1. Draw complete structure of the following natural $\alpha$-amino acid at pH 7.0 in appropriate charged form. (8 pts)

A basic amino acid

A polar, but not basic, amino acid

2. Rank the following compounds on their ability to undergo hydrolysis at pH 1 (H$^+$/H$_2$O). Use 1 for most easily hydrolyzable and 3 for least. (9 pts)

2 3 1

3. Write the Henderson–Hasselbach equation for the following equilibrium. Define the terms involved. (12 pts)

$$R_3NH^+ + H_2O \rightleftharpoons R_3N + H_3O^+$$

$$\log \frac{[R_3N]}{[R_3NH^+]} = pH - pK_A$$

where $pK_a = -\log K_a$ (or negative log of the acid dissociation constant); $pH = -\log [H^+]$ (or a measure of the concentration of protons); $[R_3N]$ is the concentration of the base and $[R_3NH^+]$ is the concentration of the conjugate acid at equilibrium.

4. The three major functions of lipids are (6 pts)

1) formation of lipid bilayer (cellular membrane / membranes)
2) provide energy (energy storage)
3) perform secondary messenger functions
5. Draw product(s) of the following hydrolytic reactions assuming that complete hydrolysis. Write appropriate charges on functional groups formed in the reaction. If there is no product, write NONE. (16 pts)

A) \[
\text{H}_3\text{C} - \text{CH}_3
\]
\[
\text{CH}_3 - \text{CH}_3
\]
\[
\text{H}_2\text{O/OH}, \text{pH 8}
\]
\[
\text{COO}^-
\]
\[
\text{COO}^-
\]

B) \[
\text{R} - \text{N} - \text{S} - \text{CH}_3 - \text{CH}_3
\]
\[
\text{R} - \text{N} - \text{S} - \text{CH}_3 - \text{CH}_3
\]
\[
\text{H}_2\text{O/OH}, \text{pH 12}
\]
\[
\text{COO}^-
\]
\[
\text{R} - \text{O} - \text{H}
\]

6. Predict the major product (not all the products) in the following reactions. If there is no product, write NONE. **NOTE:** More than one major product would fetch negative points. (15 pts)

A) \[
\text{O}
\]
\[
\text{O}
\]
\[
\text{Cl}
\]
\[
\text{NO}_2
\]
\[
\text{nitration}
\]

B) \[
\text{Cl} - \text{SO}_2\text{NHCH}_3
\]
\[
\text{Cl} - \text{SO}_2\text{NHCH}_3
\]
\[
\text{bromination}
\]

C) \[
\text{Cl} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2
\]
\[
\text{Cl} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2
\]
\[
\text{metabolic oxidation}
\]

7. Identify the class of the following lipids (8 pts)

- Sphingolipid
- Steroid

8. HDL particles are different from LDL particles in \#4 (4 pts)
   1) their overall composition
   2) their density
   3) their size
   4) all of the above

9. Two phase I metabolic reactions include **hydrolysis** and **oxidation or reduction**, while two phase II metabolic reactions include **glucuronidation, sulfation, glutathionylation** and _____________________________.(8 pts)
10. Predict the order of melting transition of following three natural lipids (all double bonds are cis). Use 1 for lowest melting and 3 for highest melting (9 pts).

\[ \text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{COOH} \] _2_____ \\
\[ \text{CH}_3(\text{CH}_2)_5\text{CH}==\text{CH}(\text{CH}_2)_7\text{COOH} \] _1_____ \\
\[ \text{CH}_3(\text{CH}_2)_9\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{COOH} \] _3_____ \\

11. Name the type of the following metabolic reactions. (8 pts)

a) \( \text{CH}_3(\text{CH}_2)_5\text{COOCH}_3 \rightarrow \text{CH}_3(\text{CH}_2)_5\text{COOH} + \text{CH}_3\text{OH} \)  
Ester Hydrolysis

b) \( \text{PhOCH}_3 \rightarrow \text{PhOH} + \text{HCHO} \)  
O-Dealkylation

c) \( \text{PhCH(NH}_2\text{)CH}_3 \rightarrow \text{PhCOCH}_3 + \text{NH}_3 \)  
Deamination

d) \( \text{PhSCH}_3 \rightarrow \text{PhS(O)CH}_3 \)  
S-oxidation / Sulfoxidation

12. Circle the part of the following structures that is aromatic. Clearly identify the part. If the entire molecule is aromatic, encircle the whole molecule. **Note:** Negative points for identifying wrong parts as aromatic. (8 pts)

13. The four most important constituents of lipoprotein particles are cholesterol, cholesteryl ester, phospholipids and apolipoprotein (8 pts). These constituents are held together through non-covalent interaction or hydrophobic interaction (identify the type of interaction) (2 pts). The surface of lipoprotein particles is lined with polar groups (2 pts). This makes lipoprotein particles highly soluble in aqueous medium (2 pts).

14. In not more than 5 sentences explain why lipid I is likely to be more beneficial for a human body in comparison to lipid II? (5 pts)

\[ \text{I} \quad \text{CH}_3(\text{CH}_2)_3\text{CH}==\text{CHCH}==\text{CH}(\text{CH}_2)_7\text{COOH} \] \\
\[ \text{II} \quad \text{CH}_3(\text{CH}_2)_5\text{CH}==\text{CH}(\text{CH}_2)_7\text{COOH} \]

Lipid I has lower melting transition than lipid II because of the presence of an additional double bond. The extra double bond in I lowers its melting transition more than II, which introduces greater fluidity (or plasticity) in the membrane (or reduces membrane rigidity). This enhanced fluidity is thought to be very important for membrane communication.

15. Circle the acid that is expected to exhibit higher pKa in the following pair of acids. (5 pts)

\[ \text{Cl} \quad \text{Cl} \quad \text{COOH} \] \\
\[ \text{Cl} \quad \text{Cl} \quad \text{COOH} \]
16. Rank the molecules/ions in each series according to their acidity. Use 1 for the least acidic, 2 for slightly higher, and so on. (28 pts)

a) 
\[
\begin{align*}
\text{COOH} & : 1/2 \\
\text{NO}_2 \text{COOH} & : 4 \\
\text{CH}_2\text{NO}_2 \text{COOH} & : 2/1 \\
\text{CHO} \text{COOH} & : 3
\end{align*}
\]

b) 
\[
\begin{align*}
\text{OH} & : 1 \\
\text{OH} \text{NO}_2 & : 5 \\
\text{OH} \text{N(CH}_3)_2 & : 1 \\
\text{OH} \text{CN} & : 2 \\
\text{OH} & : 4
\end{align*}
\]

c) 
\[
\begin{align*}
\text{OH} & : 1 \\
\text{COOH} & : 5 \\
\text{O} \text{H} \text{CON} \text{H}_2 \text{N} \text{COOH} & : 3 \\
\text{COOH} & : 4 \\
\text{O} \text{C} \text{CO} & : 2
\end{align*}
\]

17. Why does molecule I hydrolyze faster in our body than molecule II? (6 pts)

In molecule I, the two sterically bulky groups are on the same side of the carbonyl carbon, while in molecule II, they are on the opposite side. Thus, OH⁻ or H₂O attack (in alkaline or acidic conditions) is sterically hindered from both sides for molecule II, while one face of the carbonyl carbon is open to attack for molecule I. Thus, molecule I hydrolyzes faster than molecule II.

18. Rank the following compounds on their ability to undergo hydrolysis under basic conditions (H₂O/OH⁻). Use 1 for least hydrolyzable and 3 for most. (9 pts)

\[
\begin{align*}
\text{Me} & : 3 \\
\text{Me} & : 1 \\
\text{Me} & : 2
\end{align*}
\]
19. The pH of kidney ranges from 4.5 to 8.0. In the un-metabolized form, which of the following two compounds below will most rapidly excreted and why? (8 pts)

In the pH range 4.5 to 8.0, molecule I will always be protonated (quaternary ammonium ion), while molecule II will not be protonated (aniline derivative ... pKa 3 – 5). Thus, molecule I will be highly soluble and excreted rapidly in urine (mostly water).

20. Circle ionizable functional group(s) (pH range 0 -14) in the following molecules and indicate their approximate pKₐ value or range. If there are no ionizable groups, write NONE. (14 pts)