 points) Clearly draw the most stable conformation of the following molecules. You may use Newman projections, when appropriate. No explanation is necessary.

3 pts each:

- \[
\begin{align*}
\text{H}_2\text{C} & \quad \text{SiMe}_3 \\
\text{CH}_3 & \\
\end{align*}
\]

- \[
\begin{align*}
\text{H}_2\text{C} & \quad \text{SiMe}_3 \\
\text{CH}_3 & \\
\end{align*}
\]

- \[
\begin{align*}
\text{HN} & \quad \text{CH}_3 \\
\text{CH} & \quad \text{CH}_3 \\
\end{align*}
\]

- \[
\begin{align*}
\text{HO} & \quad \text{Et} \\
\text{Et} & \\
\end{align*}
\]

- \[
\begin{align*}
\text{H} & \quad \text{OH} \\
\text{Et} & \\
\end{align*}
\]
2. (18 points)
(a) Based on your chemical intuition, please name and draw the HOMO and LUMO of water (H₂O).

<table>
<thead>
<tr>
<th>Name of HOMO of H₂O:</th>
<th>Picture of HOMO of H₂O:</th>
</tr>
</thead>
<tbody>
<tr>
<td>lone pair on oxygen (x2)</td>
<td><img src="image1" alt="HOMO of H₂O" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of LUMO of H₂O:</th>
<th>Picture of LUMO of H₂O:</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image2" alt="LUMO of H₂O" /></td>
<td><img src="image2" alt="LUMO of H₂O" /></td>
</tr>
</tbody>
</table>

(b) Please rationalize why H₂O is bent using Molecular Orbital Theory. Your answer should include molecular orbital diagrams of linear and bent H₂O. Please draw the molecular orbitals and their relative energies on the diagram below.

![Molecular Orbital Diagram](image3)
3. (20 points) Molander reported the following useful method for the stereoselective formation of product 2 (JACS 1991, 113, 3608). In this reaction, Me₃SiOTf acts as a catalytic Lewis acid. Importantly, the OCH₃ group is critical for diastereoselectivity.

Molander reported the following useful method for the stereoselective formation of product 2 (JACS 1991, 113, 3608). In this reaction, Me₃SiOTf acts as a catalytic Lewis acid. Importantly, the OCH₃ group is critical for diastereoselectivity.

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>Ratio of 2 : 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>Me</td>
<td>1.5 : 1</td>
</tr>
<tr>
<td>i-Pr</td>
<td>Me</td>
<td>5 : 1</td>
</tr>
<tr>
<td>i-Pr</td>
<td>i-Pr</td>
<td>15 : 1</td>
</tr>
</tbody>
</table>

(a) What type of stereoisomers are 2 and 3?

(b) Please draw a reasonable arrow-pushing mechanism for the transformation of 1 to 2. Be sure your answer includes an explanation for the role of the OCH₃ group.
(c) Please explain the observed stereoselectivity, including the trend shown in the table. Your answer should include clearly drawn structures and less than 10 words. (Hint: The stereoselectivity is not dependent on the relative stability of the products.)

As $R'$ and $R^2$ get bigger, the lowest energy conformation is more greatly favored.

2pts: $OR'$ seeks to minimize steric clash w/ $R^2$
4. (15 points) Phosphites (1) are known to undergo 1,4- additions to α,β-unsaturated carbonyls (2), ultimately resulting in the formation of phosphorane 4. The rate of this reaction depends on Step 1, so you only need to consider Step 1. Please explain the relative rates of the phosphites shown in the table. Hint: Because you are considering what would stabilize the transition state, you can consider either the forward (1+2 → 3) or the reverse (3 → 1+2) reaction.

<table>
<thead>
<tr>
<th>Phosphite</th>
<th>Relative Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>OMe P(OEt)₃ (A)</td>
<td>1</td>
</tr>
<tr>
<td>OMe P(OEt)₃ (B)</td>
<td>125</td>
</tr>
<tr>
<td>OMe P(OEt)₃ (C)</td>
<td>250</td>
</tr>
<tr>
<td>OMe P(OEt)₃ (D)</td>
<td>750</td>
</tr>
</tbody>
</table>

Consider reverse reaction... \( \text{P-O} \to \sigma_{P-C}^* \) weakens P-C bond. 
Up to 3 \( \text{P-O} \to \sigma_{P-C}^* \) possible but not enforced.

+5: anomeric effect
5. (20 points) For this question, please consider the equilibrium of 1 and 2.

(a) Please draw the lowest energy conformations of 1 and 2.

(b) Based on values we discussed in lecture, please predict an approximate $\Delta G^\circ$ for this equilibrium. Please clearly explain your reasoning (remember: a picture is worth 1000 words!).

(c) Please clearly describe the experiment and data analysis you would do to experimentally determine $\Delta G^\circ$, $\Delta H^\circ$, and $\Delta S^\circ$ for this equilibrium.
6. (15 points) (a) Please draw a reasonable arrow-pushing mechanism for the following reaction (Grossman, Chapter 3, #4i).

(b) Please explain the stereochemistry of the new stereocenters formed in the product.
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