I. (4 points) In connection with our research directed at probing the molecular mechanism of chemical carcinogenesis, we carried out a series of synthetic reactions shown below. Arrange these four compounds in order of their \( R_f \) values when analyzed by thin-layer chromatography (TLC) on silica gel-coated plates using \( \text{CH}_2\text{Cl}_2 \) as the developing solvent. No partial credit is given to this question.

II. (8 points) Silica gel thin layer chromatography (TLC) is often used to monitor the progress of an organic reaction. For the following reduction, a solvent system is selected to give the starting material an \( R_f \) value of about 0.5. Fill in the spots that would be expected when the reduction is 50% compete and 100% complete. Visualization of all of the organic compound spots on TLC can be made upon exposure of each solvent-dried plate to a 254 nm-UV lamp.

On each TLC plate, a student has placed a sample of the starting material (5) as a reference on the left of the plate, a spot of the reaction mixture on the right, and a co-spot in the center of each. Co-spotting is where some of 5 and some of the reaction mixture are spotted together in order to make better comparisons.
III. (12 points) Lithium diisopropylamide (LDA) is commonly used to generate the dilithium dienolate from β-keto ester under mild conditions (see below). However, it is essential to use exactly a one to two molar ratio of a keto ester and LDA for the effective generation of the dienolate.

$$\text{H}_3C\overset{\text{O}}{\text{C}}\overset{\text{O}}{\text{O}}\text{C}_2\text{H}_5\overset{\text{O}}{\text{O}}\text{C}_2\text{H}_5 + 2\overset{\text{Li}}{\overset{\text{N}}{\text{N}}}\text{LDA} \rightarrow \overset{\text{O}}{\text{O}}\text{O}_2\text{C}_2\text{H}_5\overset{\text{2Li}^+}{\text{O}} + 2\overset{\text{N}}{\text{N}}\text{Li}_2\text{+}$$

ethyl acetoacetate (7)  LDA  tetrahydrofuran (solvent)  dilithium dienolate (8)

(1) (4 points) What volume of a 2.0 M solution of LDA in tetrahydrofuran is required for the quantitative formation of dilithium dienolate (8) from 13.0 g of ethyl acetoacetate (7)? Show your work.

Molecular weight of ethyl acetoacetate (7) is 130 g/mol. So, 13 g of 3 is 0.1 moles.

Therefore, 0.2 moles of LDA is required for the formation of dilithium dienolate (8).

$$2.0 \text{ moles} / \text{L} \times X \text{ L} = 0.2 \text{ moles} \rightarrow X = 0.1 \text{ L} = 100 \text{ mL}$$

Answer: 100 mL

(2) (4 points) Treatment of dilithium dienolate (8) with 1 mol equivalent of benzyl bromide (9) followed by work-up with aqueous NH₄Cl provides the monobenzylated product, (10). If the dienolate (8) generated from 13.0 g of ethyl acetoacetate (7) is used for this reaction, how many grams of benzyl bromide are required for the quantitative formation of the monobenzylated product, (10)? Show your work.

Molecular weight of benzyl bromide (9) is 171 g / mol.

0.1 moles of benzyl bromide is required for the above reaction.

Thus, 0.1 moles x 171 g / mol = 17.1 g

Answer: 17.1 g

(3) (4 points) What is the theoretical yield of monobenzylated product, (10), for the reaction described in (2)? Show your work.

The reaction should produce 0.1 moles of the monobenzylated product, (10).

Molecular weight of (10) is 220 g / mol.

Thus, 0.1 moles x 220 g / mol = 22.0 g

Answer: 22.0 g
IV. (14 points) For each of the following two sets of compounds, match each compound to its expected IR frequency for the C=O bond stretching absorption and provide a brief explanation to your answer. If your explanation involves the resonance concept, make certain to draw relevant resonance structures and if your explanation includes the inductive effect, make sure to indicate to which direction electrons move inductively.

(1) 1761, 1740, or 1720 cm$^{-1}$

![Normal ester!](1760 cm$^{-1}$) ![Conjugated ester.](1720 cm$^{-1}$) ![Normal ester!](1740 cm$^{-1}$)

νC=O is more single bonded due to these resonance contributors. Therefore, lower cm$^{-1}$ than a normal ester νC=O.

In this res structure, C-C σ e's are inductively withdrawn towar O+. => C=O becomes shorter, stronger => higher νC=O cm$^{-1}$ than a normal ester νC=O. Alternatively, the lone pair on the Ar-O oxygen atom is shared with the aromatic π e's, thus diminishing the contribution of these lone-pair e's to the resonance with the C=O. => less single-bonded C=O than a normal ester C=O, thus raising the νC=O cm$^{-1}$.

(2) 1692, 1674, or 1657 cm$^{-1}$

![This res contributor makes C=O even more single bonded, thus a lower νC=O cm$^{-1}$](1657 cm$^{-1}$) ![This res contributor makes C=O even more single bonded, thus a lower νC=O cm$^{-1}$](1674 cm$^{-1}$) ![This res contributor makes C=O even more single bonded, thus a lower νC=O cm$^{-1}$](1692 cm$^{-1}$)

In this res contributor, C-C σ e's are inductively withdrawn towards C+ => C=O becomes shorter, stronger => a higher νC=O cm$^{-1}$ than 1674 cm$^{-1}$

Alternatively, C=C and arom π e's are withdrawn towards the NO$_2$ group, thus diminishing the contribution of those π e's to the resonance with the C=O => less single-bonded C=O => a higher νC=O than 1674 cm$^{-1}$

Therefore, a lower νC=O cm$^{-1}$ than a normal α,β-unsat'd νC=O cm$^{-1}$(1685 cm$^{-1}$).
V. (11 points) Treatment of hydroxy-acid 11 with a catalytic amount of \( p \)-toluenesulfonic acid (\( p \)-TsOH; \( \text{pKa} = 0.5 \)) at reflux in benzene produces the intramolecular esterification product, lactone 12 in 95% yield. Provide in the box below a step-by-step mechanism for the formation of lactone 12 from 11. You may use H-A and A- to represent the acid catalyst and its conjugate base, respectively.

\[
\begin{align*}
\text{HO} & \quad \text{HO} \\
\text{HO} & \quad \text{HO} \\
\text{H} & \quad \text{H} \\
11 & \\
\end{align*}
\]

\[
\begin{align*}
\text{p-toluenesulfonic acid (\( p \)-TsOH) (catalytic)} & \quad \text{benzene, reflux} \\
\text{H}_2\text{O} & \\
12 & \\
\end{align*}
\]

Mechanism:

VI. (4 points) The solubility of compound A in ethanol is 0.8 g per 100 mL at 0 °C and 5.0 g per 100 mL at 78 °C. What is the minimum amount of ethanol needed to recrystallize a 12.0-g sample of this compound? How much would be lost in the recrystallization, that is, would remain in the cold solvent? Show your work.

\[
\cdot 5 \text{ g} / 100 \text{ mL} = 12 \text{ g} / X \text{ mL} \quad \text{Thus, } X = (12 \times 100) / 5 = 240 \text{ mL} \\
\text{Answer: 240 mL of ethanol needed for recrystallization}
\]

\[
\cdot 0.8 \text{ g} / 100 \text{ mL} = Y \text{ g} / 240 \text{ mL} \quad \text{Thus, } Y = (240 \times 0.8) / 100 = 1.92 \text{ g} \\
\text{Answer: 1.92 g of compound A would remain in the solvent at 0 °C.}
\]

VII. (3 points) In a couple of experiments you have performed in the lab, recrystallization is carried out using a mixture of solvents such as ethanol and water. Under what general circumstances is a mixture of solvents instead of a single solvent used for recrystallization?

High solubility of a compound at or near the boiling point and its low solubility at room temperature are the required properties of a solvent for recrystallization. When no single solvent that satisfies such properties can be found, a solvent pair is used for recrystallization.
VIII. (12 points) For each of the following aldol condensation reactions, draw in the boxes provided the structure of the expected major organic product or the starting compound.


(2) Synlett 2008, 260.

(3)

IX. (12 points) Given below are infrared (IR) spectra of four compounds (all in liquid film). The compounds are among those structures given on page 8. Assign each spectrum to its compound by putting the letter corresponding to the compound in the answer box next to the spectrum. The table of characteristic infrared frequencies appears on pages 9 and 10.

1 C

wavenumbers

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NH₂
\((\text{N-N-H})\)

1616

atom νC=O

Too low cm⁻¹ to be νC=O

\(\text{Sp}^2\text{N-C-H₅}\)

\(\text{Sp}^2\text{N-C-H₅}\)
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IX. (continued)

2. B Answer

3. F Answer

4. I Answer
### IX. (continued)

| A. | \[
\text{CH}_2\text{OH}
\] |
| B. | \[
\text{CH}_2\text{OH}
\] |
| C. | \[
\text{CH}_2\text{NH}_2
\] |
| D. | \[
\text{CH}_2\text{OCH}_3
\] |
| E. | \[
\text{CH}_2\text{CH}_2\text{CO}_2\text{H}
\] |
| F. | \[
\text{CH}_3\text{CH}_2\text{CO}_2\text{H}
\] |
| G. | \[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3
\] |
| H. | \[
\text{CH}_3\text{CO}_2\text{CH}_3
\] |
| I. | \[
\text{CH}_2\text{CH}_2\text{CH}_2\text{N}_2\text{H}_3
\] |
| J. | \[
\text{CH}_2\text{CH}_2\text{N}_2\text{H}_3
\] |
| K. | \[
\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_3
\] |
| L. | \[
\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_3
\] |