1. Fill in the blanks from among the choices provided. If you believe that more than one choice is valid, choose the best answer. (30 points)

a. An acid with a $pK_a$ of 4.76: $\text{CH}_3\text{COOH}$
   choices: HCl, NH$_3$, CF$_3$COOH, CH$_3$CH$_2$OH, CH$_3$COOH, H$_2$O

b. An ionic compound: $\text{NaOCH}_3$
   choices: BF$_3$, Et$_2$O, CCl$_4$, CH$_4$, CH$_2$=CH$_2$, NaOCH$_3$

c. A Lewis acid: $\text{BF}_3$
   choices: BF$_3$, Et$_2$O, CCl$_4$, CH$_4$, CH$_2$=CH$_2$, NaOCH$_3$

d. A typical value of a bond dissociation energy: $100 \text{ kcal/mol}$
   choices: 1 kcal/mol, 3 kcal/mol, 10 kcal/mol, 30 kcal/mol, 100 kcal/mol, 300 kcal/mol

e. A typical energy barrier to rotation about a carbon-carbon single bond: $3 \text{ kcal/mol}$
   choices: 1 kcal/mol, 3 kcal/mol, 10 kcal/mol, 30 kcal/mol, 100 kcal/mol, 300 kcal/mol

f. A chiral molecule: $2$-$\text{chlorohexane}$
   choices: 3-bromopentane, cis-1,3-dichlorocyclopentane, 2-chlorohexane, 2,3-dimethylbutane, methylcyclohexane, 1-propanol

g. A typical carbon-carbon bond length: $1.5 \text{ Å}$
   choices: 0.5 Å, 1.5 Å, 3 Å, 5 Å, 10 Å, 15 Å (Note: Å = angstrom)

h. A good reactant in an $S_{N}1$ reaction: $1$-$\text{chloro-1-methylcyclohexane}$
   choices: iodobenzene, 1-chloro-1-methylcyclohexane, 2-fluorobutane, CH$_2$=CHBr, 1-bromohexane, chlorocyclobutane

i. A good reactant in an $S_{N}2$ reaction: $1$-$\text{bromohexane}$
   choices: iodobenzene, 1-chloro-1-methylcyclohexane, 2-fluorobutane, CH$_2$=CHBr, 1-bromohexane, chlorocyclobutane

j. A good reactant in an E1 reaction: $1$-$\text{chloro-1-methylcyclohexane}$
   choices: iodobenzene, 1-chloro-1-methylcyclohexane, 2-fluorobutane, CH$_2$=CHBr, 1-bromohexane, chlorocyclobutane
2. Write the missing reactants, reagents, and products in the boxes. If NO REACTION OCCURS, write N.R. (18 points)

\[
\text{Br}_2 + \text{CH}_3\text{I} \rightarrow \text{S}^+ \quad \text{or} \quad \text{S}^+ \quad \text{or other strong base}
\]

\[
\text{Cl} + \text{NaOCH}_3 \rightarrow \text{N.R.} \quad \text{(+ CH}_3\text{O H}) \quad \text{(+ NaCl)}
\]

\[
\text{Br} + \text{NaCN} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3\quad \text{CN}
\]

\[
\text{Br}_2 + \text{O}_2, \text{combustion} \rightarrow 4\text{CO}_2 + 5\text{H}_2\text{O}
\]
3. Diethyl malonate can be prepared from chloroacetic acid in the four-step synthesis shown below. (23 points)

a. Complete the synthesis by filling in the missing reagents in step 1, step 2, and step 4.

\[
\text{chloroacetic acid} \xrightarrow{\text{NaO} \cdot \text{H}} \text{Na} \quad \xrightarrow{\text{NaCN}} \quad \text{Na} \quad \xrightarrow{\text{H}_2\text{O}} \quad \text{diethyl malonate}
\]

b. Diethyl malonate is relatively acidic. Draw the three most important resonance structure for its conjugate base. Make sure to show all charges and lone pairs of electrons.

\[
\begin{align*}
\text{diethyl malonate} & \quad \xrightarrow{\text{NaOEt}} \\
\end{align*}
\]

c. The conjugate base of diethyl malonate is a good nucleophile. Use the template below to write a curved-arrow mechanism for its generation (step 1) and subsequent reaction with benzyl bromide (step 2). Make sure to show all charges and lone pairs of electrons that are directly involved in the reaction. (You do not need to rewrite all resonance structures of the conjugate base of diethyl malonate.)
4. Kemp's triacid (cis,cis-1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid) adopts a chair conformation in which the three methyl groups are in equatorial positions and the three carboxylic acid groups are in axial positions. (25 points)

Build a model of this molecule with your Darling (Molecular Visions) molecular models.

a. What is the distance in centimeters between the carbon atoms of two of the methyl groups? \(2.5\) cm

b. What is the distance in centimeters between the carbon atoms of two of the carboxylic acid groups? \(12.5\) cm

c. Draw Kemp's triacid in such a manner as to clearly illustrate the chair conformation of the cyclohexane ring and the correct positions of the methyl and carboxylic acid groups.

d. How many stereoisomers are there of 1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid (including Kemp's triacid shown above)? \(2\)

e. Draw skeletal structure(s) of the additional stereoisomer(s).

f. What word best describes the relationship of the additional stereoisomer(s) to Kemp's triacid? \(\text{diastereomer}\) (\(\text{diastereomeric}\))
5. One of the two stereoisomers of 2-bromo-1,3-dimethylcyclohexane shown below readily undergoes elimination upon treatment with potassium tert-butoxide. (10 points)

a. Write the products of the elimination reaction in the boxes.

\[ \text{H}_3\text{C} \quad \text{OR} \quad \text{H}_3\text{C} \]

\[ \text{Br} \quad \text{CH}_3 \quad \text{Br} \quad \text{CH}_3 \]

\[ \text{KO-t-Bu} \quad \text{t-BuOH} \]

\[ \text{+} \]

\[ \text{+} \]

\[ \text{(the enantiomer)} \]

b. Circle the stereoisomer that reacts readily.

c. Explain why that stereoisomer reacts readily while the other does not.

The circled stereoisomer can adopt a chain conformation with an anti-periplanar relationship between hydrogen and bromine for E2 elimination while the other cannot.

6. Two constitutional isomers equilibrate as shown below. (20 points)

a. Write a curved-arrow mechanism for this reaction. Make sure to show all intermediates, charges, and lone pairs of electrons. Also, make sure to draw important resonance structures where appropriate.

\[ \text{Br} \quad \text{heat} \quad \text{Br} \]

b. Do you expect the reaction to be endothermic, exothermic, or neither? **Endothermic**

Why? The more substituted double bond of the reactant is more stable than the less substituted double bond of the product.

c. Draw an energy diagram for this reaction. Clearly label the reactant, product, intermediate(s), and transition state(s).
7. Explain the following with words, equations, or structures. (18 points)

a. An undergraduate research student wants to convert a sample of enantiomerically pure \((R)-1\)-chlordodecane to enantiomerically pure \((S)-1\)-deutero-1-iodododecane and proposes to do so by treatment with an excess of sodium iodide dissolved in acetone. His research advisor agrees that only \(S_N2\) displacement will occur under the reaction conditions, but thinks that the resulting \((S)-1\)-deutero-1-iodododecane will not be enantiomerically pure and that the enantiomeric purity of the \((S)-1\)-deutero-1-iodododecane will decay with increasing exposure to the sodium iodide solution. Explain the research advisor's thinking.

Note: Deuterium (D) is an isotope of hydrogen with 1 proton and 1 neutron. It is sometimes referred to as "heavy hydrogen."

\[
\begin{align*}
\text{(R)-1-chloro-1-deuterododecane} & \quad \text{(S)-1-deutero-1-iodododecane} \\
\text{D} & \quad \text{D}
\end{align*}
\]

\[\text{Sn}_2: \text{reaction of the iododione product with I}^- \text{generates the enantiomer, leading to racemization.}\]

b. Another undergraduate research student attempts to recrystallize a sample of enantiomerically pure \((S)-1\)-bromo-2,2-dimethyl-1-phenylpropane from hot acetone. To her dismay, the optical rotation of her recrystallized product is substantially less than that of her original sample. After repeated attempts, the crystals she obtains are racemic \((S)-1\)-bromo-2,2-dimethyl-1-phenylpropane. Explain the racemization.

\[
\text{(S)-1-bromo-2,2-dimethyl-1-phenylpropane}
\]

\[
\text{Br} \quad \quad \text{Br}
\]

Racemization occurs by way of ionization to form a chiral cation.

c. Both \(\text{cis-2-butene}\) and \(\text{trans-2-butene}\) undergo an addition reaction with bromine, but the 2,3-dibromobutane produced from \(\text{cis-2-butene}\) has a different melting point and boiling point than the 2,3-dibromobutane produced from \(\text{trans-2-butene}\). Explain the difference between the 2,3-dibromobutane products.

\[
\begin{align*}
\text{cis-2-butene} & \quad \text{trans-2-butene} & \quad \text{2,3-dibromobutane} \\
\text{CH}_3-\text{CHBr}\text{CHBr}-\text{CH}_3 \\
\end{align*}
\]

\(\text{Cis- and trans-2-butene form different diastereomers of 2,3-dibromobutane, which have different mp and bp. One forms meso-2,3-dibromobutane (\(\text{meso-2,3-dibromobutane}\)) while the other forms a racemic mixture of (2R,3R)- and (2S,3S)-2,3-dibromobutane (\(\text{2R,3R- and 2S,3S-2,3-dibromobutane}\))}\)
The pinacol rearrangement occurs when pinacol (2,3-dimethylbutane-2,3-diol) is treated with a strong acid (e.g., H\textsubscript{2}SO\textsubscript{4}) and results in the formation of pinacolone (3,3-dimethyl-2-butanone). (12 points)

The mechanism of the pinacol rearrangement involves four steps. In the first step, pinacol is protonated. In the second step, a leaving group leaves. The third step (which has been drawn for you) is called a Wagner-Meerwein rearrangement or a 1,2-methyl shift. In the final step, a proton is lost.

Use the template below to write a curved-arrow mechanism for the pinacol rearrangement. Make sure to show all intermediates, charges, and lone pairs of electrons.