1. (15 pts)

a) In which direction will the acid-base equilibria lean, to the left or to the right, considering the pKa values for the molecules shown below?

\[
\begin{align*}
\text{H}_2\text{CO} & \rightleftharpoons \text{H}^+ + \text{CO}_2^- \\
pK_a &= 40 \\
\text{H}_3\text{PO}_4 & \rightleftharpoons \text{H}_2\text{PO}_4^- + \text{H}^+ \\
pK_a &= 16 \\
\end{align*}
\]

b) Calculate the enthalpy change for this S_N reaction from these approximate bond dissociation energies: (O-H = 497 kJ/mol; C-O = 385 kJ/mol; HCl = 431 kJ/mol; C-Cl = 300 kJ/mol. Show your calculation. Is this reaction exothermic (exergonic) or endothermic (endergonic)?

\[
\begin{align*}
\text{C}_6\text{H}_5\text{Cl} & \rightleftharpoons \text{H}_2\text{O} \text{H} \\
\Delta G^o &= -19 \text{ kJ/mol} \\
\end{align*}
\]

c) Allylic bromination can be accomplished with low concentrations of Br_2 by employing the NBS reagent. Use the technique of arrow pushing to describe the following bromination reaction. Additionally put the suitable resonance structures in the provided boxes.

\[
\begin{align*}
\text{Br}_2 & \text{C}_6\text{H}_5\text{Br} \text{HBr} \\
\end{align*}
\]

2. (9 pts)

a) What are the statistics for each product's formation (I, II, III) in the free-radical bromination (low Br_2 concentration) reaction shown below? What are the C-H bond strengths for each C-H bond that needs to be broken to make these products? Use the following values: 356 kJ/mol, 381 kJ/mol, 410 kJ/mol.

\[
\begin{align*}
\text{C}_6\text{H}_5 & \text{C}_6\text{H}_5 \rightleftharpoons \text{Br}_2 \text{C}_6\text{H}_5\text{Br} \\
\end{align*}
\]
b) From these relative rates for bromination (I° = 1; II° = 80; allylic > 800), calculate the relative percentage of isomer each isomer. Show your work.

\[
\begin{align*}
\text{I} & : 1600 \\
\text{II} & : 1763 \\
\text{III} & : 3 (1)
\end{align*}
\]

\[1600 \div 1763 = 91\% \quad 2(800) \quad 2(80) \quad 3(1)\]

b) If you were to chlorinate pent-1-ene instead of brominate it (see b above), would the percentage of isomer I be larger or smaller? Please explain.

3. (9 pts)

a) A mechanism for an exothermic SN1 reaction (solvolysis in ethanol) is shown below. For this reaction draw a reaction coordinate energy diagram, labeling the diagram to show \(\Delta G^\circ\), \(\Delta G^+\), intermediate(s), transition state(s), etc. \(\Delta G^\circ\) is the same as Eact). Be sure to identify the rate-determining step.

\[
\begin{align*}
\text{A} & \rightarrow \text{B} \rightarrow \text{C} \rightarrow \text{D} \\
& \text{rate step}
\end{align*}
\]

b) Hammond's postulate allows us to estimate the likely structure of a transition state. From the reaction step (C to D) depicted above in part a, and the energy diagram shown here for that step, which structure more correctly represents the transition state \(\text{TS}_1\) or \(\text{TS}_2\)? Explain.

\[
\text{TS}_1 \quad \text{TS}_2
\]
4. (24.5 pts)

a) S-4-iodopent-1-ene, a $2^0$ alkyl halide, reacts with sodium bromide to generate 4-bromopent-1-ene. What will be the stereochemistry of the product that is produced, and what type and structure of polar solvent will be needed for each of these nucleophilic substitution types? Circle your correct three answers per side.

b) Draw structures of the products that form in the following nucleophilic substitution reactions.

c) Good leaving groups are required for all nucleophilic substitution reactions and this is reflected in reaction rates. The rates for second order substitution reactions were measured as a function of leaving group and the following rates were observed (60,000; 30,000; 10,000; 200; and 1). Correctly associate the observed rate with the appropriate leaving group.

\[
\text{Cl}^{-1} = \frac{200}{30000}, \text{I}^{-1} = \frac{30000}{10000}, \text{F}^{-1} = \frac{1}{10000}, \text{Br}^{-1} = \frac{16000}{60000}
\]

d) Which will be the better nucleophile for an $S_N2$ reaction? There are two questions below. Select an answer from each rectangle.

e) In 217 we learn a name reaction called the ‘Williamson Ether Synthesis’. It is a simple example of an $S_N2$ reaction as is shown below. Which procedure would be most favorable for making the ether shown in the center, the one coming from the right or the one coming from the left? Why?

5. (16 pts)

a) Tofacitinib and Ruxolitinib, FDA approved drugs used to treat myelofibrosis and rheumatoid arthritis, have recently been shown to promote hair regrowth. This may be useful for patients who have undergone chemotherapy or other forms of trauma. Identify the configuration (R or S) for each chirality center in these two molecules.
b) What is the stereochemical relationship between the tofacitinib fragment and each isomer shown below?

```
[Chemical Structures]
```

c) Using the frameworks that are drawn below, add the elements to the correct positions to give the stereochemistry indicated in each name.

```
[Chemical Frameworks]
```

d) Draw the structure of the product(s) that form(s) when the following molecule undergoes bromination with NBS. Be sure to assign R or S-configurations as appropriate to the product(s) and identify any stereochemical relationships that may exist.

```
[Chemical Structures]
```

6. (11.5 pts)

a) Give the correct IR carbonyl absorption value for each molecule that is shown below. Use the following values: 1685, 1718 and 1747 cm\(^{-1}\).

```
[Chemical Structures]
```

b) The CNMR spectrum for a molecule of formula C\(_6\)H\(_{10}\)O\(_2\) is shown below. In the DEPT-90 all peaks have disappeared. In DEPT-135 the peaks at 125.1 and 60.78 are negative, and those at 18.3\(\delta\) and 14.3\(\delta\) are positive. There are significant peaks in the IR at 1722, 1640 and 1178 cm\(^{-1}\). Determine the structure for this molecule. Show your work and correlate your structure with the absorptions that are observed.

```
[Chemical Structures]
```