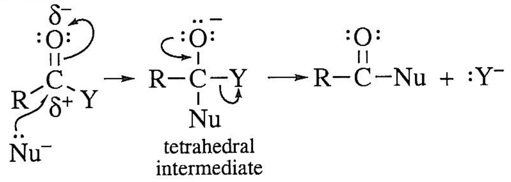
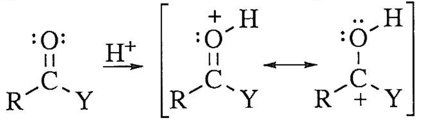
Nucleophilic Substitution at Carbonyl Groups

Carboxylic acids and their derivatives, acyl halides, anhydrides, esters, and amides, undergo the general reaction termed nucleophilic acyl substitution. The carbonyl group is polarized with the carbon atom partially positive and therefore, electrophilic. Nucleophiles can bond to the carbonyl carbon atom forming what is often referred to as a tetrahedral intermediate, because of the sp^3 hybridized carbon atom. The tetrahedral intermediate can reform the strong carbon–oxygen double bond with the loss of the leaving group $Y:^-$. The nucleophile has thus substituted for the leaving group at the acyl carbon atom.



(1)

Nucleophilic acyl substitution is subject to acid catalysis. Protonation of the carbonyl oxygen atom increases the electrophilic character of the carbonyl carbon atom as indicated by the resonance below:



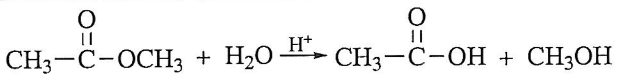
(2)

Nucleophilic attack on the protonated carbonyl compound forms the tetrahedral intermediate directly, which can then collapse with the loss of a leaving group. Under acidic conditions, protonation of a poor leaving group increases its tendency to dissociate.

Although they do not involve nucleophilic addition to carbonyl groups, the similarities of nitrile chemistry and condensation polymers formed by repeated nucleophilic acyl substitution justify their inclusion in the problems in this section.

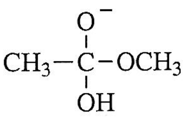
Study Questions

NC-1. Which would be a reasonable intermediate in the mechanism for this reaction?



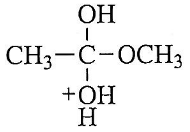
$$CH_3-\overset{O}{\overset{\|}{C}}-OCH_3 + H_2O \xrightarrow{H^+} CH_3-\overset{O}{\overset{\|}{C}}-OH + CH_3OH$$

(A)



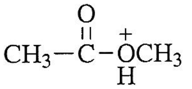
$$CH_3-\underset{OH}{\overset{O^-}{C}}-OCH_3$$

(B)



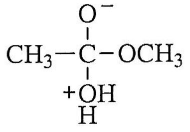
$$CH_3-\underset{+\underset{H}{O}H}{\overset{OH}{C}}-OCH_3$$

(C)



$$CH_3-\overset{O}{\overset{\|}{C}}-\overset{+}{\underset{H}{O}}CH_3$$

(D)

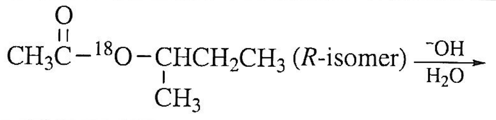


$$CH_3-\underset{+\underset{H}{O}H}{\overset{O^-}{C}}-OCH_3$$

Knowledge Required: Mechanism of the acid-catalyzed nucleophilic acyl substitution reaction that is characteristic of carboxylic acids and carboxylic acid derivatives.

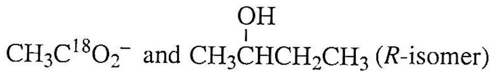
Thinking it Through: Acidic reaction conditions catalyze nucleophilic acyl substitution through protonation of the carbonyl oxygen atom. This makes the carbonyl carbon atom more electrophilic, and more susceptible to attack by the water nucleophile. Choice **(B)** would result from water attacking the protonated ester, and is the correct answer. Choices **(A)** and **(D)** would result from the nonprotonated ester being attacked by hydroxide ion and water, respectively. Choice **(C)** has the ester protonated on the wrong oxygen atom.

NC-2. What products are expected from this reaction?



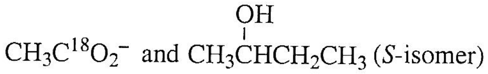
$CH_3\overset{O}{\overset{\|}{C}}-{}^{18}O-\underset{CH_3}{CH}CH_2CH_3$ (*R*-isomer) $\xrightarrow[H_2O]{^-OH}$

(A)



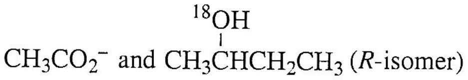
$CH_3C^{18}O_2^-$ and $CH_3\overset{OH}{C}HCH_2CH_3$ (*R*-isomer)

(B)



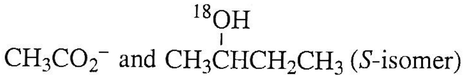
$CH_3C^{18}O_2^-$ and $CH_3\overset{OH}{C}HCH_2CH_3$ (*S*-isomer)

(C)



$CH_3CO_2^-$ and $CH_3\overset{^{18}OH}{C}HCH_2CH_3$ (*R*-isomer)

(D)



$CH_3CO_2^-$ and $CH_3\overset{^{18}OH}{C}HCH_2CH_3$ (*S*-isomer)

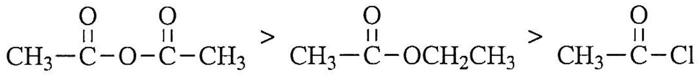
……

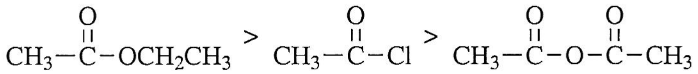
Knowledge Required: (1) Mechanism of the nucleophilic acyl substitution under basic (or neutral) conditions. (2) Configuration at a stereogenic center.

Thinking it Through: The nucleophile is the hydroxide ion, which attacks the carbonyl carbon atom of the ester, forming a tetrahedral intermediate. The tetrahedral intermediate collapses with the dissociation of the alkoxide ion. Strongly basic conditions result in immediate deprotonation of the resulting carboxylic acid. The bond is broken between the carbonyl carbon atom and the oxygen atom of the alkoxide. The labeled oxygen atom remains with the alkoxide, and the configuration at the stereogenic center (chiral center) remains the same.

Choice **(A)** is eliminated because the alkyl oxygen bond has been broken instead of the bond between the oxygen atom and the carbonyl carbon atom. Choice **(D)** shows the cleavage of the correct carbon–oxygen bond, but the configuration has been inverted. Choice **(B)** is chemically plausible, but would require an S_N2 attack by hydroxide ion on the alkyl carbon atom. This is not an observed mechanism for basic hydrolysis of esters. Only choice **(C)** shows cleavage of the correct bond and retention of configuration. It is the correct answer.

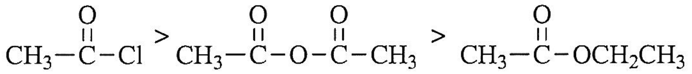
NC-3. The order from most reactive to least reactive with aqueous ammonia is

(A)

$CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 > CH_3-\overset{O}{\overset{\|}{C}}-OCH_2CH_3 > CH_3-\overset{O}{\overset{\|}{C}}-Cl$

(B)

$CH_3-\overset{O}{\overset{\|}{C}}-OCH_2CH_3 > CH_3-\overset{O}{\overset{\|}{C}}-Cl > CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3$

(C)

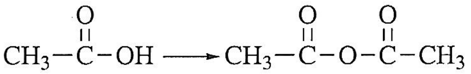
$CH_3-\overset{O}{\overset{\|}{C}}-Cl > CH_3-\overset{O}{\overset{\|}{C}}-OCH_2CH_3 > CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3$

(D)

$CH_3-\overset{O}{\overset{\|}{C}}-Cl > CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 > CH_3-\overset{O}{\overset{\|}{C}}-OCH_2CH_3$

Knowledge Required: The relative reactivity of carboxylic acid derivatives toward nucleophilic acyl substitution.

Thinking it Through: In general, the relative reactivity of the carboxylic acid derivatives follows the order: acyl chloride > acid anhydride > ester > amide. This trend may be predicted from two considerations: (1) the extent of resonance delocalization and stabilization of the starting material; and (2) the basicity of the leaving group from the tetrahedral intermediate. For example, resonance is least important for acyl chlorides, and the Cl^- is the weakest base and thus the best leaving group. Therefore choices **(A)** and **(B)** may be eliminated because the acyl chloride is not listed as the most reactive. Choice **(D)** must be the correct answer, since it has the anhydride listed as being more reactive than the ester.

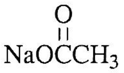
NC-4. Which would be the best reagent for this conversion?


$CH_3-\overset{O}{\overset{\|}{C}}-OH \longrightarrow CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3$

(A) NaOH

(B) Na_2SO_4 (anhydrous)

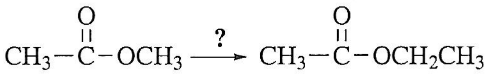
(C) $SOCl_2$ (1/2 molar equivalent)

(D)

$NaO\overset{O}{\overset{\|}{C}}CH_3$

Knowledge Required: (1) The relative reactivity of carboxylic acid derivatives. (2) Products of the reaction of carboxylic acids with thionyl chloride, $SOCl_2$.

Thinking it Through: Primarily because of the reactivity of acyl chlorides, their preparation from carboxylic acids and $SOCl_2$ is a necessary precursor to deal with many synthesis problems. Choice **(A)** is a strong base and would simply deprotonate the acid. The carboxylate anion does not undergo nucleophilic substitution, so **(A)** is eliminated. Choice **(B)** is a drying agent for small amounts of water, but cannot "dehydrate" the carboxylic acid. This eliminates **(B)**. In choice **(D)**, the acetate ion cannot displace the stronger base, OH^-, from the carboxylic acid. This leaves choice **(C)** as the correct answer. In choice **(C)**, conversion of half of the acid to the acid chloride allows the other half to provide the acetate nucleophile, and this is a reasonable synthesis of the anhydride.

NC-5. What is the best way to perform this transformation?


$CH_3-\overset{O}{\overset{\|}{C}}-OCH_3 \xrightarrow{?} CH_3-\overset{O}{\overset{\|}{C}}-OCH_2CH_3$

(A) $\xrightarrow[CH_3CH_2OH]{CH_3CH_2OK}$

(B) $\xrightarrow[CH_3OH]{CH_3OK} \xrightarrow{CH_3I}$

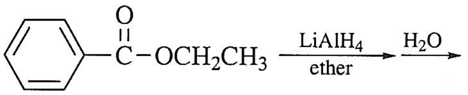
(C) $\xrightarrow{CH_3CH_2MgBr} \xrightarrow{H_2O,\ H^+}$

(D) $\xrightarrow{Br_2,\ h\nu} \xrightarrow[ether]{Mg} \xrightarrow{CH_3I}$

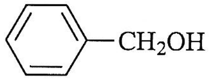
Knowledge Required: (1) The mechanism of nucleophilic acyl substitution. (2) The reaction of esters with Grignard reagents. (3) The acidic nature of hydrogen atoms on a carbon atom alpha to a carbonyl group.

Thinking it Through: The transesterification is the result of nucleophilic acyl substitution of the CH_3O^- by a $CH_3CH_2O^-$. This is exactly the reagent encountered first in **(A)**. The other choices are eliminated. Choice **(B)** treats the ester with the strong base, CH_3O^-. Deprotonation of the α–carbon atom would lead to a Claisen condensation. The Grignard reagent in choice **(C)** provides a $CH_3CH_2^-$ nucleophile, which would attack the carbonyl carbon atom. Choice **(D)** is an imaginative sequence with several flaws. The free radical bromination would give a mixture of products. Formation of a Grignard would be futile since Grignard reagents react with esters. And finally, Grignard reagents do not couple efficiently with alkyl halides. Choice **(B)** suggests that methoxide ion will deprotonate the methoxy methyl group and the resulting carbanion will then be alkylated with CH_3I. However, any deprotonation would occur at the much more acidic methyl group that is bonded to the carbonyl group.

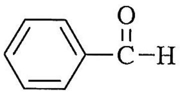
NC-6. Other than ethanol, what is the major product of this reaction sequence?



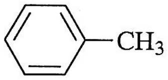
(A)



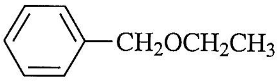
(B)



(C)



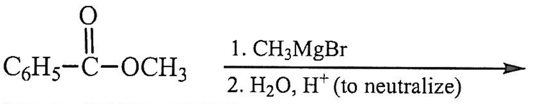
(D)



Knowledge Required: Hydride reduction of carboxylic acids and derivatives.

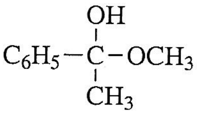
Thinking it Through: Recognizing $LiAlH_4$ as a source of the nucleophilic hydride ion, H:⁻, allows this reaction to be analyzed. Nucleophilic attack by hydride ion produces a tetrahedral intermediate, which can then collapse with the dissociation of the less basic group originally on the carbonyl carbon atom. The resulting aldehyde is then reduced further to a primary alcohol. The correct answer is **(A)**. The initially formed aldehyde is choice **(B)**. Choices **(C)** and **(D)** would require an S_N2 displacement of an ^-OH group, which is not observed.

NC-7. What is the product of this reaction?



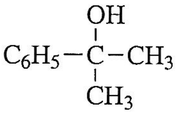
$$C_6H_5-\overset{\overset{\large O}{\|}}{C}-OCH_3 \xrightarrow[\text{2. } H_2O,\ H^+ \text{ (to neutralize)}]{\text{1. } CH_3MgBr}$$

(A)



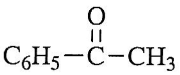
$$C_6H_5-\underset{CH_3}{\overset{OH}{C}}-OCH_3$$

(B)



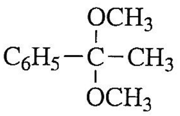
$$C_6H_5-\underset{CH_3}{\overset{OH}{C}}-CH_3$$

(C)



$$C_6H_5-\overset{\overset{O}{\|}}{C}-CH_3$$

(D)

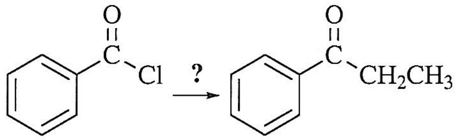


$$C_6H_5-\underset{OCH_3}{\overset{OCH_3}{C}}-CH_3$$

Knowledge Required: (1) Reactions of organometallic reagents with carboxylic acids and derivatives. (2) Relative reactivity of organometallic reagents.

Thinking it Through: The common organometallic reagents can be viewed as containing a nucleophilic carbon atom. Nucleophilic attack on the carbonyl group produces a tetrahedral intermediate that can collapse with the dissociation of the less basic group originally on the carbonyl carbon atom. Depending on the reactivity of the organometallic reagent, the resulting carbonyl group may then be attacked again, leading to an alcohol after hydrolysis. The reaction of esters with Grignard reagents and organolithium reagents are particularly useful. The product is a tertiary alcohol, with two identical alkyl groups attached to the carbon atom bearing the hydroxyl group. A tertiary alcohol is produced because the initially formed ketone is more reactive than the ester and reacts with additional reagent as fast as it is formed. Regardless of the amount of Grignard or organolithium reagent used, a tertiary alcohol is produced; however, two moles of reagent per mole of ester must be used to obtain good yields. The less reactive organocuprate reagents, R_2CuLi, react only with acyl halides, and not with the resulting ketone. The reaction of acid chlorides with organocuprate reagents is thus a useful synthesis for ketones. Choices **(A)**, **(B)**, and **(C)** could all be produced by the reaction of a Grignard reagent with an ester, but choices **(A)** and **(C)** are intermediates that will react with additional Grignard reagent to produce the tertiary alcohol in choice **(B)**, which is the correct answer. Choice **(D)** cannot be synthesized with these reactants.

NC-8. Identify the reagent that is ***best*** suited for this conversion.



(A) CH_3CH_2Li

(B) CH_3CH_2MgBr

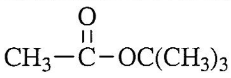
(C) CH_3CH_2ONa

(D) $(CH_3CH_2)_2CuLi$

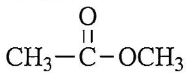
Knowledge Required: Relative reactivities of organometallic reagents toward carbonyl compounds.

Thinking it Through: A new carbon–carbon bond is being formed in this conversion of an acyl chloride to a ketone, which requires an organometallic reagent. Choice **(C)** may be eliminated because it is an alkoxide, not an organometallic reagent, and would produce an ester. The remaining three choices will all react to produce the ketone. However, the alkyllithium reagent in choice **(A)** and the Grignard reagent in choice **(B)** will subsequently react with the ketone group to yield the corresponding tertiary alcohol. This leaves choice **(D)** as the correct answer. Lithium dialkylcuprates are less reactive than alkyllithium and Grignard reagents, and will not continue to react with the ketone product.

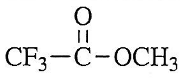
NC-9. What is the order from most reactive to least reactive for these esters towards aqueous hydroxide?


$CH_3-\overset{\overset{\large O}{\|}}{C}-OC(CH_3)_3$

1


$CH_3-\overset{\overset{\large O}{\|}}{C}-OCH_3$

2


$CF_3-\overset{\overset{\large O}{\|}}{C}-OCH_3$

3

(A) 3 > 2 > 1 (B) 1 > 2 > 3 (C) 3 > 1 > 2 (D) 2 > 3 > 1

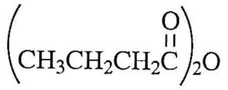
Knowledge Required: (1) Mechanism of ester hydrolysis. (2) Electronic and steric effects on hydrolysis rates.

Thinking it Through: All three esters undergo hydrolysis by the same mechanism: addition of hydroxide ion to the carbonyl carbon atom followed by expulsion of the alkoxide. Electron-withdrawing groups in the ester will increase the partial positive charge on the carbonyl carbon atom, making it more susceptible to nucleophilic attack. On the other hand, bulky groups in the ester will hinder nucleophilic attack on the carbonyl carbon atom, because the large groups are forced closer together in the tetrahedral intermediate. Inspection of the three esters reveals that the main difference between esters **2** and **3** is that ester **3** has three electron-withdrawing fluorine atoms. The fact that ester **3** should hydrolyze faster than ester **2** eliminates choices **(B)** and **(D)**. Ester **1** contains a bulky tertiary butyl group and should hydrolyze more slowly than ester **2**. This leaves choice **(A)** as the correct answer.

NC-10. What is the product of this reaction sequence?

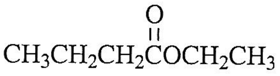
$CH_3CH_2CH_2CO_2H \xrightarrow{SOCl_2} \xrightarrow{CH_3CH_2OH}$

(A)



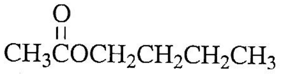
$\left(CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}\right)_2O$

(B)



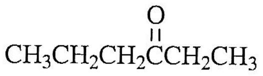
$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_3$

(C)



$CH_3\overset{\overset{O}{\|}}{C}OCH_2CH_2CH_2CH_3$

(D)



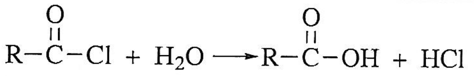
$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}CH_2CH_3$

Knowledge Required: (1) Preparation of acyl chlorides from carboxylic acids. (2) Reactions of acyl chlorides with nucleophiles.

Thinking it Through: Thionyl chloride converts the carboxylic acids into the corresponding acyl chloride. The acyl chloride then reacts with the ethanol to form the corresponding ester. Choices **(A)** and **(D)**, which are not esters, may be eliminated. Both choices **(B)** and **(C)** are esters, but choice **(C)** has the wrong number of carbon atoms in the alcohol and carboxylic acid portions. Choice **(B)** is the correct answer.

Practice Questions

1. This reaction that is typical of carboxylic acids, esters, acid halides, anhydrides, and amides is called



$R-\overset{\overset{O}{\|}}{C}-Cl + H_2O \longrightarrow R-\overset{\overset{O}{\|}}{C}-OH + HCl$

(A) nucleophilic non-acyl substitution

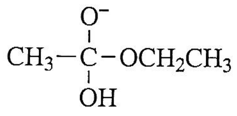
(B) nucleophilic addition

(C) nucleophilic acyl substitution

(D) electrophilic substitution

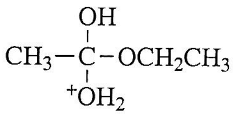
2. Which structure is a reasonable intermediate in the acid-catalyzed hydrolysis of ethyl acetate in dilute aqueous acid?

(A)



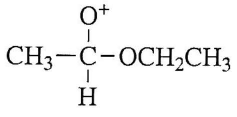
$CH_3-\overset{O^-}{\underset{OH}{C}}-OCH_2CH_3$

(B)



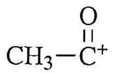
$CH_3-\overset{OH}{\underset{^+OH_2}{C}}-OCH_2CH_3$

(C)



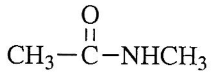
$CH_3-\overset{O^+}{\underset{H}{C}}-OCH_2CH_3$

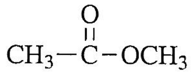
(D)

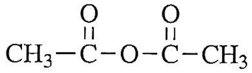


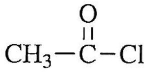
$CH_3-\overset{\overset{O}{\|}}{C^+}$

3. Which would be hydrolyzed ***most slowly*** with aqueous NaOH?

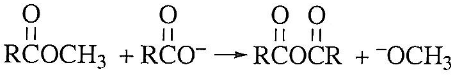
(A)

$CH_3-\overset{\overset{O}{\|}}{C}-NHCH_3$

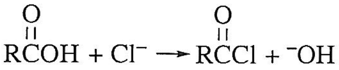
(B)

$CH_3-\overset{\overset{O}{\|}}{C}-OCH_3$

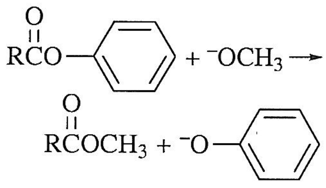
(C)

$CH_3-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}-CH_3$

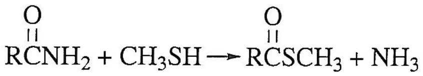
(D)

$CH_3-\overset{\overset{O}{\|}}{C}-Cl$

4. Using your knowledge of base strengths, predict which of these reactions would be most likely to occur.

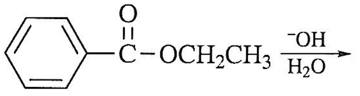
(A)

$R\overset{\overset{O}{\|}}{C}OCH_3 + R\overset{\overset{O}{\|}}{C}O^- \rightarrow R\overset{\overset{O}{\|}}{C}O\overset{\overset{O}{\|}}{C}R + {}^-OCH_3$

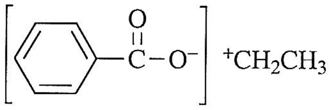
(B)

$R\overset{\overset{O}{\|}}{C}OH + Cl^- \rightarrow R\overset{\overset{O}{\|}}{C}Cl + {}^-OH$

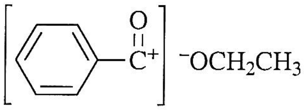
(C)


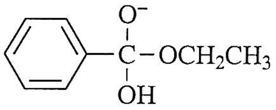
(D)

$R\overset{\overset{O}{\|}}{C}NH_2 + CH_3SH \rightarrow R\overset{\overset{O}{\|}}{C}SCH_3 + NH_3$

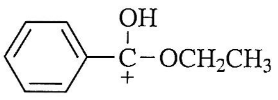
5. Which intermediate is involved in the mechanism of this base-promoted hydrolysis?



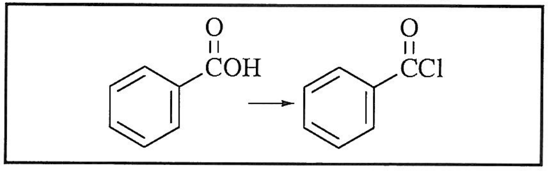
(A)


(B)


(C)


(D)


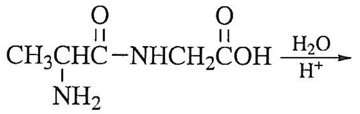
6. With which reagent is benzoic acid readily converted into benzoyl chloride in high yield?

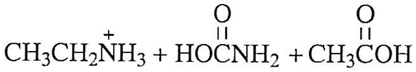


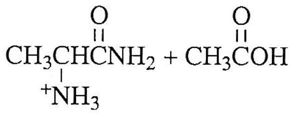
(A) HCl **(B)** $SOCl_2$

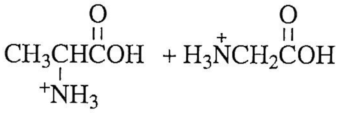
(C) Cl_2 **(D)** NaCl

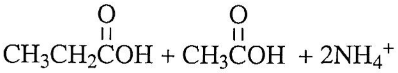
7. Which set of products is obtained from this acid hydrolysis?


$CH_3\underset{NH_2}{\underset{|}{C}}H\overset{\overset{O}{\|}}{C}-NHCH_2\overset{\overset{O}{\|}}{C}OH \xrightarrow[H^+]{H_2O}$

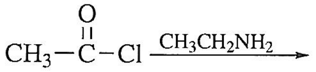
(A)

$CH_3CH_2\overset{+}{N}H_3 + HO\overset{\overset{O}{\|}}{C}NH_2 + CH_3\overset{\overset{O}{\|}}{C}OH$

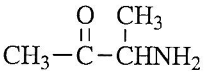
(B)

$CH_3\underset{{}^+NH_3}{\underset{|}{C}}H\overset{\overset{O}{\|}}{C}NH_2 + CH_3\overset{\overset{O}{\|}}{C}OH$

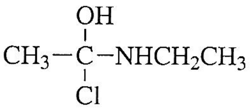
(C)

$CH_3\underset{{}^+NH_3}{\underset{|}{C}}H\overset{\overset{O}{\|}}{C}OH + H_3\overset{+}{N}CH_2\overset{\overset{O}{\|}}{C}OH$

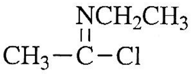
(D)

$CH_3CH_2\overset{\overset{O}{\|}}{C}OH + CH_3\overset{\overset{O}{\|}}{C}OH + 2NH_4^+$

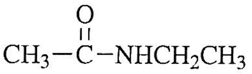
8. What product would you isolate from these reactants?


$CH_3-\overset{\overset{O}{\|}}{C}-Cl \xrightarrow{CH_3CH_2NH_2}$

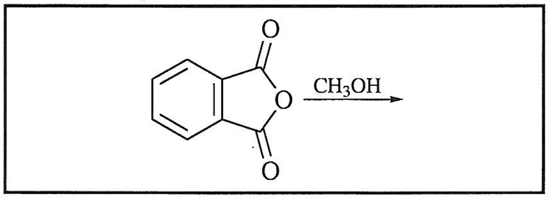
(A)

$CH_3-\overset{\overset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{C}HNH_2$

(B)

$CH_3-\underset{\underset{Cl}{|}}{\overset{\overset{OH}{|}}{C}}-NHCH_2CH_3$

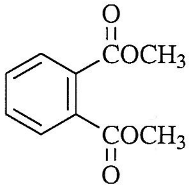
(C)

$CH_3-\overset{\overset{NCH_2CH_3}{\|}}{C}-Cl$

(D)

$CH_3-\overset{\overset{O}{\|}}{C}-NHCH_2CH_3$

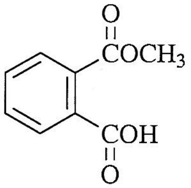
9. Predict the product formed from this reaction:



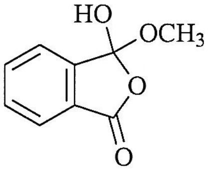
(A)



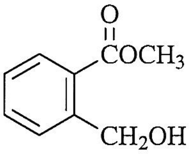
(B)



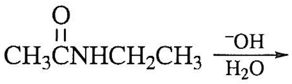
(C)



(D)

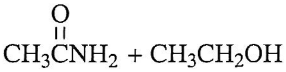


10. What are the products of this reaction?



$CH_3\overset{O}{\overset{\|}{C}}NHCH_2CH_3 \xrightarrow[H_2O]{^-OH}$

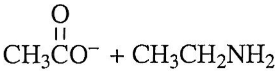
(A)



$CH_3\overset{O}{\overset{\|}{C}}NH_2 + CH_3CH_2OH$

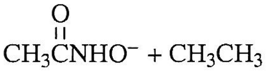
(B) $CH_3OH + NH_3 + CH_3CH_2OH$

(C)



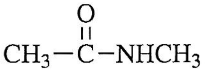
$CH_3\overset{O}{\overset{\|}{C}}O^- + CH_3CH_2NH_2$

(D)



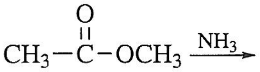
$CH_3\overset{O}{\overset{\|}{C}}NHO^- + CH_3CH_3$

11. Which of these reactions would produce this product?



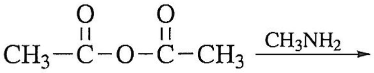
$CH_3-\overset{O}{\overset{\|}{C}}-NHCH_3$

(A)



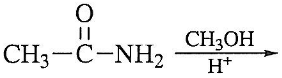
$CH_3-\overset{O}{\overset{\|}{C}}-OCH_3 \xrightarrow{NH_3}$

(B)



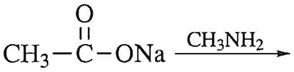
$CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{CH_3NH_2}$

(C)



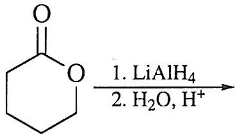
$CH_3-\overset{O}{\overset{\|}{C}}-NH_2 \xrightarrow[H^+]{CH_3OH}$

(D)

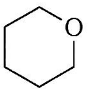


$CH_3-\overset{O}{\overset{\|}{C}}-ONa \xrightarrow{CH_3NH_2}$

12. What is the product of this reaction?



(A)



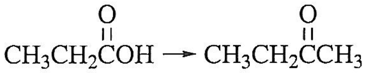
(B) $HOCH_2CH_2CH_2CH_2CH_3$

(C)

$H\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_2OH$

(D) $HOCH_2CH_2CH_2CH_2CH_2OH$

13. Which reaction sequence is preferred for this conversion?



$CH_3CH_2\overset{O}{\overset{\|}{C}}OH \rightarrow CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3$

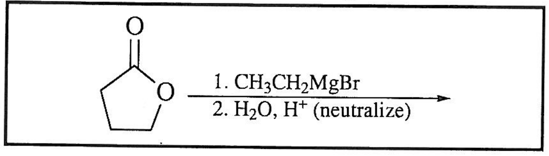
(A) $\xrightarrow{CH_3MgBr} \xrightarrow[H^+]{H_2O}$

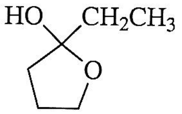
(B) $\xrightarrow{SOCl_2} \xrightarrow{(CH_3)_2CuLi}$

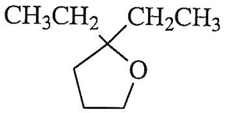
(C) $\xrightarrow{SOCl_2} \xrightarrow{CH_3Li} \xrightarrow[H^+]{H_2O}$

(D) $\xrightarrow{SOCl_2} \xrightarrow{CH_3MgBr} \xrightarrow[H^+]{H_2O}$

14. What is the product of this Grignard reaction?

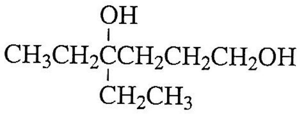


(A)


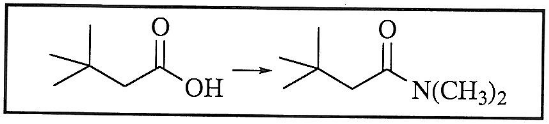
(B)


(C)

$CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2CH_2OH$

(D)

$CH_3CH_2\underset{\underset{CH_2CH_3}{|}}{\overset{\overset{OH}{|}}{C}}CH_2CH_2CH_2OH$

15. Which reaction sequence would ***best*** accomplish this transformation?



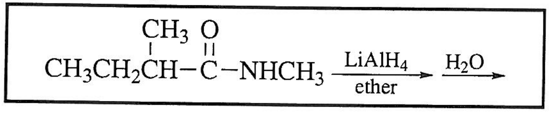
(A) $\xrightarrow{SOCl_2}\xrightarrow{(CH_3)_2NH}$

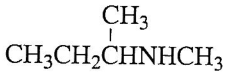
(B) $\xrightarrow{NH_3}\xrightarrow{CH_3I\text{ (excess)}}$

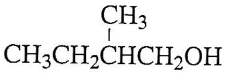
(C) $\xrightarrow{NaBH_4}\xrightarrow{(CH_3)_2NH}$

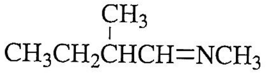
(D) $\xrightarrow{LiN(CH_3)_2}$

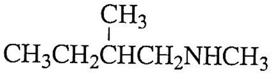
16. What is the product of this reduction?


$CH_3CH_2\overset{\overset{CH_3}{|}}{C}H-\overset{\overset{O}{\|}}{C}-NHCH_3 \xrightarrow[\text{ether}]{LiAlH_4}\xrightarrow{H_2O}$

(A)

$CH_3CH_2\overset{\overset{CH_3}{|}}{C}HNHCH_3$

(B)

$CH_3CH_2\overset{\overset{CH_3}{|}}{C}HCH_2OH$

(C)

$CH_3CH_2\overset{\overset{CH_3}{|}}{C}HCH=NCH_3$

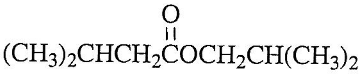
(D)

$CH_3CH_2\overset{\overset{CH_3}{|}}{C}HCH_2NHCH_3$

17. What product is formed from this reaction sequence?

$(CH_3)_2CHCH_2Li \xrightarrow[2.\ H_2O,\ H^+]{1.\ CO_2}$

(A)

$(CH_3)_2CHCH_2\overset{\overset{O}{\|}}{C}OH$

(B)

$(CH_3)_2CHCH_2\overset{\overset{O}{\|}}{C}OCH_2CH(CH_3)_2$

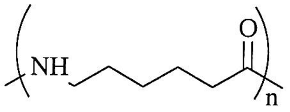
(C)

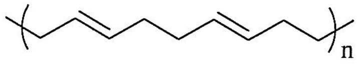
$(CH_3)_2CHCH_2\overset{\overset{O}{\|}}{C}H$

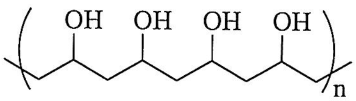
(D)

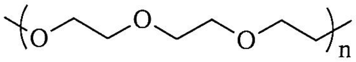
$(CH_3)_2CHCH_2O\overset{\overset{O}{\|}}{C}OH$

18. Which of these polymers could be readily prepared by condensation polymerization?

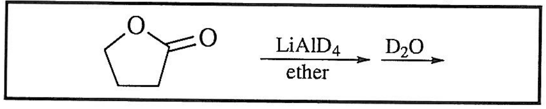
(A)


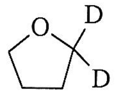
(B)


(C)


(D)


19. Predict the product from this reaction sequence.



(A)


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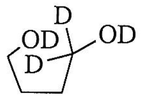
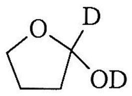
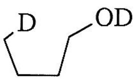
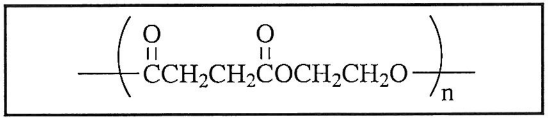


(C)


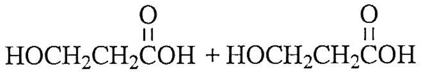
(D)


20. What monomers are needed to produce this polymer?



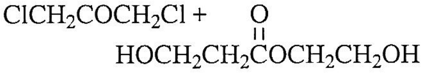
$$-\!\left(\overset{\overset{O}{\|}}{C}CH_2CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_2O\right)_{n}\!-$$

(A)



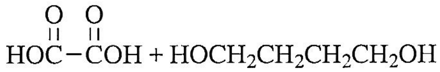
$HOCH_2CH_2\overset{\overset{O}{\|}}{C}OH + HOCH_2CH_2\overset{\overset{O}{\|}}{C}OH$

(B)



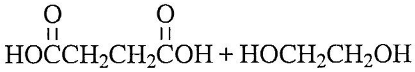
$ClCH_2COCH_2Cl + HOCH_2CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_2OH$

(C)



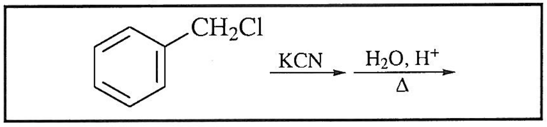
$HO\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}OH + HOCH_2CH_2CH_2CH_2OH$

(D)

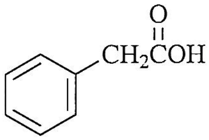


$HO\overset{\overset{O}{\|}}{C}CH_2CH_2\overset{\overset{O}{\|}}{C}OH + HOCH_2CH_2OH$

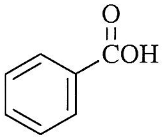
21. What is the product of this reaction?



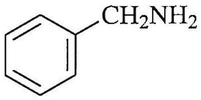
(A)



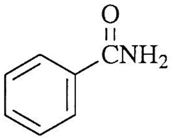
(B)



(C)



(D)



Answers to Study Questions

1. B
2. C
3. D
4. C
5. A
6. A
7. B
8. D
9. A
10. B

Answers to Practice Questions

1. C
2. B
3. A
4. C
5. C
6. B
7. C
8. D
9. B
10. C
11. B
12. D
13. B
14. D
15. A
16. D
17. A
18. A
19. B
20. D
21. A