QUIZ #3
March 27, 1997
(5 questions, 33 points)

*1. (4 pts) Quiana is a condensation polymer with the following structure. Draw the two monomer units used in the synthesis of quiana.

\[
\begin{array}{c}
\text{CH}_2\text{N} \quad \text{N} \\
\text{O} \quad \text{N} \\
\text{(CH}_2\text{)}_6 \quad \text{O} \\
\text{O} \\n\text{n}
\end{array}
\]

2. (6 pts) Choose from the following list of reaction types to identify each of the following reactions: Aldol, Malonic ester synthesis, Dieckmann, Claisen, Robinson annulation, Michael reaction.

-\[
\text{CH}_3\text{CH} = \text{CH} \quad \text{H} \\
\text{OH} \quad \text{NaOH, EtOH} \quad \text{H} \quad \text{CH}_3\text{CH} = \text{CH} \quad \text{CO}_2\text{Me}
\]

-\[
\text{MeO} \quad \text{CH} \quad \text{CH} \quad \text{CH} \quad \text{CH}_3\text{CH} = \text{CH} \quad \text{H} \\
\text{O} \quad \text{H} \quad \text{NaOMe} \quad \text{O} \quad \text{O} \quad \text{CO}_2\text{Me}
\]

-\[
\text{CH} = \text{CH} \quad \text{CH} = \text{CH} \quad \text{MeO} \quad \text{NaOMe} \quad \text{O} \quad \text{CO}_2\text{Me}
\]

-\[
\text{CH} = \text{CH} \quad \text{O} \quad \text{CO}_2\text{Me} \quad \text{NaOMe} \quad \text{O} \quad \text{CO}_2\text{Me}
\]
3. (15 pts) Fill in either starting materials, reagents or major products for each of the following reactions. Show stereochemistry where relevant.

1. NaOEt, CH₃I
2. H₃O⁺,

(2 compounds)

LiAlH₄

PhMgBr (excess)
*4. (4 pts) Show the two-step mechanism for the following reaction.

\[
\overset{\text{NaOEt}}{\text{EtOH}} \quad \overset{\text{ClCH}_2\text{CO}_2\text{C}_2\text{H}_5}{\text{NaOEt}} \quad \overset{\text{EtOH}}{\text{NaOEt}} \quad \overset{\text{EtOH}}{\text{NaOEt}}
\]

*5. (4 pts) Use a malonic ester synthesis to prepare ethyl cyclobutane carboxylate.
1. (30 pts) Multiple choice.
   
a) Propanoic anhydride would react with sodium ethoxide to give:
   1- propyl ethanoate and acetic acid
   2- ethyl propanoate and acetic acid
   3- ethyl propanoate and propanoic acid
   4- two equivalent of propanoic acid

b) The correct structure for N,N-dimethylbutanamide is:

   ![Structures](image)

   a.  
   b.  
   c.  
   d.  

   ![Reaction](image)

   1- a Dieckmann cyclization
   2- an SN2 substitution
   3- an Aldol reaction
   4- a nucleophilic acyl substitution

d) The final product of the reaction in part (c) is:
   1- an ether
   2- a lactone
   3- a lactam
   4- an anhydride

e) Which of the following carbonyl compounds has the most acidic hydrogen?

   ![Compounds](image)

   1.  
   2.  
   3.  
   4.  

f) The product of a Michael addition of a ketone enolate to an α,β-unsaturated ketone is?

   1- a 1,5-diketone
   2- an α-substituted acetate
   3- a β-hydroxy ketone
   4- a β-keto ester
g) The ester shown below can be formed by a Dieckmann cyclization. The starting material would be:

1- diethyl-1,6-hexanedioate
2- cyclohexanone
3- diethyl-1,8-octanedioate
4- diethyl-1,7-heptanedioate

h) The Robinson annulation consists of:
   1- a Dieckmann followed by an Aldol
   2- a Michael followed by an Aldol
   3- an Aldol followed by a Michael
   4- a Claisen followed by a Michael

i) Ribose is a:
   1- ketohexose
   2- aldohexose
   3- ketopentose
   4- aldopentose

j) The following disaccharide has a:

1- 1, 3' linkage
2- 2, 3' linkage
3- 3, 1' linkage
4- 3, 2' linkage

2. (8 pts) Show the mechanism for the base-catalyzed Aldol reaction of benzaldehyde (PhCHO) and methyl phenyl ketone (MeCOPh). Stop at the alcohol product.
3. (12 pts) Answer the following questions regarding D-allose.

![D-allose structure]

a) Draw the cyclic form (six-membered ring) of D-allose as a Haworth projection. Name the anomer you have drawn.

b) Draw a Fischer projection of the product of the reaction of D-allose with the following set of reagents: 1. H₂NOH; 2. (CH₃CO)₂O, CH₃CO₂Na; 3. NaOCH₃. What is the name of this reaction sequence?

c) Draw the chair form of the product of the reaction of D-allose with CH₃OH and acid.

d) Is the product in part (c) a reducing or a non-reducing sugar?
4. (19 pts) Make the following compounds by the specified method. You may use any reagents necessary.

a) \( \text{\includegraphics[width=0.2\textwidth]{image_a.png}} \) via an acetoacetic ester synthesis

b) \( \text{\includegraphics[width=0.2\textwidth]{image_b.png}} \) via an enolate alkylation

c) \( \text{\includegraphics[width=0.2\textwidth]{image_c.png}} \) use a Dieckmann and alkylation
   Why would this method work better than method (b)?

d) \( \text{\includegraphics[width=0.2\textwidth]{image_d.png}} \) via an Aldol
5. (15 pts) Fill in either products, reagents or starting materials for the following reactions.

1. \( \text{BrCH}_2\text{CH} = \text{CH}_2 \)  
2. \( \text{H}_3\text{O}^+ \)

\[
\text{CH}_3\text{CH}_2\text{CO} \rightarrow \text{CH}_3\text{CH} = \text{CH}\text{CO}.
\]

\[
\text{Ph}_2\text{CuLi} \rightarrow \text{CH}_3\text{CH} = \text{CH}\text{CO}.
\]

\[
\text{HOH}_2\text{C} \rightarrow \text{H}_2\text{O}, \text{Br}_2 \rightarrow \text{HOH}_2\text{C}.
\]

\[
\text{PhCOOMe} + \text{CH}_3\text{CH} = \text{CH}\text{COOMe} \rightarrow \text{PhCOOMe}.
\]
6. (16 pts) Give short answers to the following questions.

a) Addition of 2-methylcyclohexanone slowly to a flask of LDA, followed by addition of methyl iodide, gives 2,6-dimethylcyclohexanone as the major product. However, if LDA is added slowly to a solution of 2-methylcyclohexanone, followed by addition of methyl iodide, the major product is 2,2-dimethylcyclohexanone. Explain.

b) N,N-Dimethylformamide (HCONMe₂) shows two signals in the proton NMR for the two methyl groups. Explain why the two methyls are not equivalent.

c) Maltose is a disaccharide, with an α-glycosidic linkage. It can be oxidized by bromine in water to maltobionic acid (MBA). When MBA is treated with methyl iodide and base, followed by acid hydrolysis, the products are 2,3,4,6-tetramethyl-D-glucose and 2,3,5,6-tetramethyl-D-gluconic acid. Provide a three-dimensional structure for maltose.

d) If glucose is left in basic solution, over a period of time, it is converted to a mixture of glucose, mannose, and fructose (a ketone). Use structures, and explain what is happening.
7. (5 pts extra credit) The following reaction sequence was used in the synthesis of a series of HIV protease inhibitors (AIDS drugs) being developed at Pharmacia & Upjohn (J. Med. Chem., 1996, 39, 4630). Provide the missing structures and intermediate, and supply mechanism arrows for the last step.

* NaH pulls off the more acidic proton, then BuLi pulls off the less acidic proton to give a dianion. Reaction then occurs at the less hindered carbon.

an HIV protease inhibitor
*1. (4 pts) Fill in the missing compounds in the following synthetic sequence.

\[
\begin{array}{c}
\text{NH} \\
\text{O} \\
\text{O} \\
\text{KOH} \\
\text{PhCH}_2\text{Br} \\
\text{KOH} \\
\end{array}
\]

*2. (6 pts) Show the mechanism for the reaction of pentanoyl chloride with NaN\(_3\), followed by heat and then H\(_2\)O. (three steps)

\[
\begin{array}{c}
\text{1) } \text{Na}^+ \cdot \text{N}=\text{N}=\text{N}^- \\
\uparrow \\
\text{heat} \\
\text{H}_2\text{O} \\
\end{array}
\]
3. (12 pts) Fill in either products, starting materials or reagents for the following reactions.

\[
\begin{align*}
\text{1. } & \text{HNO}_2, \text{H}_2\text{SO}_4 \\
& \text{2. CuCN, KCN}
\end{align*}
\]

\[
\begin{align*}
\text{1. xs CH}_3\text{I} \\
& \text{2. KOH}
\end{align*}
\]

4. (4 pts) Which of the following reactions would proceed to the right? Circle the amine which is the strongest base.

(a) \[
\begin{align*}
\text{pKa} &= 9.33 \\
\text{pKa} &= 10.0
\end{align*}
\]

(b) \[
\begin{align*}
\text{pKa} &= 10.71 \\
\text{pKa} &= 10.0
\end{align*}
\]
5. (3 pts) Which of the compounds below fits the following spectral data?

Mass spec: \( m/z \) 165, 150, 135

\(^1\)H-NMR: \( \delta \) 1.12 (d, 6H), 2.88 (septet, 1H), 3.1 (broad s, 1H), 3.4 (s, 3H), 7.21 (d, 2H), 7.62 (d, 2H).

6. (4 pts) Valine has the is an \( \alpha \)-amino acid with an isopropyl as the "R" group on the \( \alpha \)-carbon.

a) Draw the zwitterionic form of valine.

b) Draw the form of valine that is found in strongly basic solution.