Final Exam Worksheet

Chapter 16 Concepts: Reactions of Aromatic Compounds
- mechanisms (2-step) of electrophilic aromatic substitutions
- effects of aromatic substituents on regioselectivity
  - ortho, para, meta
  - inductive, resonance, reactivity
- types of electrophilic aromatic substitutions
  - halogenation
  - nitration
  - sulfonation
  - friedel-crafts alkylation
  - friedel-crafts acylation
- reactions of other benzene derivatives

Chapter 17 Concepts: Introduction to Carbonyl Chemistry, Organometallic Reagents, and Oxidation and Reduction
- Types of Carbonyl Compounds and General Reactions
  - nucleophilic addition: aldehydes and ketones
  - nucleophilic substitution: carbonyl compounds with leaving groups
  - Reactivity of Aldehyde vs Ketone
- Oxidation Reactions
  - def) an increase in the number of C–Z bonds (usually C–O bonds)
    - ex. aldehydes to carboxylic acids
- Reduction Reactions
  - def) a decrease in the number of C–Z bonds
  - Hydride reduction via nucleophilic addition (LiAlH4, NaBH4)
    - aldehydes and ketones
  - Catalytic hydrogenation to 1° and 2° alcohols (H2, Pd-C)
    - α,β-unsaturated aldehydes and ketones
  - Enantioselective reduction (S-CBS, R-CBS)
    - ketones
    - other reactions of acid chlorides, esters, carboxylic acids to 1° alcohols, amides to amines
- Preparation and Reactions with Organometallic Reagents
- Protecting Groups

Chapter 18 Concepts: Aldehydes and Ketones - Nucleophilic Addition
- Nucleophilic Addition Reactions
  - Addition of Hydride (H-) (18.7)
  - Addition of organometallic reagents (R-) (18.7)
  - Addition of cyanide (CN-) (18.8)
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- Wittig reaction (18.9)
- Addition of 1° amines (18.10)
- Addition of 2° amines (18.11)
- Addition of H2O -Hydration (18.12)
- Addition of alcohols (18.13)

- Other reactions
  - Synthesis of wittig reagents (18.9A)
  - Conversion of cyanohydrins to aldehydes and ketones (18.8)
  - Hydrolysis of nitriles (18.8)
  - Hydrolysis of imines and enamines (18.11)
  - Hydrolysis ofacetals (18.13)

Chapter 19 Concepts: Carboxylic Acids and Nitriles
- pKa and effects of resonance, inductive effects, etc on pKa
- Protonation of carbonyl O
- Hydrolysis of Nitriles
- Reduction of Nitriles
- Addition of Nitriles to Organometalllics

- Nucleophilic Acyl Substitution
  - Acid chlorides, anhydrides, carboxylic acids, esters, amides
- Nitrile Synthesis
- More Reaction of Nitriles
  - Hydrolysis, reduction, reaction with organometallic reagents
  - Nucleophilic Acyl Substitution
  - Structure, bonding, rates
  - Carbonyl Reactivity and L.G ability
- Acyl Chloride Reactions
  - DCC, Et3N, and pyridine as solvents
  - Mechanism
- Acid Anhydrides
- Fischer Esterification
  - Ester Hydrolysis
- Saponification
- Hydrolysis of Amides
- Multistep Synthesis
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Chapter 21 Concepts: Enols and Enolates
  - 21.1-4 Enol/Enolate Chemistry
    - Tautomerization
      - Acid-Catalyzed
  - 21.5 Racemization of alpha-carbon
  - 21.7 Halogenation at alpha-carbon
    ○ Subsequent elimination of halogen
  - 21.8 Kinetic vs Thermodynamic Enolates
  - 21.9-10 Malonic/Acetoacetic Esters

Chapter 22 Concepts: Carbonyl Condensation Reactions
  - The aldol reaction
  - Crossed aldol reactions
  - Directed aldol reactions
  - Intramolecular aldol reactions
  - The Claisen reaction
  - The crossed Claisen and related reactions
  - The Dieckmann reaction
  - The Michael reaction
  - The Robinson annulation

Chapter 23 Concepts: Amines
  - Properties of amines (basicity) and other compounds
  - Synthesis reactions
    - Direct nucleophilic substitution with NH3 and amines
    - Gabriel synthesis
    - Reduction methods
    - Reductive amination
  - Reactions of amines
    - Reaction as a base
    - Nucleophilic addition to aldehydes and ketones
    - Nucleophilic substitution with acid chlorides and anhydrides
    - Hofmann elimination
    - Reaction with nitrous acid
  - Reactions of diazonium salts
1. What starting material(s) is (are) needed to synthesize each compound using an aldol or similar reaction?

a. 

b. 

c. 
2. What crossed Claisen product is formed from each pair of compounds?

a. CH₃CH₂COOEt and HCO₂Et
b. CH$_3$(CH$_2$)$_5$CO$_2$Et and HCO$_2$Et

c. (CH$_3$)$_2$C – – O and CH$_3$CO$_2$Et

d. [Image of a cyclic compound with a ketone group] and [Image of a benzyl group with an ethoxy group]
3. Draw a stepwise mechanism for the formation of one C – C bond in polytulipalin
4. Octinoxate is an unsaturated ester used as an active ingredient in sunscreens. (a) What carbonyl compounds are needed to synthesize this compound using a condensation reaction? (b) Devise a synthesis of octinoxate from the given organic starting materials and any other needed reagents.
4. Treatment of the amino alcohol $X$ with diethyl carbonate forms the heterocycle $Y$. Draw a stepwise mechanism for this process.
5. (a) Both monomers needed for the synthesis of nylon 6,6 can be prepared from 1,4-dichlorobutane. Write out the steps illustrating these syntheses. (b) Devise a synthesis of adipic acid from cyclohexene.

\[
\text{Cl} - \text{Cl} \quad \rightarrow \quad \text{Cl} - \text{Cl} \quad \rightarrow \quad \text{H}_2\text{N} - \text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2 \quad \text{and} \quad \text{HO} - \text{CO} - \text{CH}_2\text{CH}_2\text{COOH}
\]

hexamethylenediamine  
adipic acid

6. Draw the product of each reductive amination reaction

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C} &= \quad \rightarrow \quad \text{NH}_2 \\
\text{NaBH}_3\text{CN}
\end{align*}
\]

a. 
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b. 

\[ \text{Cyclic ketone} \xrightarrow{\text{(CH}_3\text{)}_2\text{NH, NaBH}_3\text{CN}} \]

c. 

\[ \text{Phenylglyoxal} \xrightarrow{\text{NH}_3, \text{NaNBH}_3\text{CN}} \]

d. 

\[ \text{Acetone} \xrightarrow{\text{ NaNBH}_3\text{CN}} \]
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7. A chiral amine A having the R configuration undergoes Hofmann elimination to form an alkene B as the major product. B is oxidatively cleaved with ozone, followed by CH₃SCH₃, to form CH₂=O and CH₃CH₂CH₂CHO. What are the structures of A and B?

8. Draw a stepwise mechanism for the following reaction.

\[
\text{OH} \quad \overset{\text{H}_2\text{C}=\text{O}}{\text{mild acid}} \quad \overset{\text{H}_2\text{O}}{\text{OH}} \quad + \quad \text{H}_2\text{O}
\]
9. Complete the following reactions. **Consider Stereochemistry.**

a.

![Keto-enol tautomerization](image)

b.

![Phosphine addition to ketone](image)

10. Complete the following oxidation/reduction reactions in a **single step**.

a.

![Alcohol to aldehyde](image)

b.

![Hydroxylation](image)

c.

![Oxidation with CrO₃](image)
11. Draw the correct product(s).

a. 

b. 

12. Draw the organic products formed in each reaction.

a. 

b. 

[1] CH₃OH, H⁺  
[2]  
[3] H₂O

13. Draw the enol tautomers for each compound

a. 

b. 

c. (mono enol form)
14. Draw the organic products formed in each reaction

a. 

\[
\text{NaOEt, EtOH} \\
(\text{CH}_3)_2\text{C}=0
\]

b. 

\[
\text{NaOEt, EtOH} \\
\text{CH}_3\text{OH}
\]

c. 

\[
\text{[1] LDA} \\
\text{[2]CH}_3\text{CH}_2\text{CHO} \\
\text{[3]H}_2\text{O}
\]

d. 

\[
\text{NaOEt, EtOH} \\
\text{[2]H}_2\text{O}^+
\]

e. 

\[
\text{[1] NaOEt, EtOH} \\
\text{[2]H}_2\text{O}^+
\]
15. Draw the organic products formed in each reaction

d. 

\[
\text{OCH}_2\text{CH}_2\text{NH}_2 + \text{NH}_3 \xrightarrow{\text{excess}} \]


e. 

\[
\text{OCH}_2\text{CH}_2\text{NH}_2 \xrightarrow{[1] \text{KOH}} \xrightarrow{[2] \text{(CH}_3\text{)}_2\text{CHCH}_2\text{Cl}} \xrightarrow{[3] \cdot \text{OH, H}_2\text{O}} 
\]

f. 

\[
\text{BrCH}_2\text{NO}_2 \xrightarrow{\text{Sn}} \xrightarrow{\text{HCl}} 
\]

g. 

\[
\text{CH}_3\text{CH}_2\text{CN} \xrightarrow{[1] \text{LiAlH}_4} \xrightarrow{[2] \text{H}_2\text{O}} 
\]

h. 

\[
\text{NH} \xrightarrow{\text{NaNH}_2} \xrightarrow{\text{HCl}} 
\]
Extra Practice:

16. Synthesize each compound from benzene.

a. 

\[
\begin{array}{c}
\text{CH}_2\text{CH}_3 \\
\text{CH}_3 \\
\text{SO}_3\text{H} \\
\text{C} \\
\text{O}
\end{array}
\]

b. 

\[
\begin{array}{c}
\text{Br} \\
\text{CH}_2\text{CH}_3
\end{array}
\]

c. 

\[
\begin{array}{c}
\text{Cl} \\
\text{CHO}
\end{array}
\]
17. Explain why the pKa of compound A is lower than the pKa's of both compounds B and C.