1. Hemoglobin is the key molecule in biological oxygen transport, and the key part of hemoglobin is an Fe$^{3+}$ ion as part of its structure. A simple model suggests that the iron ion acts as a Lewis acid, bonding reversibly to oxygen. Think about the bonding of oxygen to the iron ion.

A. Draw the oxygen molecule using Lewis structures and show all bonds, non-bonding electrons and formal charges. Then draw next to it a picture of oxygen bound to a Lewis acid; please use BF$_3$ as your Lewis acid instead of Fe$^{3+}$ (the picture will be simpler). Show all non-bonding electrons and formal charges.

![Lewis structure of oxygen and BF$_3$](image)

Sodium cyanide (NaCN) and carbon monoxide are toxic because they compete with the oxygen in binding to the iron ion.

B. There are two reasonable resonance structures for cyanide anion, one with two bonds and one with three. Draw both resonance structures, showing all bonds, non-bonding electrons, and formal charges. Indicate the hybridization at C and at N. State which structure you feel is the more stable, and explain the basis for your choice briefly.

![Resonance structures of cyanide anion](image)

more stable: N is a little more electronegative than C, and therefore putting (-) on N is a little better than putting it on (C). However, the structure on the left has one more bond, a big stabilizing factor.

C. There are two reasonable resonance structures for CO, one with two bonds and one with three. Draw both resonance structures of CO, showing all bonds, non-bonding electrons, and formal charges. Indicate the hybridization at C and at O. State which structure you feel is the more stable (more important in the hybrid), and explain the basis for your choice briefly.

![Resonance structures of CO](image)

O is more electronegative than C, and therefore putting (-) on O is better than putting it on (C). However, the structure on the left has one more bond, a stabilizing factor. Not easy to decide which is more stable from this analysis.

D. Draw a structure for cyanide anion bound to BF$_3$. Note that there are two "ends" to cyanide anion. Explain why you chose one particular end over the other to bind the Lewis acid. Show all bonds, non-bonding electrons, and formal charges. Indicate the hybridization at the boron atom

![Structure for cyanide anion bound to BF$_3$](image)

E. Draw a representation of carbon monoxide bound to BF$_3$. Note that there are two "ends" to carbon monoxide. Explain why you chose one particular end over the other to bind the Lewis acid. Show all bonds, non-bonding electrons, and formal charges.
F. Which do you predict will bind more strongly to BF₃: oxygen, cyanide anion, or carbon monoxide? Explain your reasoning briefly.

*Cyanide: Formal negative charge, less electronegative atoms*

2. Consider the isomers with the molecular formula C₃H₆O₂
   a. write the isomer which is much more soluble in 0.1 M NaOH compared to pure water. Explain your choice briefly.

   **Criteria for solubility in water:**
   - best--ionic
   - next--H-bonding

   With two O to play with, you can construct a carboxylic acid unit, and deprotonate it in base.

   ![Carboxylic acid deprotonation](image)

   **Strong association with water through H-bond donation from water to the anion.**

   b. write the isomer which is least soluble in water.

   Least soluble in water means least polar (no polarized pi bonds) and minimum H-bonding. Need one pi bond or ring to fit the empirical formula

   ![Possible isomers](image)

3. using any combination of 5 carbon atoms, any number of hydrogens, and two nitrogen atoms, construct the uncharged molecule with:
   a. the highest solubility in cyclohexane

   minimum H-bonding, minimum polarity, no ions; no N-H units

   Design molecule with N as tertiary amino groups

   ![Tertiary amino group alternatives](image)

   b. the least basic nitrogen atom

   Least basic: minimum availability of non-bonding electron pair.

   Inductive stabilization by electron withdrawing groups nearby
   Resonance stabilization by delocalizing the lone pair

   Most (s) character for the lone pair (sp>sp2>sp3)

   ![Least basic nitrogen alternatives](image)

   Hard to be sure which of these is the better answer
c. the most electron deficient carbon atom
Most electron deficient carbon atom--attach as many electro negative atoms as possible
\[ \text{N} \equiv \text{C} \equiv \text{N} \]

d. the most acidic proton
Maximum delocalization of anion, especially onto electronegative atoms
maximum electron withdrawing inductive effect at anion site
more s character
wierd and wonderful
\[ \text{N} \leftarrow \text{H} \]

I should have been more careful to specific "uncharged" molecules, because one could obviously generate all sorts of funny charged species that would love to give up a proton.

4. Compare the acidity of molecules A and B. Identify the most acidic proton on each.

A more acidic

The anion has two good resonance structures

5. Phenol is a moderately acidic molecule, and was used in water solution by Pasteur as the first antiseptic.
Assuming the acidity is the feature responsible for the antibiotic activity, would it have been more or less effective to use solution of phenol in DMSO instead of water? Explain by showing off your expertise regarding solvent effects on acid-base reactions.

The relative acidity of a molecule depends on its ability to dissociate into a proton and an anion (or neutral lone pair). Protic solvents strongly favor the ionization by H-bonding to both the proton and the anion. Aprotic solvents are less favorable, even if polar, because there is no H-bond donation to stabilize the anion, less ionization. DMSO is a polar aprotic solvent, gives less dissociation of phenol, less effect acidic solution. Use water!

6. Normally, when causing an acidic molecule to form its conjugate base by proton abstraction with base, it is possible to neutralize the solution and re-generate the original acid. We also imply this reversibility in the equilibrium expression:
Strange, when the weak acid C was treated with base and then neutralized with acid, C was re-generated but two new molecules were also found, D and E. Propose structures for D and E and explain how they formed.

\[
\text{base} \quad \text{conjugate base of C} \quad \text{acid to neutralize} \quad C + D + E
\]

7. Consider the following pairs of molecules. Note the bond indicated by the arrow in each structure. For each pair, circle the one in which the indicated bond is longer and give one important reason for the difference (hybridization, delocalization, steric effects, inductive effects. Explain briefly. If you choose delocalization, draw the relevant structure(s).

A. longer (less shortened by resonance delocalization; the resonance structure is not as "good" and for the N case.)
B. \[ \text{H}_3\text{C}-\text{C}≡\text{C}-\text{CH}_3 \quad \text{H}≡\text{C}-\text{CH}_2-\text{CH}_3 \]

shorter (sp-sp3)

more s character, tighter and shorter bond

C. \[
\begin{array}{c}
\text{partial double} \\
\text{bond, delocalized}
\end{array}
\quad \text{vs} \quad \begin{array}{c}
\text{normal double bond,}
\text{shorter}
\end{array}
\]

D. In a related analysis, draw the structure of a molecule with six carbons, any number of hydrogens, no other atoms, and no formal charge which has the SHORTEST carbon-carbon SINGLE BOND distance. Explain your choice briefly. Indicate clearly which bond you think is the shortest.

\[ \text{sp-sp overlap} \]