Statistics:

- **Average:** 70 pts (70%);
- **Highest:** 95 pts (95%); **Lowest:** 25 pts (25%)
- Number of students performing at or above average: 26 (59%)
- Number of students at 55% or below: 9 (20%)

1. (5 pts) Mark as true (T) or false (F) the following statements. Do not explain!
   - (F) Carboxylic acids are not *Brønsted* acids;
   - (T) Base-promoted hydrolysis of esters is irreversible;
   - (F) Esters can be formed from carboxylic acids and alcohols in both acid-catalyzed and base-promoted reactions;
   - (F) Lactones are cyclic amides;
   - (F) β-ketoesters are more acidic than carboxylic acids;

2. Circle ALL that apply:
   A. (3 pts) The following reactions are used to generate carbon – carbon bonds:
      a. **Aldol condensation**;
      b. **Claisen condensation**;
      c. Ester saponification;
      d. Lactam formation;
   B. (3 pts) Circle the reagents that CANNOT be used to convert a carboxylic acid to an acid chloride:
      a. Thionyl chloride;
      b. Alkyl chloride;
      c. Sodium chloride;
      d. Phosphorus pentachloride;
   C. (3 pts) The following compounds CANNOT undergo aldol self-condensation:
      a. Acetone;
      b. Acetaldehyde;
      c. Formaldehyde;
      d. Benzaldehyde;
   D. (3 pts) The following esters CANNOT form enolates:
      a. Ethyl acetate;
      b. Ethyl formate;
      c. Diethyl carbonate;
      d. Ethyl propanoate;

3. (5 pts) Provide the correct structure, matching each of the following names:

   - Acetic formic anhydride
   - Urea
   - Acetonitrile
   - N-methylformamide
   - Malonic ester

5. Write the complete equation for each of the following reactions:
   a. (2 pts) Reaction of succinic anhydride with ethanol, in the presence of pyridine.

      \[
      \text{O} \quad \text{O} \quad \text{H} \\
      \text{H}_{2}\text{N} \quad \text{NH}_{2} \quad \text{H}_{3}\text{C} \quad \text{C=N} \\
      \text{O} \quad \text{O} \\
      \text{C}_{2}\text{H}_{5}\text{O} \quad \text{C}_{2}\text{H}_{5}\text{O} \\
      \text{acetic formic anhydride} \quad \text{urea} \quad \text{acetonitrile} \quad \text{N-methylformamide} \quad \text{malonic ester}
      \]

   b. (2 pts) Saponification of 4-butanolide;
c. (2 pts) Cyclopentanone and formaldehyde, in the presence of KOH/ethanol, upon heating;

\[
\begin{align*}
\text{HCHO} + \text{C}_5\text{H}_5\text{O} & \overset{\text{KOH}}{\rightarrow} \text{C}_5\text{H}_7\text{O} \\
\end{align*}
\]

d. (2 pts) Ethyl propanoate and ethyl formate, in the presence of NaOCC_2H_5/C_2H_5OH, followed by acid;

\[
\begin{align*}
\text{C}_2\text{H}_5\text{OCOC}_2\text{H}_5 + \text{HOCOC}_2\text{H}_5 & \overset{1) \text{NaOCC}_2\text{H}_5}{\rightarrow} \text{C}_2\text{H}_5\text{OCOC}_2\text{H}_5 \\
& \overset{2) \text{H}_3\text{O}^+}{\rightarrow} \text{C}_2\text{H}_5\text{OCOC}_2\text{H}_5
\end{align*}
\]

6. (32 pts) Write the principal organic product of each of the following reactions:
7. (3 pts) Although nitrogen centers are generally more basic than oxygen centers, protonation of amides in acid occurs at oxygen rather than nitrogen. Suggest a structural rationalization.

![Structural diagram showing protonation at oxygen and nitrogen]

8. (4 pts) Lactones are cyclic esters. Taking this into account, suggest a mechanism for the following reaction.

![Mechanism diagram for lactone synthesis]

9. (9 pts) Show how to synthesize each of the following compounds using either the acetoacetic or the malonic ester synthesis.

a. 4-Phenyl-2-butanone;

![Synthesis of 4-Phenyl-2-butanone]

b. 2-Methylhexanoic acid;

![Synthesis of 2-Methylhexanoic acid]

c. Cyclobutyl methyl ketone;

![Synthesis of Cyclobutyl methyl ketone]

10. (5 pts) Propose a synthesis of the following isotope-labeled compounds, using any necessary reagents (Note: The reagents/conditions that you propose should not lead to scrambling of the label, i.e. its appearance in more than one type of substance and/or position).

![Isotope-labeled synthesis diagram]
11. Suggest a plausible synthetic sequence for the preparation of each of the following compounds from the indicated starting material. Use any other necessary organic or inorganic reagents.

A. (4 pts) Acetic acid $\rightarrow$ Malonic acid.

\[ \text{O} \quad \text{O} \quad \text{Cl} \quad \text{O} + \text{H}^{18}\text{O} \quad \text{pyr} \rightarrow \text{O} \quad \text{O} \quad \text{Cl} \quad \text{O} + \text{H}^{18}\text{O} \quad \text{pyr} \]

1. $\text{Br}_2/\text{PBr}_3$
2. $\text{H}_2\text{O}$

B. (4 pts) Propanedioic acid $\rightarrow$ pentanedioic acid;

\[ \text{O} \quad \text{O} \quad \text{OH} \quad \text{OH} \quad \text{1) LiAlH}_4 \quad \text{ OH} \quad \text{OH} \quad \text{2) H}_2\text{O} \quad \text{Br} \quad \text{Br} \quad \text{1. NaCN/DMSO} \quad \text{2. H}_3\text{O}^+, \text{heat} \]

C. (4 pts)

\[ \text{O} \quad \text{C} \quad \text{OH} \quad \text{CH}_3 \quad \text{O} \quad \text{C} \quad \text{OH} \quad \text{SOCl}_2 \quad \text{OC} \quad \text{NH}_3 \quad \text{P}_4\text{O}_{10} \quad \text{heat} \quad \text{1. CH}_3\text{MgBr/ether} \quad \text{2. H}_3\text{O}^+ \]

12. (5 pts) The two isomeric carboxylic acids ($\text{C}_5\text{H}_{10}\text{O}_2$), whose $^1\text{H}$ NMR spectra are shown below, were produced using the malonic ester synthesis.

a. Propose structures for the acids.

b. What alkyl halide(s) was (were) used in each case?
Another interesting reaction of nitriles is the von Ritter reaction, which takes place between a nitrile and a tertiary alcohol, in the presence of acid catalyst, and leads to the formation of an N-alkyl amide. Propose a detailed mechanism for the reaction below (Hint: Start with protonation of the alcohol).

\[ \text{C} = \text{N} + \text{OH} \xrightarrow{\text{H}_3\text{O}^+} \text{CONH} \]

The reaction works with tertiary alcohols because they form relatively stable carbocations.