This is a long exam. It has been designed so that no one question will make or break you. The best strategy is to work steadily, starting with those problems you understand best. Make sure you show all of your work. Draw in any lone pairs of electrons, formal charge and curved arrows to show electron movement where appropriate. Partial credit is given for any partially correct responses. Do your best to show me what you know in the time available.

The wise does at once what the fool does at last. Baltasar Gracian
1. Provide an acceptable name for the following molecule. Only specify R and S where shown as 3D. (30 pts)

(4E,6R,8R,9S) 3-(2-methylbutoxy)-4-(2-methyl-3-benzyl-4-nitrosooctyl)-5-phenyl-6-hydroxy-8-amino-9-mercapto-
10-ethyl-12-bromododec-4-enyl 2-amido-3-nitro-6,11-dioxo-7-(4-chlorocarbonyl-7-propylthiocyclonona-4E,7Z-dienyl)-
8-cyano-9-(3-methoxycarbonylcyclopentyl)undec-7Z-en-4-ynoate

2. Indicate all formal charges present in the following structures. Assume all electrons are shown as lines or dots. If other reasonable resonance structures are possible, draw the best other resonance structure using the proper arrow conventions. Indicate which resonance structure is better or if they are equivalent with a brief reason why. (18 pts)
3. Draw all possible chair conformations of trans-1-methoxy-3-isopropylcyclohexane. The axial energy of a methoxy group is 0.6 kcal/mole and the axial energy of isopropyl is 2.1 kcal/mole. The gauche energy of methoxy/isopropyl is 0.9 kcal/mole. Make the left most ring carbon C1 and number towards the front. Show all axial and equatorial groups in the first chair. Which conformation is more stable? Provide a reason for your answer. Draw a Newman projection of the least stable conformation using the C1→C6 and C3→C4 bonds to sight along. Point out any gauche interactions of the substituents shown in your Newman projection. Sketch an energy diagram that shows how the energy changes (lower to higher) with the conformational changes and estimate the ratio of the two conformations at equilibrium. Show your work.

a. (15 pts)

\[ \Delta H_{total} = \Delta H_{methoxy} + \Delta H_{isopropyl} = 2.1 - 0.6 = 1.5 \text{ kcal/mole} \]

\( \Delta H = +1.5 \text{ kcal/mole} \)

\( \Delta H_{total} = 2.1 \text{ kcal/mole} \)

b. Newman projection (C1→C6 and C3→C4) – least stable, point out any gauche interactions with the substituent(s). (5 pts)

\[ \Delta H \approx 3.3 - 7.1 = -3.8 \text{ kcal/mole} \]

\[ K = 10^{\frac{-3.8}{1380}} = 10^{0.082} = 1.087 \]

\[ K = 92\% \]

\[ K = 8\% \]

c. Energy diagram and relative percents (K_{eq} = ?) (5 pts)

\[ K = 10^{\frac{-3.8}{1380}} = 10^{-1.087} \]

\[ K = 0.082 \]

\[ K = 1 / 12 \]

\[ \approx 92\% \]

\[ \approx 8\% \]

d. Calculate an approximate \( \Delta H \) difference between the two conformations. Use that value to estimate a \( K_{eq} \). (Assume R = 2 cal/mol-K and T = 300 K.) Use energy values provided in the box. Show your work. (5 pts)
4. Use a Newman projection of the C3 → C4 bond of 2,2,3-trimethyl-4-phenylhexane to show the most stable conformation first. Rotate through all of the eclipsed and staggered conformations. Using the energy values provided in the tables below, calculate the relative energies of the different conformations. Plot the changes in energy in the graph diagram provided. Calculate a ratio of least stable to most stable based on ΔH values. Hint: Draw a 2D structure first and “bold” the bond viewed in your Newman projection, then decide your line of sight. (25 pts)

![Newman projections of 2,2,3-trimethyl-4-phenylhexane](image)

**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>
<th>Br</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>1.0</td>
<td>1.4</td>
<td>1.5</td>
<td>1.6</td>
<td>3.5</td>
<td>1.7</td>
<td>1.6</td>
</tr>
<tr>
<td>Me</td>
<td>1.4</td>
<td>2.5</td>
<td>2.7</td>
<td>3.0</td>
<td>8.5</td>
<td>3.3</td>
<td>2.8</td>
</tr>
<tr>
<td>Et</td>
<td>1.5</td>
<td>2.7</td>
<td>3.3</td>
<td>4.5</td>
<td>10.0</td>
<td>3.8</td>
<td>3.1</td>
</tr>
<tr>
<td>i-Pr</td>
<td>1.6</td>
<td>3.0</td>
<td>4.5</td>
<td>7.8</td>
<td>13.0</td>
<td>8.1</td>
<td>3.6</td>
</tr>
<tr>
<td>t-Bu</td>
<td>3.5</td>
<td>8.5</td>
<td>10.0</td>
<td>13.0</td>
<td>23.0</td>
<td>13.5</td>
<td>9.1</td>
</tr>
<tr>
<td>Ph</td>
<td>1.7</td>
<td>3.3</td>
<td>3.8</td>
<td>8.1</td>
<td>13.5</td>
<td>8.3</td>
<td>4.2</td>
</tr>
<tr>
<td>Br</td>
<td>1.6</td>
<td>2.8</td>
<td>3.1</td>
<td>3.6</td>
<td>9.1</td>
<td>4.2</td>
<td>3.0</td>
</tr>
</tbody>
</table>

**Approximate Gauche 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>
<th>Br</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.1</td>
<td>0.2</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Me</td>
<td>0</td>
<td>0.8</td>
<td>0.9</td>
<td>1.1</td>
<td>2.7</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Et</td>
<td>0.1</td>
<td>0.9</td>
<td>1.1</td>
<td>1.5</td>
<td>2.9</td>
<td>1.7</td>
<td>1.2</td>
</tr>
<tr>
<td>i-Pr</td>
<td>0.2</td>
<td>1.1</td>
<td>1.5</td>
<td>2.4</td>
<td>3.5</td>
<td>2.1</td>
<td>1.6</td>
</tr>
<tr>
<td>t-Bu</td>
<td>0.5</td>
<td>2.7</td>
<td>2.9</td>
<td>3.5</td>
<td>7.2</td>
<td>3.9</td>
<td>3.3</td>
</tr>
<tr>
<td>Ph</td>
<td>0</td>
<td>1.4</td>
<td>1.7</td>
<td>2.1</td>
<td>3.9</td>
<td>2.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Br</td>
<td>0.1</td>
<td>1.0</td>
<td>1.2</td>
<td>1.6</td>
<td>3.3</td>
<td>1.9</td>
<td>1.1</td>
</tr>
</tbody>
</table>

**Approximate Eclipsing Energy Values (kcal/mole)**

Some were estimated by me.

**Approximate Gauche Energy Values (kcal/mole)**

Some were estimated by me.

ΔG = ΔH

K_\text{eq} = 10^{-\Delta H / 2.3RT}

ΔH = 17.2 - 5.1 = 12.1 kcal/mole

K_\text{eq} = 10^{-12.100 / 580} = 10^{-20.77} = 1.7 \times 10^{-9} = 1 / 590,000,000 = (least) / (most)
5. Use the following set of Fischer projections to answer each of the questions below by circling the appropriate letter(s) or letter combination(s). Hint: Redraw the Fischer projections with the longest carbon chain in the vertical direction and having similar atoms in the top and bottom portion. Classify all chiral centers in the first structure as R or S absolute configuration. (30 pts)

![Fischer projections](image)

(a. Which are optically active? A B C D E) (17 pts)
(b. Which are meso? A B C D E) (5 pts)
(c. Which is not an isomer with the others? A B C D E) (5 pts)
(d. Which pairs are enantiomers? AB AC AD AE BC BD BE CD CE DE) (3 pts)
(e. Which pairs are identical? AB AC AD AE BC BD BE CD CE DE) (3 pts)
(f. Which pairs are diastereomers? AB AC AD AE BC BD BE CD CE DE) (3 pts)
(g. Which pairs, when mixed in equal amounts will not rotate plane polarized light? AB AC AD AE BC BD BE CD CE DE) (3 pts)

(h. Draw any stereoisomers of 3-chlorooohexan-2,4-ol as Fischer projections, which are not shown above. If there are none, indicate this. (5 pts)

![Additional Fischer projections](image)

(i. An ester of a bile acid was recently synthesized. Circle all of the chiral centers. How many stereoisomers are possible? Show work. (5 pts)

![Ester of bile acid](image)

chiral centers are sp³ atoms with 4 different groups attached

# chiral centers = 10

# possible stereoisomers = 2¹⁰ = 1024
6. Draw two additional “better” 2D resonance structures of the given structure. Assume all nonhydrogen atoms have full octets unless + is written next to carbon. Add in any necessary lone pairs and use proper curved arrows to show electron movement. Which structure(s) is(are) best and why? Draw a 3D structure for the given resonance structure. Show bonds in front of the page as wedges, bonds in back of the page as dashed lines and bonds in the page as simple lines. Show orbitals for pi bonds and lone pairs along with their electrons. Identify the hybridization, bond angles and descriptive shape for all numbered atoms in the given structure. (30 pts)

(6 pts) 3rd best - fewer bonds

(14 pts)

Use the given (first) Lewis structure to answer this part. (12 pts)

<table>
<thead>
<tr>
<th>Atom</th>
<th>Shape</th>
<th>Hybridization</th>
<th>Bond Angles</th>
<th># sigma bonds</th>
<th># pi bonds</th>
<th># lone pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>trigonal planar</td>
<td>sp²</td>
<td>120</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>trigonal planar</td>
<td>sp²</td>
<td>120</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>trigonal planar</td>
<td>sp²</td>
<td>120</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>linear</td>
<td>sp</td>
<td>180</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>linear</td>
<td>sp</td>
<td>180</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>tetrahedral</td>
<td>sp³</td>
<td>109</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Explain the different C-F bond energies. Use structures in your explanation. Include any necessary lone pairs, formal charge, curved arrows, etc. What is the hybridization of the fluorine atom in A and B? (4 pts)
7. Draw an acceptable Lewis structure (2D) for the following structure. Show all single, double and triple bonds with one, two or three lines. Include all lone pairs of electrons as two dots. Include formal charge, if present at the atom where present. (25 pts)

8. Match each letter with its common name. Some letters may be used twice. (25 pts)

Use the given molecular formula to calculate the degree of unsaturation. Show work. \( C_{21}H_{24}BrClF_{3}N_{5}O_{5} \), (3 pts)
9. a. The active site of an important liver enzyme has just been discovered. Several key regions are shown in the enzyme active site, just below. As an employee of Bronco Pharmaceutical, you are trying to design an inhibitor molecule that will strongly bind to the key regions of the active site so that the normal substrate cannot get in and react. Four possible inhibitors are shown below. Pick the molecule you think will block the enzyme cavity the best and draw it in the active site. Dashes represent “behind” the page, heavy lines indicate in “front” of the page and simple lines are “in” the page. R represents a nonpolar group. Give a very brief explanation for why your choice will work best. (7 pts)

[Diagram of enzyme active site with interactions labeled]

B works best. All 6 interactions match up well using B, so it should have a high affinity for the enzyme active site and bind strongly. All of the others have some mismatches.

b. Propyl amine, ethylmethylamine and trimethyl amine have boiling points of 7°C, 35°C and 51°C. Match each temperature with the correct compound and provide an explanation for your answer. (7 pts)

[Chemical structures of propyl amine, ethylmethylamine, and trimethyl amine]

The first structure has 2 polar hydrogen atoms (bonded to the nitrogen) that can hydrogen bond, so has stronger attractions with its neighbors (higher boiling point), the second structure has 1 polar hydrogen atom, so has weaker attractions than the first but stronger than the third which has zero polar hydrogen atoms, and the lowest boiling point.

c. 1,3-dichlorobenzene and 1,4-dichlorobenzene have melting points of -22 and 53°C, in no particular order. Match each temperature with the correct compound and provide an explanation for your answer. (5 pts)

[Chemical structures of 1,3-dichlorobenzene and 1,4-dichlorobenzene]

The linear symmetry (more symmetrical shape) of the 1,4-dichloro isomer allows closer packing in the lattice structure. Since the molecules are closer they have stronger interactions that have to be overcome before the lattice breaks down at the melting point. That requires more energy, which we see as a higher melting point.
10. Logic arguments of organic and biochemistry

a. The first molecule in each row is a reference point. Explain if the indicated substitution will be stabilizing, destabilizing or have no effect relative to the reference structure. Provide an explanation for your answer. (10 pts)

i. 

\[
\text{ref. structure: } \begin{array}{c}
\text{H} \\
\text{C} \\
\text{H}
\end{array}
\]

A

\[
\text{ref. structure: } \begin{array}{c}
\text{H} \\
\text{C} \\
\text{H}
\end{array}
\]

B

All of the structures are very electron deficient carbocations that would like to have more electron density. "R" groups are inductively electron donating relative to hydrogen atoms, so structure A should help stabilize the carbocation by shifting its sigma electron towards the electron deficient carbon. The problem with the "R" groups in B is that the fluorines are all pulling electrons AWAY from the electron deficient carbocation and that would be very destabilizing. Structure A more stable than the reference compound and structure B is less stable than the reference carbocation.

ii. 

\[
\text{ref. structure: } \begin{array}{c}
\text{H} \\
\text{C} \\
\text{H}
\end{array}
\]

C

D

All of the structures have too much electron density. In structure C the R groups are pushing even more electron density towards the negative charge which is destabilizing. In structure D the fluorines are all trying to pull more electron density towards themselves, away from the negative charge, which stabilizes the excess charge on the oxygen.

b. Which atom has the higher first ionization potential and why? (F or S) (16 pts, 4 pts each)

F is farther to the right (higher \(Z_{eff}\)) and higher in a column (closer to the nucleus). Both of those predict a stronger attraction for electrons, so ionization potentials are \(F > S\). \(IP_1 (F) = 402 \text{ kcal/mole}\) and \(IP_1 (S) = 239 \text{ kcal/mole}\)

c. Which neutral atom has the larger atomic radius and why? (S or Cl)

Sulfur and chlorine are in the same row. S has a \(Z_{eff}\) of +6 and Cl has a \(Z_{eff}\) of +7, so Cl will hold on to its electrons tighter than S. This should contract the electron cloud making the radius of sulfur \((r_S = 88 \text{ pm})\) larger than chlorine \((r_{Cl} = 79 \text{ pm})\).

d. Which anion has the larger radius and why? (Br\(^{-1}\) or Se\(^{-2}\))

Both Br\(^{-1}\) and Se\(^{-2}\) are in the same row and have a full \(n=3\) shell (full octets). Selenium has \(Z_{eff}\) of +6 and bromine has a \(Z_{eff}\) of +7, so Br will hold on to its electrons tighter than Se so bromine is smaller than selenide. Also there is an excess of 2 electrons instead of 1 electron The radius of selenide \((r_{Se^{2-}} = 184 \text{ pm})\) is larger than bromide \((r_{Br^{-}} = 182 \text{ pm})\)

e. Which cation has the larger radius and why? (Na\(^{+}\) or Mg\(^{+2}\))

Both Na\(^{+}\) and Mg\(^{+2}\) have lost all of their \(n=3\) valence electrons and have full \(n=1\) and 2 shells (core electrons = 1s\(^2\), 2s\(^2\),2p\(^6\)). Na has \(Z_{eff}\) of +1 and Mg has a \(Z_{eff}\) of +2, so Mg will hold on to its electrons tighter than Na. The radius of Mg\(^{+2}\) \((r_{Mg^{+2}} = 86 \text{ pm})\) should be smaller than Na\(^{+}\) \((r_{Na^{+}} = 116 \text{ pm})\).

You can't build a reputation on what you are going to do. Henry Ford