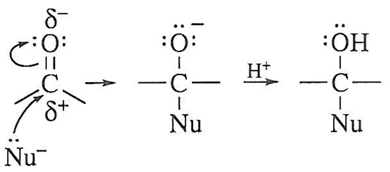
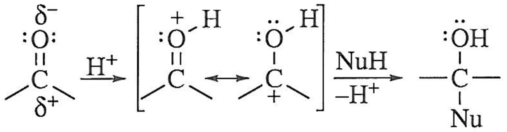
Nucleophilic Addition at Carbonyl Groups

The carbonyl group is polar with the electronegative oxygen atom creating a partial positive charge on the carbon atom. Nucleophiles are attracted to the electrophilic carbon atom. The formation of a sigma bond between the nucleophilic atom and the carbonyl carbon atom breaks the carbon–oxygen π bond, which localizes the π-bonding electrons as nonbonding electrons on the oxygen atom. The resulting alkoxide species is often referred to as a tetrahedral intermediate (equation *1*). In protic environments, the alkoxide becomes protonated and the addition to the carbonyl group is complete. The ease of nucleophilic attack at the carbonyl carbon atom is subject to steric hindrance and electronic considerations.



(1)

The nucleophilic addition is catalyzed by acid. Protonation of the carbonyl oxygen atom results in an even more electrophilic carbon atom as suggested by the resonance structure in equation *2*. Nucleophilic attack forms the addition product directly.



(2)

If the nucleophile is a weak base, and therefore a good leaving group, the nucleophilic addition is reversible. An equilibrium is established that reflects the relative stabilities of the carbonyl compound and the adduct. Since the substituents are closer together in the tetrahedral intermediate than in the starting material, steric effects may be important in assessing relative stabilities. In addition, the stability of the carbonyl compound is greatly affected by the electronic nature of the substituent attached to the carbonyl carbon atom. Electron-releasing groups diminish the positive charge on the carbonyl group, which is a stabilizing factor. Electron-withdrawing groups intensify the positive charge on the carbon atom, and destabilize the carbonyl group.

If the nucleophile is a primary amine or a so-called derivative of ammonia (Y–NH_2), the tetrahedral intermediate can lose water to form the carbon–nitrogen double bond of an **imine**. A secondary amine can lose water from the carbon–carbon double bond giving an **enamine**.

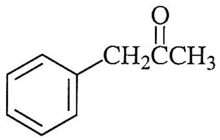
The formation of acetals and imines can be favored by the removal of the water, which is also a product of the reactions. Reversing the process, acetals, imines, and enamines can be hydrolyzed back to the carbonyl compound using an aqueous acid solution.

Aldehydes and ketones that are α,β-unsaturated may undergo either 1,2-additon or 1,4-addition with nucleophiles. The *kinetic* product results from 1,2-nucleophilic addition, while the *thermodynamic* product results from 1,4-nucleophilic addition. Strongly basic nucleophiles such as Grignard and organolithium reagents and complex metal hydrides generally give 1,2-additions. Weakly basic nucleophiles and organocuprates (R_2CuLi) generally give 1,4-additions.

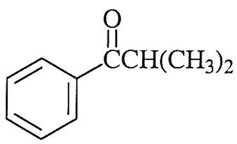
Study Questions

NA-1. Which compound exists to the greatest extent as its hydrate when dissolved in aqueous solution?

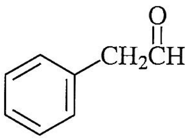
(A)



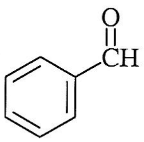
(B)



(C)



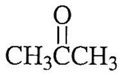
(D)



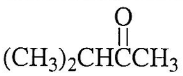
Knowledge Required: (1) Mechanism of nucleophilic addition to a carbonyl group. (2) Electron-releasing characteristic of alkyl groups. (3) Steric factors in formation of reaction intermediate. (4) Stabilizing effect of conjugation.

Thinking it Through: The nucleophilic attack by water at the carbonyl carbon atom to form the tetrahedral intermediate is reversible. The relative concentrations of reactants and products reflect their relative stabilities. Ketones have two electron-releasing groups attached to the carbonyl carbon atom and therefore, that carbon atom is less electrophilic than the carbonyl carbon atom of an aldehyde. In addition, the two alkyl or aryl groups of the ketone must come closer to each other as the tetrahedral intermediate forms. Steric repulsion between these groups is greater than the repulsion between one alkyl (or aryl) group and a hydrogen atom in an aldehyde. Both the electronic effect and the steric effect suggest that the carbonyl group of ketones is more stable than the carbonyl group of aldehydes, so less of the ketone adduct would be present at equilibrium. On this basis, choices **(A)** and **(B)** are eliminated. Of the two aldehydes shown, choice **(D)** is conjugated, and therefore more stable than choice **(C)**, which is the correct answer.

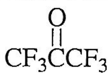
NA-2. Arrange the ketones in order of decreasing reactivity toward cyanohydrin formation with HCN/KCN.


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

1


$(CH_3)_2CH\overset{O}{\overset{\|}{C}}CH_3$

2


$CF_3\overset{O}{\overset{\|}{C}}CF_3$

3

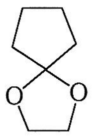
(A) 1 > 2 > 3 (B) 2 > 1 > 3 (C) 3 > 1 > 2 (D) 3 > 2 > 1

Knowledge Required: (1) Mechanism of nucleophilic addition to a carbonyl group. (2) Electron-withdrawing characteristic of fluoroalkyl groups. (3) Steric factors in formation of reaction intermediate.

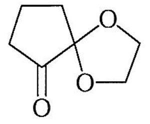
Thinking it Through: The three structures shown are all ketones, and the reaction involves nucleophilic addition of HCN to the carbonyl group. Nucleophilic attack at the carbonyl carbon atom is a consequence of the electrophilic character of the carbonyl carbon atom. The electron-withdrawing trifluoromethyl group greatly increases the electrophilic character of the carbonyl carbon atom in ketone **3** relative to that of the other two ketones. Therefore, choices **(A)** and **(B)** are eliminated. The intermediate for ketone **2** is more sterically hindered than the intermediate for ketone **1**, so ketone **2** should be less reactive. This gives the sequence **3** > **1** > **2** as the correct answer, which is choice **(C)**.

NA-3. What is the principal product of the acid-catalyzed reaction of cyclopentanone with ethylene glycol ($HOCH_2CH_2OH$)?

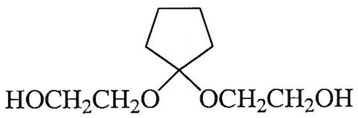
(A)



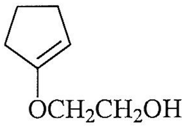
(B)



(C)



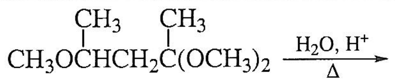
(D)



Knowledge Required: (1) Mechanism of nucleophilic addition to a carbonyl group. (2) Relative rates of intramolecular and intermolecular reactions.

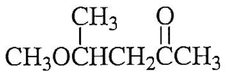
Thinking it Through: The general mechanism of nucleophilic addition under acidic conditions begins with protonation of the carbonyl group, which activates it toward nucleophilic attack by the alcohol, forming a hemiacetal. Under acidic conditions, the hydroxyl group of the hemiacetal is protonated, and loses water to give a resonance-stabilized carbocation. *Intramolecular* nucleophilic attack by the remaining hydroxyl would lead to the acetal shown in choice **(A)**. Choice **(C)** is an acetal, but results from *intermolecular* reaction of a second ethylene glycol with the carbocation. The intramolecular reaction proceeds much more rapidly than the intermolecular reaction, which eliminates choice **(C)**. Choice **(D)** is not an acetal, but an enol ether that would react to form the resonance stabilized carbocation, then choice **(A)**. Therefore, choice **(D)** is eliminated. Choice **(B)** contains both ketone and acetal functional groups, and it would not form under any conceivable reaction conditions. This leaves choice **(A)** as the only correct answer.

NA-4. Which is the product that can be isolated from the reaction shown?



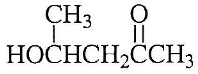
$CH_3O\overset{CH_3}{\overset{|}{C}}HCH_2\overset{CH_3}{\overset{|}{C}}(OCH_3)_2 \xrightarrow[\Delta]{H_2O,\ H^+}$

(A)



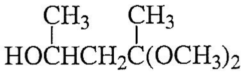
$CH_3O\overset{CH_3}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}CH_3$

(B)



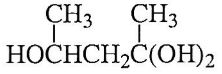
$HO\overset{CH_3}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}CH_3$

(C)



$HO\overset{CH_3}{\overset{|}{C}}HCH_2\overset{CH_3}{\overset{|}{C}}(OCH_3)_2$

(D)

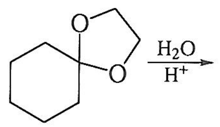


$HO\overset{CH_3}{\overset{|}{C}}HCH_2\overset{CH_3}{\overset{|}{C}}(OH)_2$

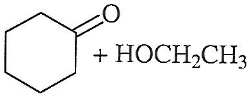
Knowledge Required: (1) Structure of acetal functional group. (2) Mechanism of acid-catalyzed hydrolysis of acetals. (3) Stability of simple ethers to mild acidic conditions.

Thinking it Through: Many nucleophilic addition reactions are reversible. This question deals with the reverse reaction of acetal formation. The reactant molecule contains both an acetyl functional group and a simple ether functional group. Only the acetal group is reactive under mild acidic conditions. Simple ethers require extreme conditions for hydrolysis. Choices **(B)**, **(C)**, and **(D)** are eliminated as possible products because each shows the simple ether as having been hydrolyzed. Only choice **(A)** is left as a possible answer. Choice **(A)** correctly shows the product of the acetal hydrolysis to be a ketone group as well as showing the simple ether as having not reacted.

NA-5. What are the products of the hydrolysis reaction shown?

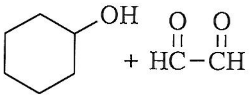


(A)



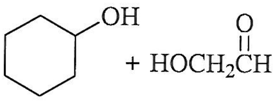
$+ HOCH_2CH_3$

(B)



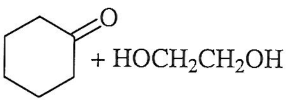
$+\ H\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}H$

(C)



$+\ HOCH_2\overset{O}{\overset{\|}{C}}H$

(D)



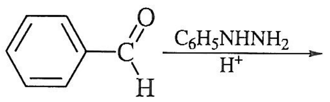
$+ HOCH_2CH_2OH$

Knowledge Required: (1) Mechanism of nucleophilic addition to a carbonyl group. (2) Mechanism of acid-catalyzed hydrolysis of acetals.

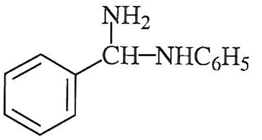
Thinking it Through: This is another example of the reverse reaction for nucleophilic addition. This question considers the reverse of the reaction in which an acetal is formed from a ketone. The first thing is to recognize that the cyclic compound is an acetal that could only have formed from a diol. In the hydrolysis reaction, protonation on one of the oxygen atoms of the acetal produces a good leaving group (an alcohol), which can dissociate to a resonance-stabilized carbocation.

Nucleophilic attack on the carbocation by water then produces a hemiacetal. Subsequent protonation on the alkoxyl oxygen atom again produces a good leaving group, which then dissociates to the protonated carbonyl group. The overall result is that hydrolysis of the carbon atom bearing the two alkoxyl groups converts it to a carbonyl group, and the alkoxyl groups become alcohol groups. Either two alcohol molecules or a diol must be counted among the products. Choice (**A**) has the correct ketone, but only one alcohol group among the products. Choices (**B**) and (**C**) have the carbonyl group appearing in the wrong fragment. Choice (**D**) has the correct ketone, and there are two alcohol groups in the diol. It is the correct answer.

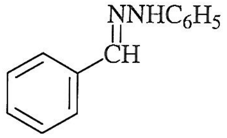
NA-6. Which is the product that can be isolated from the reaction shown?



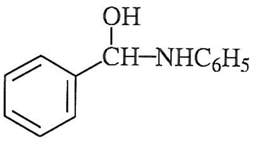
(A)



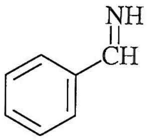
(B)



(C)



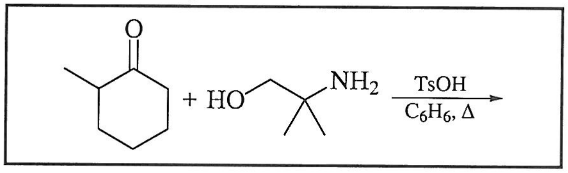
(D)



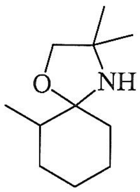
Knowledge Required: Mechanism of nucleophilic addition to a carbonyl group when the nucleophile is a primary amine (Y–NH_2).

Thinking it Through: The reaction shows an aldehyde reacting with phenylhydrazine, a primary amine, in the presence of an acid. Acid-catalyzed nucleophilic addition would give a species with a hydroxyl and an amine attached to what was the carbonyl carbon atom. Protonation of the hydroxyl and loss of water forms a resonance-stabilized carbocation that can lose a proton from the nitrogen atom to give a carbon–nitrogen double bond. Choices (**A**) and (**C**) are immediately eliminated because they do not contain a carbon–nitrogen double bond. Choice (**B**) results if the terminal N–H bond is broken during the elimination of water, and is the correct answer. Choice (**D**) would form if the N–N bond were broken, which cannot happen under these conditions.

NA-7. What is the most reasonable structure for product of the reaction shown?



(A)



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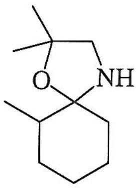

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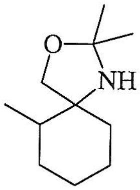
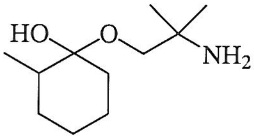


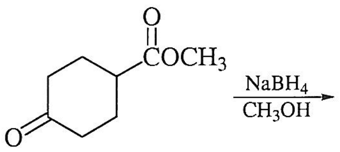
(D)

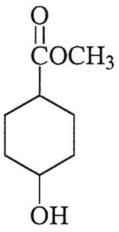


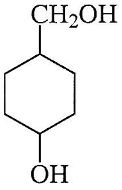
Knowledge Required: (1) Mechanism of nucleophilic addition to a carbonyl group. (2) Relative strengths of alcohol oxygen atoms and amine nitrogen atoms as nucleophiles.

Thinking it Through: Under acidic reaction conditions, the carbonyl group of the ketone becomes protonated. The nitrogen atom is an intrinsically better nucleophile (stronger base) than the oxygen atom, and preferentially attacks the carbonyl carbon atom, producing a hemiaminal (analogous to a hemiacetal). In analogy to the mechanism of acetal formation with a diol, the hemiaminal undergoes protonation of the hydroxyl group followed by rapid *intramolecular* nucleophilic attack at the carbocation by the hydroxyl oxygen atom. The product is the mononitrogen analogue of an acetal, and must have both a nitrogen atom and an oxygen atom directly attached to the carbon atom. Choice (**C**) is eliminated because a methylene group is shown between the carbonyl carbon atom and the oxygen atom. Choice (**D**) is eliminated because it shows initial nucleophilic attack by the hydroxyl oxygen atom, with no further reaction. Considering choices (**A**) and (**B**), the difference is in the linkage of the nitrogen atom and oxygen atom to the tertiary carbon atom. Choice (**A**) correctly shows the nitrogen atom directly connected to the tertiary carbon atom, while (**B**) shows the nitrogen atom connected through a methylene group.

NA-8. What is the product of the $NaBH_4$ reduction shown?



(A)


(B)


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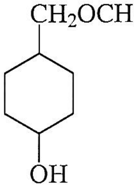
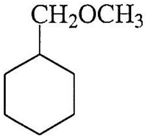
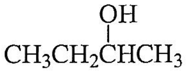


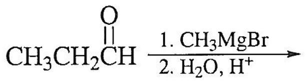
(D)


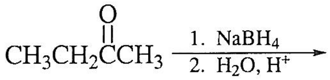
Knowledge Required: Relative reactivity and selectivity of hydride reagents.

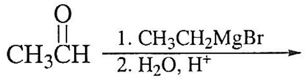
Thinking it Through: Sodium borohydride, $NaBH_4$, is a source of hydride ion and reduces aldehydes and ketones by hydride attack at the carbonyl group. In general, $NaBH_4$ does not readily reduce esters. Choice **(A)** shows the reduction of the ketone without reaction with the ester and is the correct answer. Choice **(B)** shows reduction of both the ketone and ester groups. The reaction shown in choices **(C)** and **(D)** indicates the ester reduction product to be an ether, which would not occur. If the reduction did occur, an alcohol would result, as in choice **(B)**. Note that $LiAlH_4$ is a more reactive source of hydride and readily reduces aldehydes, ketones, esters, and carboxylic acids.

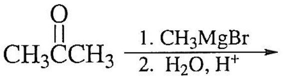
NA-9. Which combination would *not* produce the alcohol shown?


$CH_3CH_2\overset{OH}{\overset{|}{C}}HCH_3$

(A)

$CH_3CH_2\overset{O}{\overset{\|}{C}}H \xrightarrow[2.\ H_2O,\ H^+]{1.\ CH_3MgBr}$

(B)

$CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[2.\ H_2O,\ H^+]{1.\ NaBH_4}$

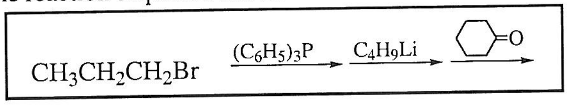
(C)

$CH_3\overset{O}{\overset{\|}{C}}H \xrightarrow[2.\ H_2O,\ H^+]{1.\ CH_3CH_2MgBr}$

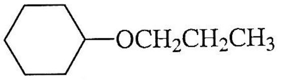
(D)

$CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[2.\ H_2O,\ H^+]{1.\ CH_3MgBr}$

Knowledge Required: (1) Mechanism of nucleophilic addition to a carbonyl group. (2) Organomagnesium compounds (Grignard reagents) as sources of alkyl nucleophiles. (3) $NaBH_4$ as a source of nucleophilic hydride.

Thinking it Through: A systematic approach to the synthesis of alcohols is to focus on transformation of a carbonyl group into the carbon atom bearing the hydroxyl. The third substituent attached to the carbon atom bearing the hydroxyl is introduced as the nucleophile reacting with the carbonyl group. Carbon nucleophiles can derive from Grignard reagents or organolithium reagents. The nucleophilic hydrogen atom can come from $NaBH_4$ or $LiAlH_4$. This notion of "thinking backwards" is called **retrosynthetic analysis**. Mentally disconnect one of the substituents attached to the carbon atom bearing the hydroxyl. That substituent is the nucleophile and the carbon atom bearing the hydroxyl becomes the carbonyl carbon atom. In this question, however, it is necessary to examine each of the combinations to determine which is incorrect. The final secondary alcohol contains a methyl group and an ethyl group attached to the original carbonyl carbon atom. Choice **(A)** begins with propanal and adds a methyl group, so it will produce the desired 2-butanol. Choice **(C)** produces the same result by beginning with ethanal and adding an ethyl group. Choice **(B)** already has the correct substituents on the carbonyl carbon atom, and the hydride reduction converts the ketone group to an alcohol group. Choice **(D)** forms a tertiary alcohol (2-methyl-2-propanol) rather than a secondary alcohol, and is the correct answer.

NA-10. What is the product of the reaction sequence shown?



(A)


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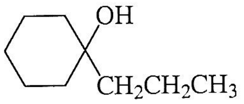
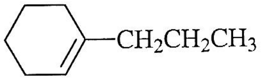
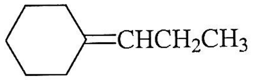
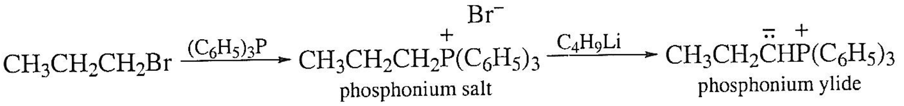


(C)


(D)


Knowledge Required: The formation of Wittig reagents and their reaction with aldehydes and ketones.

Thinking it Through: The Wittig reaction is an important method for the synthesis of alkenes. The overall transformation converts a carbon–oxygen double bond into a carbon–carbon double bond. In a Wittig reaction, an aldehyde or ketone reacts with a phosphonium ylide. An ylide is a species with positive and negative charge on adjacent atoms. In a phosphonium ylide, a phosphorus atom is positive and a carbon atom is negative, and therefore nucleophilic. The ylide is formed by the deprotonation of a phosphonium salt, which is first formed by the reaction of a trivalent phosphorus compound with an alkyl halide. This sequence is shown below for the reagents in this question.

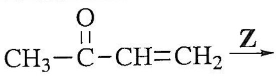


$$CH_3CH_2CH_2Br \xrightarrow{(C_6H_5)_3P} \underset{\text{phosphonium salt}}{CH_3CH_2CH_2\overset{+}{P}(C_6H_5)_3\ \ Br^-} \xrightarrow{C_4H_9Li} \underset{\text{phosphonium ylide}}{CH_3CH_2\overset{\cdot\cdot\,-}{C}H\overset{+}{P}(C_6H_5)_3}$$

The ylide is the nucleophile that attacks the carbonyl carbon atom of aldehydes and ketones in the key step of the Wittig reaction. A new carbon–carbon bond is formed that eventually becomes a carbon–carbon double bond with the elimination of oxygen and phosphorus. Formally, one carbon atom of the carbon–carbon double bond derives from the carbonyl carbon atom and the other carbon atom is from the alkyl halide to which the halogen had been attached.

Choice **(A)** is immediately eliminated because it would require a nucleophilic attack on the carbonyl oxygen atom instead of the carbonyl carbon atom. Choice **(B)** suggests a nucleophilic attack at the carbonyl carbon atom, but there is no logical basis for the elimination of the phosphorus atom. Choice **(C)** indicates formation of an alkene after a nucleophilic attack, but the double bond involves the wrong carbon atom. Choice **(D)** would result from the nucleophilic attack of the carbon atom from the phosphonium ylide on the carbonyl carbon atom, followed by removal of the oxygen atom by triphenylphosphine, and it is the correct answer.

NA-11. Which nucleophilic reagent, **Z**, will give the most 1,4-addition product with methyl vinyl ketone?



$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-CH=CH_2 \xrightarrow{\mathbf{Z}}$$

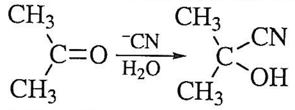
(A) $LiAlH_4$ (B) NaCN (C) CH_3MgBr (D) $(C_6H_5)_3\overset{+}{P}\overset{\cdot\cdot\,-}{C}H_2$

Knowledge Required: The factors that control whether 1,2-addition or 1,4-addition is the major mode of reaction of nucleophiles with α,β-unsaturated carbonyl compounds.

Thinking it Through: Methyl vinyl ketone is a conjugated ketone and may undergo either 1,2-addition or 1,4-addition with nucleophiles. Kinetically, 1,2-additions are favored over 1,4-additions. When the nucleophile is strongly basic, the initial1,2-addition is irreversible and the1,2-addition product is the dominant product. However, when the nucleophile is less basic, the initial 1,2-addition is reversible and the thermodynamically more stable 1,4-addition product is the dominant product. The reagents in choices **(A)**, **(C)** and **(D)** are strongly basic and give mostly 1,2-addition. The cyanide ion, in choice **(B)**, is a much weaker base ($pK_a = 9$ for HCN) and gives predominantly 1,4-addition. Choice **(B)** is the correct answer.

Practice Questions

1. The reaction shown is classified as



(A) a nucleophilic substitution.

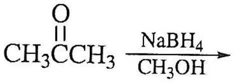
(B) an electrophilic substitution.

(C) a nucleophilic addition.

(D) an electrophilic addition.

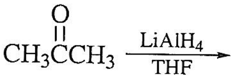
2. In which of these reactions would the addition of the nucleophile be expected to be reversible?

(A)



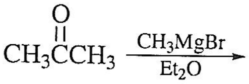
$CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[CH_3OH]{NaBH_4}$

(B)



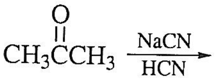
$CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[THF]{LiAlH_4}$

(C)



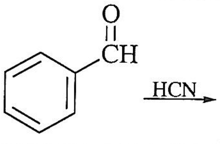
$CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[Et_2O]{CH_3MgBr}$

(D)

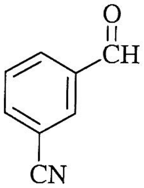


$CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[HCN]{NaCN}$

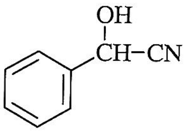
3. What product is formed in the reaction shown?



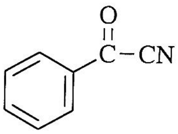
(A)



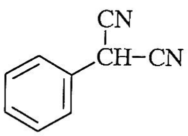
(B)



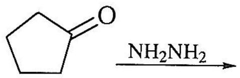
(C)



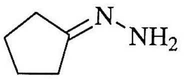
(D)



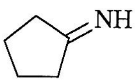
4. What product is expected from this reaction?



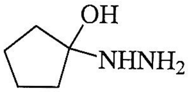
(A)



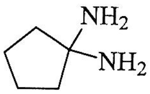
(B)



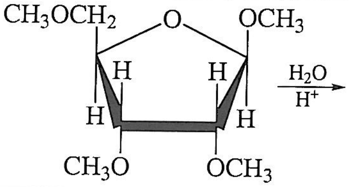
(C)



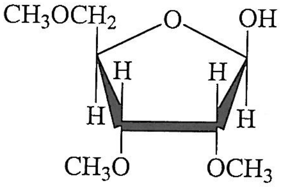
(D)



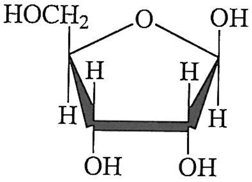
5. What is the product of the reaction shown?



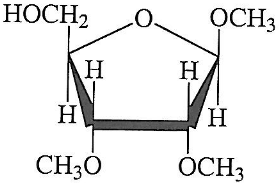
(A)



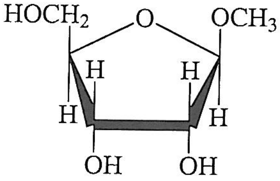
(B)



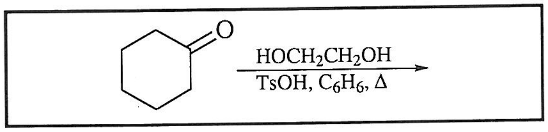
(C)



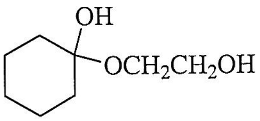
(D)



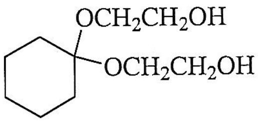
6. Which is the *main* product that can be isolated from the reaction shown?



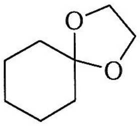
(A)



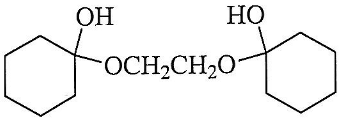
(B)



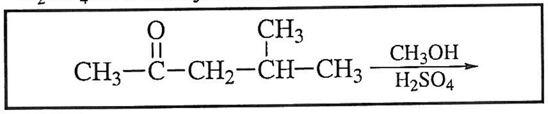
(C)



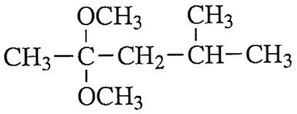
(D)



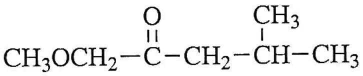
7. The initial stable product from the reaction of 4-methyl-2-pentanone and excess methanol with H_2SO_4 as a catalyst would be


$CH_3-\overset{O}{\overset{\|}{C}}-CH_2-\overset{CH_3}{\overset{|}{CH}}-CH_3 \xrightarrow[H_2SO_4]{CH_3OH}$

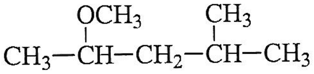
(A)


$CH_3-\underset{OCH_3}{\overset{OCH_3}{C}}-CH_2-\overset{CH_3}{CH}-CH_3$

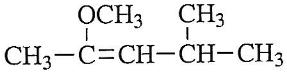
(B)


$CH_3OCH_2-\overset{O}{\overset{\|}{C}}-CH_2-\overset{CH_3}{CH}-CH_3$

(C)


$CH_3-\overset{OCH_3}{CH}-CH_2-\overset{CH_3}{CH}-CH_3$

(D)


$CH_3-\overset{OCH_3}{C}=CH-\overset{CH_3}{CH}-CH_3$

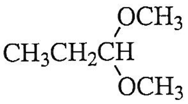
8. Which compound would be most rapidly hydrolyzed by aqueous HCl to give methanol as one of the products?

(A) $CH_3OCH_2CH_2CH_3$

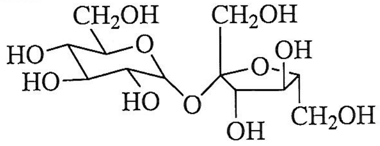
(B) $CH_3OCH_2CH_2OCH_3$

(C) $CH_3OCH_2CH_2OH$

(D)

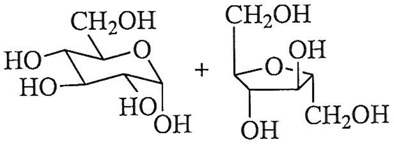

$CH_3CH_2\underset{OCH_3}{\overset{OCH_3}{CH}}$

9. Table sugar is (+)-sucrose. Which of these products forms as the result of enzymatic or acid-catalyzed test-tube hydrolysis?

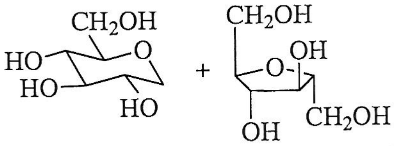


(+)-sucrose

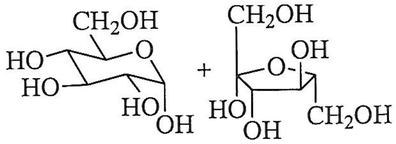
(A)



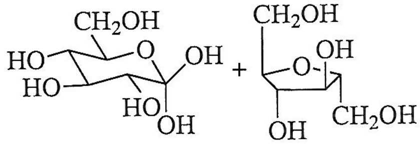
(B)



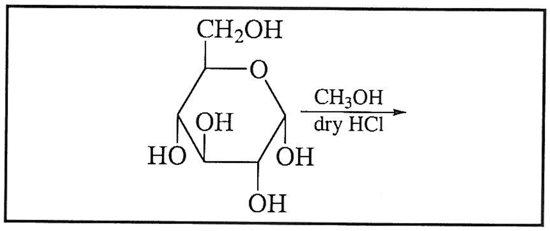
(C)



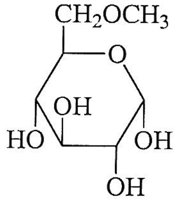
(D)



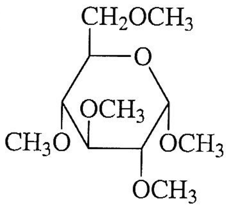
10. Which is a major product of the reaction shown?



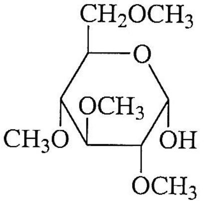
(A)



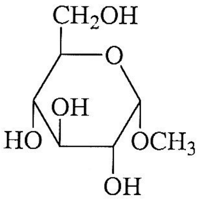
(B)



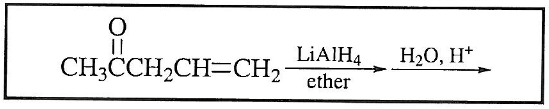
(C)



(D)

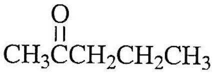


11. What is the product for the reaction shown?



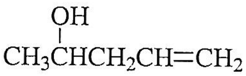
$CH_3\overset{O}{\overset{\|}{C}}CH_2CH{=}CH_2 \xrightarrow[\text{ether}]{LiAlH_4} \xrightarrow{H_2O,\ H^+}$

(A)



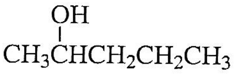
$CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3$

(B)



$CH_3\overset{OH}{\overset{|}{C}}HCH_2CH{=}CH_2$

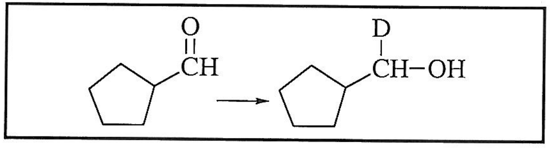
(C)



$CH_3\overset{OH}{\overset{|}{C}}HCH_2CH_2CH_3$

(D) $CH_3CH_2OH + CH_3CH_2CH_3$

12. Which is the best reagent for this conversion?



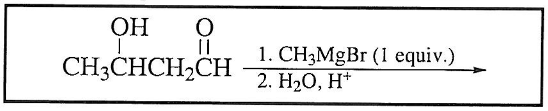
(A) D_2O, containing catalytic amounts of HCl

(B) $NaBD_4$ in CH_3CH_2OH (and an aqueous workup)

(C) NaOD in CH_3CH_2OD (and an aqueous workup)

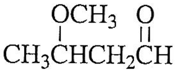
(D) D_2O_2 in CH_3CO_2H

13. Predict the products of the reaction shown.



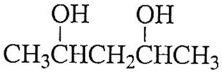
$CH_3\overset{OH}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}H \xrightarrow[\text{2. } H_2O,\ H^+]{\text{1. } CH_3MgBr\ \text{(1 equiv.)}}$

(A)



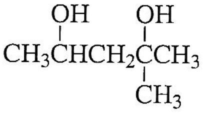
$CH_3\overset{OCH_3}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}H$

(B)



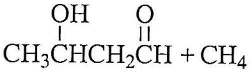
$CH_3\overset{OH}{\overset{|}{C}}HCH_2\overset{OH}{\overset{|}{C}}HCH_3$

(C)



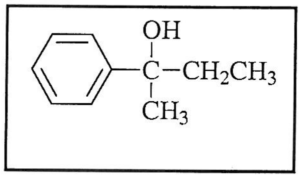
$CH_3\overset{OH}{\overset{|}{C}}HCH_2\underset{\underset{CH_3}{|}}{\overset{\overset{OH}{|}}{C}}CH_3$

(D)

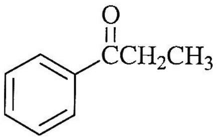


$CH_3\overset{OH}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}H + CH_4$

14. What combination of reagents would ***not*** form the alcohol shown after an aqueous workup?

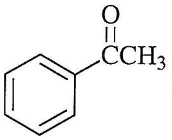


(A)



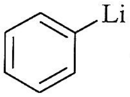
+ CH_3MgBr

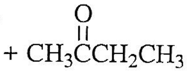
(B)



+ CH_3CH_2MgBr

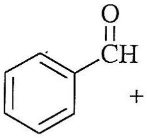
(C)

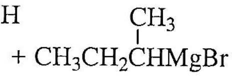




+ $CH_3\overset{O}{\overset{\|}{C}}CH_2CH_3$

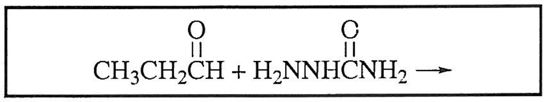
(D)





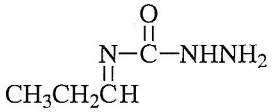
+ $CH_3CH_2\overset{CH_3}{\overset{|}{C}}HMgBr$

15. What is the major product of the reaction shown?



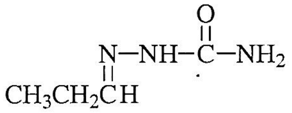
$CH_3CH_2\overset{\overset{O}{\|}}{C}H + H_2NNH\overset{\overset{O}{\|}}{C}NH_2 \longrightarrow$

(A)



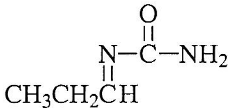
$CH_3CH_2CH{=}N-\overset{\overset{O}{\|}}{C}-NHNH_2$

(B)



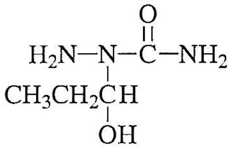
$CH_3CH_2CH{=}N-NH-\overset{\overset{O}{\|}}{C}-NH_2$

(C)



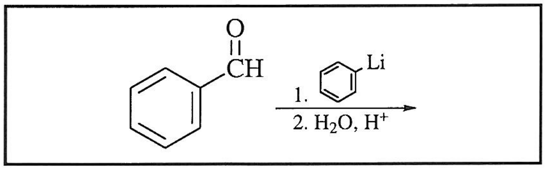
$CH_3CH_2CH{=}N-\overset{\overset{O}{\|}}{C}-NH_2$

(D)

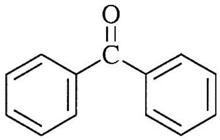


$H_2N-\underset{\underset{CH_3CH_2\underset{\underset{OH}{|}}{C}H}{|}}{N}-\overset{\overset{O}{\|}}{C}-NH_2$

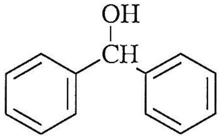
16. What would be the product from this reaction?



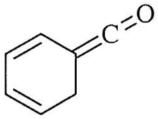
(A)



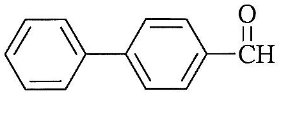
(B)



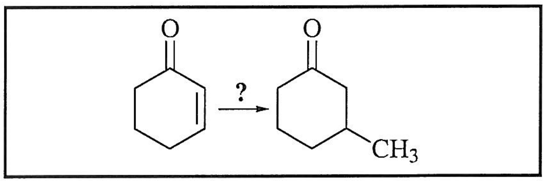
(C)



(D)



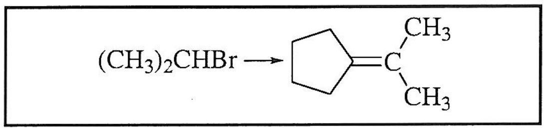
17. Which reagent will accomplish the conversion shown?

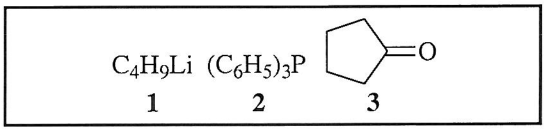


(A) CH_3I **(B)** CH_3MgBr

(C) CH_3Li **(D)** $(CH_3)_2CuLi$

18. Which reagent sequence will effect the transformation shown?

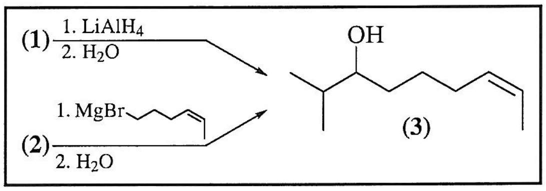




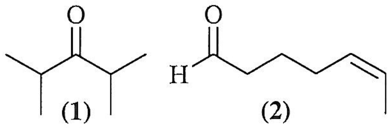
(A) 1, 2, 3 **(B)** 1, 3, 2

(C) 2, 1, 3 **(D)** 2, 3, 1

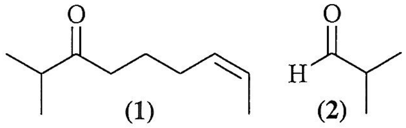
19. What set of ketone (1) and aldehyde (2) will provide the same alcohol product (3) when submitted to the reaction conditions shown?



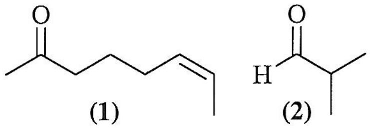
(A)



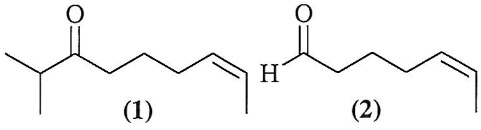
(B)



(C)



(D)

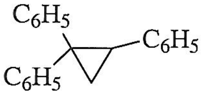


20. What is the product of this reaction sequence?

$C_6H_5CH_2Cl \xrightarrow{(C_6H_5)_3P} \xrightarrow{(CH_3)_3COK} \xrightarrow{(C_6H_5)_2C=O}$

(A) $(C_6H_5)_3COH$

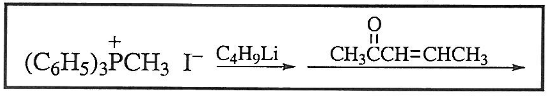
(B)



(C) $(C_6H_5)_2C=CHC_6H_5$

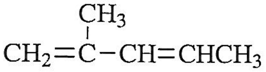
(D) $(C_6H_5)_3COCH_2C_6H_5$

21. What is the product of this reaction sequence?



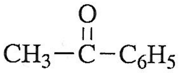
$(C_6H_5)_3\overset{+}{P}CH_3\ I^- \xrightarrow{C_4H_9Li} \xrightarrow{CH_3\overset{O}{\overset{\|}{C}}CH=CHCH_3}$

(A)



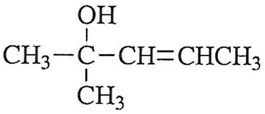
$CH_2=\overset{CH_3}{\overset{|}{C}}-CH=CHCH_3$

(B)



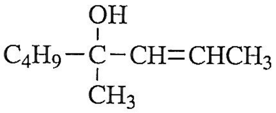
$CH_3-\overset{O}{\overset{\|}{C}}-C_6H_5$

(C)



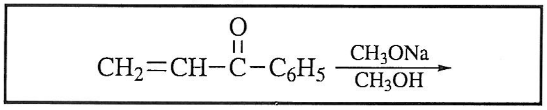
$CH_3-\underset{CH_3}{\underset{|}{\overset{OH}{\overset{|}{C}}}}-CH=CHCH_3$

(D)



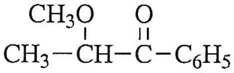
$C_4H_9-\underset{CH_3}{\underset{|}{\overset{OH}{\overset{|}{C}}}}-CH=CHCH_3$

22. Which is the *major* product of this reaction?



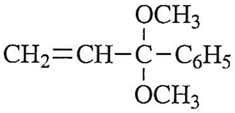
$CH_2=CH-\overset{O}{\overset{\|}{C}}-C_6H_5 \xrightarrow[CH_3OH]{CH_3ONa}$

(A)



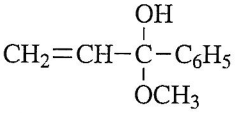
$CH_3-\overset{CH_3O}{\overset{|}{C}H}-\overset{O}{\overset{\|}{C}}-C_6H_5$

(B)



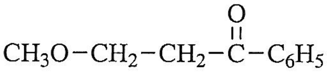
$CH_2=CH-\underset{OCH_3}{\underset{|}{\overset{OCH_3}{\overset{|}{C}}}}-C_6H_5$

(C)



$CH_2=CH-\underset{OCH_3}{\underset{|}{\overset{OH}{\overset{|}{C}}}}-C_6H_5$

(D)



$CH_3O-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-C_6H_5$

Answers to Study Questions

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

Answers to Practice Questions

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