51C FINAL Review Packet

1.) State whether the following substituents are electron withdrawing or electron donating and whether they will direct ortho/para or meta

2.) Provide reagents for the following synthesis.
   a.)
3.) Predict the product for the following Gabriel Synthesis.

4.) Predict the product of the following Robinson Annulation.

*any nucleophile that undergoes reversible addition to carbonyls will add 1,4 to α,β unsaturated carbonyls
ROH, RNH₂, RSH, cuprates, CN

*nucleophiles that undergo irreversible addition to carbonyls will add 1,2 to α,β unsaturated carbonyls
R-MgBr, R-Li, LiAlH₄, NaBH₄, R=CO

→Michael Run followed by Aldol condensation
5.) Predict the product of the following Henry Reactions.

![Henry Reaction Diagram]

5a.) Predict the product of the following Henry Reactions.

![Henry Reaction Diagram]
• not stable as enolate anion so enamine = safe alternative
6c)  

\[
\begin{align*}
R - C &\equiv N \\
\text{1. LiAlH}_4 &\rightarrow R - \text{CH}_2 - \text{NH}_2 \\
\text{2. H}_2\text{O} &\rightarrow R - C &\equiv N \\
\text{3. H}_2\text{O} &\rightarrow \text{protonate O} \\
\text{4. LiAlH}_4 &\rightarrow R - C &\equiv N \\
\text{5. H}_2\text{O} &\rightarrow \text{epoxide} \\
\text{1. mCPBA} &\rightarrow \text{epoxide} \\
\text{2. C &\equiv N} &\rightarrow \text{strong Nuc: attack @ least Subst.}
\end{align*}
\]

6d) Challenge Synthesis  

\[
\begin{align*}
\text{HNO}_3, \text{H}_2\text{SO}_4 &\rightarrow \\
\text{2. Br}_2, \text{FeBr}_3 &\rightarrow \\
\text{3. H}_2, \text{Pd} &\rightarrow \\
\text{4. NaNO}_2, \text{HCl} &\rightarrow \\
\text{5. CuCN} &\rightarrow \\
\text{6. LiAlH}_4 &\rightarrow \\
\text{7. H}_2\text{O} &\rightarrow \\
\end{align*}
\]
7.) Provide the 2 best reagent for the following retrosynthetic analysis of a Michael reaction. Label which reagent is the Michael donor and Michael acceptor.

Michael reaction: $\text{enolate} + \alpha, \beta \text{ unsaturated carbonyl}$

- Break $\beta - \gamma$ bond
- Double bond in $\alpha, \beta$
- $(-)$ charge on $\gamma$

Michael donor: $\text{CN}$
Michael acceptor: $\text{C}=\text{O}$
8.) Rank the following in terms of basicity.

\[ \text{db} = \text{double bond} \]

- **A**: \text{sp}^3
- **B**: \text{sp}^2
- **C**: \text{sp}^3

**C > B > A**

9.) Rank the following in terms of basicity.

- **A**: \text{sp}^2
- **B**: \text{sp}^3
- **C**: \text{sp}^2
- **D**: \text{sp}^3

**B \succ D \succ A \succ C**
10.) Provide the 2 best reagents for the following Robinson annulation. Provide the mechanism between the reagents that results in this product.

**Robinson Annulation:** Michael $\rightarrow$ aldol

1. **Aldol:** Break $\alpha$, $\beta$ bond $\rightarrow$ put carbonyl on $\beta$ $\rightarrow$ (-) charge $\alpha$

2. **Michael:** Break $\beta-\gamma$ bond $\rightarrow$ db on $\alpha$, $\beta$ $\rightarrow$ (-) on $\gamma$

11.) Consider the reactions of the following esters. Provide a mechanism for the synthesis of the product in D.
A. Ester → enolate

B. NO RXN!

NO enolizable H's!

C. Ester

1, 3 dicarbonyl

*Not e - no ester groups

D. No RXN!
12.) Predict the starting reagents used to make the Michael acceptor in Part A and the Michael Donor in Part B.

A. Michael acceptor

$\text{NaOEt}$

$\Delta$

$\text{CH}_2$ $\text{CH}_2$ $\text{CH}_3$

Michael donor

B. $\begin{align*}
\text{OEt} & \quad \text{OEt} \\
\text{B} & \quad \text{OEt}
\end{align*}$

$\text{H}_3\text{O}^+$

1) Break α, β bond  
2) Put carboxyl in β position  
3) (-) charge in α position

13) Circle the following amine that would react quickest with benzyl bromide if in excess.

b) Draw the resulting product(s) of the reaction between benzyl bromide and the amine from A.

c) What alternative reagent can be used to avoid overalkylation?
14.) Draw a mechanism for the following Mannich Reaction.