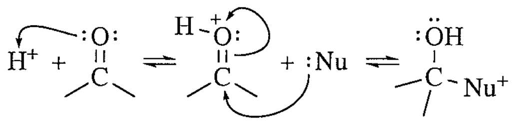
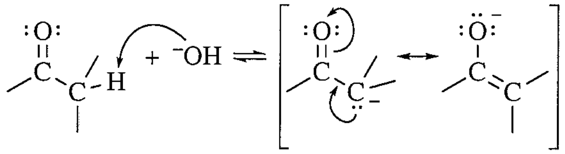
Enols and Enolate Ion Reactions

All carbonyl compounds with at least one α–hydrogen atom are in equilibrium with their respective enol tautomers. At equilibrium the amount of enol tautomer is vanishingly small with the exception of β–dicarbonyl compounds, for which the enol tautomer may even be the dominant tautomer. The rate of interconversion of the tautomers is greatly accelerated by the presence of a trace of either acid or base.

There are two "hot spots" for reactivity in aldehydes and ketones: (1) The carbonyl carbon atom is subject to addition reactions by nucleophiles (equation *1*); (2) the α–carbon atom can be deprotonated, converting it into a nucleophile. A hydrogen atom on an sp^3 carbon atom α to a carbonyl group is thirty orders of magnitude more acidic than a hydrogen atom on an sp^3 carbon atom of an ordinary hydrocarbon! Resonance, of course, provides the explanation (equation *2*).



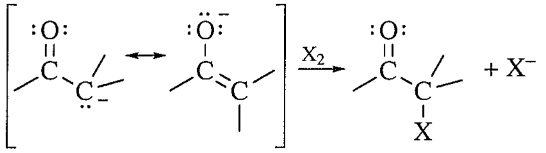
(1)



(2)

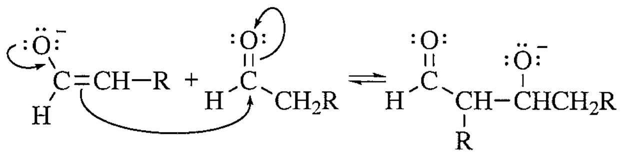
Bases such as alkoxide ions produce only small amounts of the enolates of simple carbonyl compounds, but bases that are significantly stronger than alkoxide ions quantitatively convert simple carbonyl compounds into their enolates. LDA, $[(CH_3)_2CH]_2N^- Li^+$, and sodium hydride, NaH, are examples of strong bases that produce enolates.

A nucleophilic α–carbon atom can be halogenated or alkylated. A halogenation is shown in equation *3*.

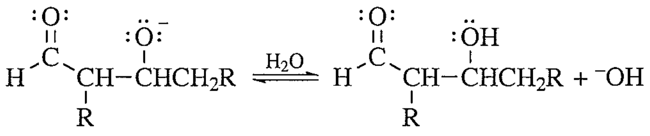


(3)

Many other examples of nucleophilic addition to the carbonyl group are provided in the *Nucleophilic Addition at Carbonyl Groups* chapter. The nucleophilic α–carbon atom of one aldehyde can attack the carbonyl carbon atom of another aldehyde molecule in a dimerization reaction called an aldol reaction (or aldol condensation if an α,β–unsaturated carbonyl compound is the product). The mechanism of the aldol condensation is shown in equations *4* through *6*. As in the general nucleophilic additions to the carbonyl group, aldehydes are more reactive than ketones for both steric and electronic reasons.



(4)



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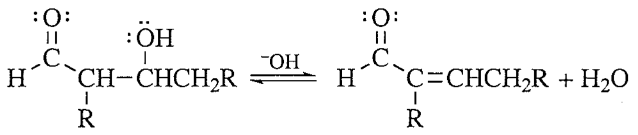


(6)

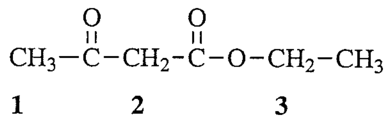
If the carbonyl-containing compound is an ester, the alcohol portion can be displaced in a nucleophilic substitution reaction by the α–carbon atom in a reaction called the Claisen condensation.

There are many different combinations of aldehydes, ketones, esters, nitriles, nitroalkanes, and β–dicarbonyl compounds that undergo aldol-type or Claisen-type reactions. When confronted with a combination not previously seen, one can usually predict the correct product this way: First, write the formula for the anion of the component with the most acidic α–hydrogen atom. Then, write the formula for the product that would form following attack on the carbonyl group of the other component. This second step can be either an addition reaction or a substitution reaction.

Although less nucleophilic than enolate ions, enols may act as nucleophiles towards very reactive electrophiles such as halogens or protonated carbonyl groups.

Study Questions

EE-1. Consider the hydrogen atoms attached to three different carbon atoms (labeled **1**, **2**, and **3**). Rank the attached hydrogen atoms in order from most acidic to least acidic.

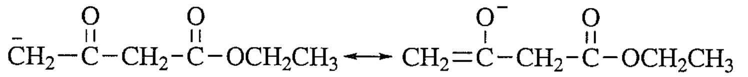

$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-O-CH_2-CH_3$

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

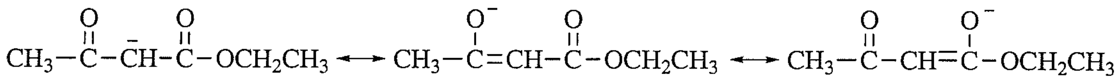
Knowledge Required: Resonance stabilization of enolate anions.

Thinking it Through: The acidities of each of the three types of hydrogen atoms depend on the relative stabilities of the conjugate bases that result from removal of the proton. The stability of each conjugate base depends on the number of the resonance structures that can be drawn for it, and on the stability of each resonance structure.

Removing a proton from carbon atom **1** yields a conjugate base with two resonance structures.

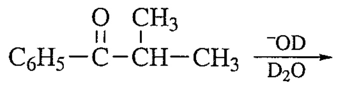

$\overset{-}{C}H_2-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OCH_2CH_3 \longleftrightarrow CH_2=\overset{\overset{O^-}{|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OCH_2CH_3$

Removing a proton from carbon atom **2** yields a conjugate base with three resonance structures, so this hydrogen atom is more acidic than the hydrogen atom attached to carbon atom **1**. Thus, choice **(A)** may be eliminated.

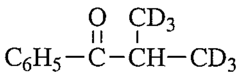

$CH_3-\overset{\overset{O}{\|}}{C}-\overset{-}{C}H-\overset{\overset{O}{\|}}{C}-OCH_2CH_3 \longleftrightarrow CH_3-\overset{\overset{O^-}{|}}{C}=CH-\overset{\overset{O}{\|}}{C}-OCH_2CH_3 \longleftrightarrow CH_3-\overset{\overset{O}{\|}}{C}-CH=\overset{\overset{O^-}{|}}{C}-OCH_2CH_3$

The conjugate base formed by removing a proton from carbon atom **3** has no resonance structures, so it must be the least acidic of the three. This eliminates choices **(B)** and **(C)**, leaving choice **(D)** as the correct answer.

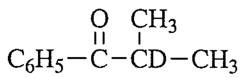
EE-2. What would be the major product of this reaction?


$C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{CH}-CH_3 \xrightarrow[D_2O]{^-OD}$

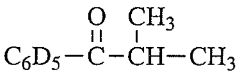
(A)


$C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{CD_3}{|}}{CH}-CD_3$

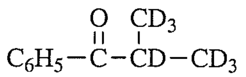
(B)


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

(C)

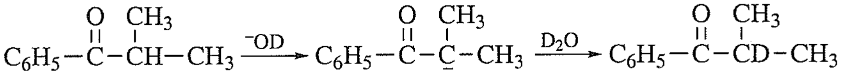

$C_6D_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{CH}-CH_3$

(D)


$C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{CD_3}{|}}{CD}-CD_3$

Knowledge Required: (1) The identity and acidity of hydrogen atoms α to a carbonyl group. (2) Ability of α–hydrogen atoms to undergo deuterium exchange with deuterated solvents.

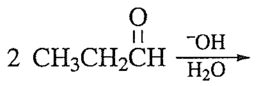
Thinking it Through: In the substrate there is only one α–hydrogen atom. This proton can be removed by the base, ^-OD, leaving the resonance-stabilized enolate ion.



$$C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{CH}-CH_3 \xrightarrow{^-OD} C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{\underline{C}}-CH_3 \xrightarrow{D_2O} C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{CD}-CH_3$$

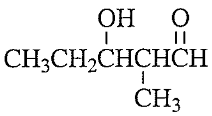
Deuteration of the negatively charged α–carbon atom can only be accomplished by deuterium in the D_2O medium. Choice **(B)** is the only possible correct answer, because it is the one choice that shows replacement of only the α–hydrogen atom with a deuterium atom.

EE-3. What would be the product of this reaction?



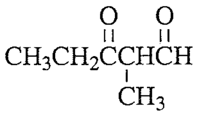
$$2\ CH_3CH_2\overset{\overset{O}{\|}}{C}H \xrightarrow[H_2O]{^-OH}$$

(A)



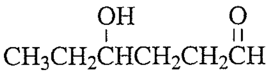
$$CH_3CH_2\overset{\overset{OH}{|}}{C}H\underset{\underset{CH_3}{|}}{C}H\overset{\overset{O}{\|}}{C}H$$

(B)



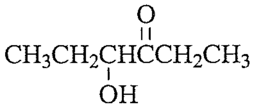
$$CH_3CH_2\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{C}H\overset{\overset{O}{\|}}{C}H$$

(C)



$$CH_3CH_2\overset{\overset{OH}{|}}{C}HCH_2CH_2\overset{\overset{O}{\|}}{C}H$$

(D)

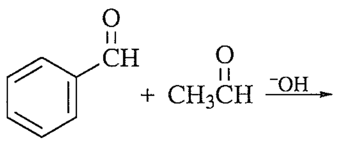


$$CH_3CH_2\underset{\underset{OH}{|}}{C}H\overset{\overset{O}{\|}}{C}CH_2CH_3$$

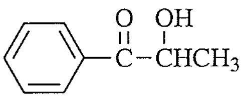
Knowledge Required: (1) How to identify the most acidic hydrogen atoms. (2) The mechanism of the aldol reaction.

Thinking it Through: First, an enolate ion is formed by abstraction an α–hydrogen atom, and then the enolate ion attacks the carbonyl carbon atom of another aldehyde to form a new carbon–carbon bond. Protonation of the new oxygen anion by water gives the aldol product. This sequence will yield the atom connectivity in choice **(A)**, which is the correct answer. Choice **(B)**, a β–keto aldehyde, is incorrect because it would require the initial enolate ion to displace the strongly basic hydride ion from the carbonyl carbon atom of another aldehyde in a substitution reaction. At first glance, Choice **(C)** may appear reasonable because it contains an aldehyde and an alcohol function; but, its formation would require the abstraction of a β–hydrogen atom instead of an α–hydrogen atom. Furthermore, an aldol condensation yields a β-hydroxy carbonyl compound. The structure shown is a γ-hydroxy carbonyl compound. Choice **(D)** would require the abstraction of the hydrogen atom attached to the carbonyl carbon atom to produce an anion, which would then react with another aldehyde molecule. Choices **(B)**, **(C)** and **(D)** are all commonly chosen wrong answers for this type of question.

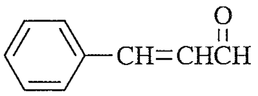
EE-4. What would be the major product of this reaction?



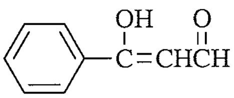
(A)



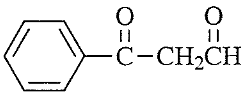
(B)



(C)

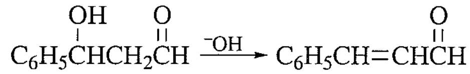


(D)



Knowledge Required: (1) The identity of the α–hydrogen atom. (2) The mechanism of the aldol reaction.

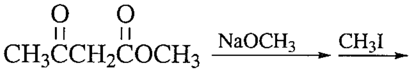
Thinking it Through: In the present case, only the acetaldehyde has an α–hydrogen atom, so it forms the enolate ion. Then the enolate ion adds to the carbonyl group of the benzaldehyde, producing the aldol product shown below. This aldol product does not match any of the choices, so something more must be involved. Recall that aldol products may undergo base-catalyzed dehydration to give α,β–unsaturated carbonyl compounds if left in contact with base, especially at elevated temperature.



$$C_6H_5\overset{OH}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}H \xrightarrow{^-OH} C_6H_5CH{=}CH\overset{O}{\overset{\|}{C}}H$$

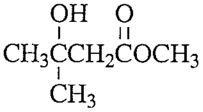
This dehydration occurs spontaneously even at normal temperatures when the new double bond extends the conjugation of another π system (a benzene ring in this instance) with the carbonyl group. The dehydrated aldol shown here matches the structure in choice **(B)**, and is the correct answer. Choice **(A)** would require the abstraction of the hydrogen atom attached to the carbonyl carbon atom of the benzaldehyde to produce an anion that would then add to the acetaldehyde carbonyl group. However, this hydrogen atom is much less acidic than an α–hydrogen atom, eliminating choice **(A)**. Choice **(D)** would require the enolate ion to displace the strongly basic hydride ion from the benzaldehyde carbonyl group in a substitution reaction, so it is eliminated. Choice **(C)** would require the loss of a molecule of hydrogen instead of a molecule of water from the initial aldol adduct, which is not logical.

EE-5. What is the product of this reaction sequence?



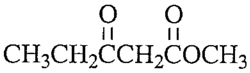
$$CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow{NaOCH_3} \xrightarrow{CH_3I}$$

(A)



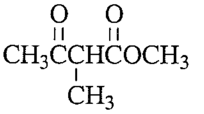
$$CH_3\underset{CH_3}{\underset{|}{\overset{OH}{\overset{|}{C}}}}CH_2\overset{O}{\overset{\|}{C}}OCH_3$$

(B)



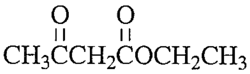
$$CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_3$$

(C)



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

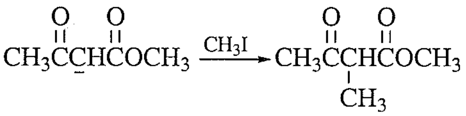
(D)



$$CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$$

Knowledge Required: (1) Relative acidities of α–hydrogen atoms. (2) Products of alkylation of enolate carbon atoms.

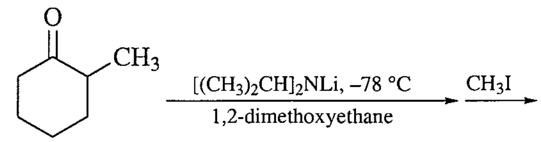
Thinking it Through: As discussed in the first study question, the hydrogen atoms on a carbon atom flanked by two carbonyl groups are the most acidic. One is removed by sodium methoxide to yield the enolate ion shown below. In this resonance structure, the carbon atom is negatively charged and can act as a nucleophile toward the CH_3I added in the second step.



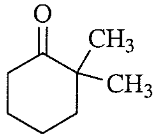
$$CH_3\overset{O}{\overset{\|}{C}}\underset{-}{C}H\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow{CH_3I} CH_3\overset{O}{\overset{\|}{C}}\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_3$$

Choice **(C)** matches the product formed by this sequence, and is the correct answer. Choices **(B)** and **(D)** are eliminated because they would require the formation of much less stable anions, followed by methylation with CH_3I. The product of Choice **(A)** is eliminated because it would require the addition of a nucleophilic methyl anion (some type of a methyl organometallic reagent).

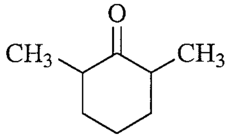
EE-6. What would be the product of this reaction sequence?



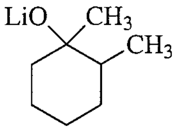
(A)



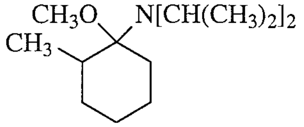
(B)



(C)

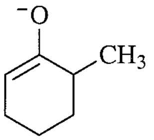


(D)



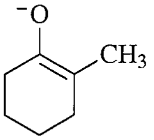
Knowledge Required: (1) Formation of kinetic *vs.* thermodynamic enolate ions. (2) Alkylation of enolate ions with alkyl halides.

Thinking it Through: The strong base lithium diisopropylamide, $[(CH_3)_2CH]_2NLi$, is used to form the enolate of the cyclohexanone reactant quantitatively. Two enolates ions are possible. The one that is formed in this reaction arises from removal of the secondary hydrogen atom, which is more accessible to the bulky diisopropylamide base. This enolate is formed more rapidly, and the reaction is not reversible. Consequently, it is referred to as the *kinetic* enolate ion. The *thermodynamic* enolate ion is more stable as a result of its more highly substituted double bond, and is formed with weaker bases (e.g. alkoxide ions) under conditions where the kinetic enolate is in equilibrium with the starting ketone. The nucleophilic α–carbon atom of the kinetic enolate ion reacts with the methyl group, displacing iodide ion, to form choice **(B)**. Choice **(A)** is eliminated because it would have been the product formed by alkylation of the thermodynamic enolate ion. Choice **(C)** is eliminated because its formation would require the organometallic reagent CH_3Li. Choice **(D)** is unlikely, and is eliminated, because the bulkiness of diisopropylamide makes it a poor nucleophile



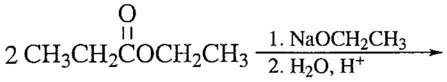
kinetic enolate

or



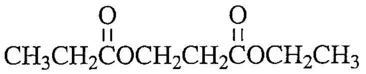
thermodynamic enolate

EE-7. What would be the major product of this reaction?



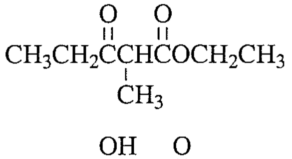
$2\,CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2.\ H_2O,\ H^+]{1.\ NaOCH_2CH_3}$

(A)



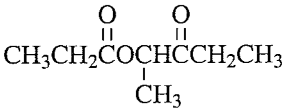
$CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$

(B)



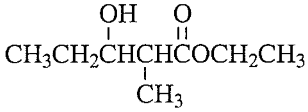
$CH_3CH_2\overset{O}{\overset{\|}{C}}\underset{CH_3}{\underset{|}{C}H}\overset{O}{\overset{\|}{C}}OCH_2CH_3$

(C)



$CH_3CH_2\overset{O}{\overset{\|}{C}}O\underset{CH_3}{\underset{|}{C}H}\overset{O}{\overset{\|}{C}}CH_2CH_3$

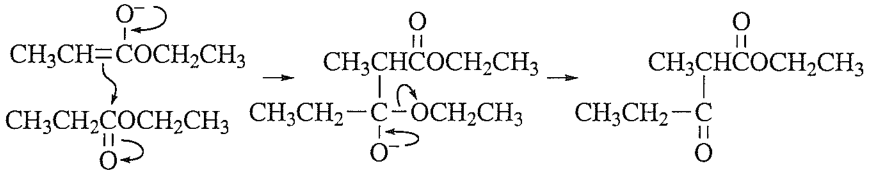
(D)



$CH_3CH_2\overset{OH}{\overset{|}{C}H}\underset{CH_3}{\underset{|}{C}H}\overset{O}{\overset{\|}{C}}OCH_2CH_3$

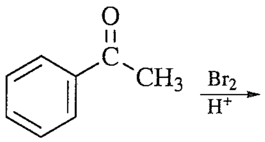
Knowledge Required: (1) Formation of enolate ions from esters that contain α–hydrogen atoms. (2) Product of reaction between ester enolates ions and the carbonyl group of other esters (Claisen condensation).

Thinking it Through: The ester reacts with $NaOCH_2CH_3$ to produce a small amount of the enolate ion. This enolate ion is nucleophilic, just as is the enolate formed from a ketone or aldehyde, and it adds to the carbonyl group of another ester molecule to give a tetrahedral intermediate. Unlike the tetrahedral intermediates formed from the addition of nucleophiles to ketones or aldehydes, this tetrahedral intermediate has a reasonable leaving group (ethoxide ion) so the carbonyl group reforms, expelling ethoxide ion, to give the Claisen condensation product.

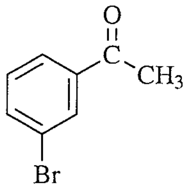


The product is a β–keto ester that immediately reacts with the expelled ethoxide ion to form a very stable enolate ion, which must be neutralized with aqueous acid to obtain the β–keto ester itself. The β–keto ester shown above is identical to that in choice **(B)**, and is the correct answer. Choices **(A)** and **(C)** are eliminated because they require the formation of non-stabilized carbanions (on the β–carbon atom for **(A)** and on the ethoxy methylene carbon atom for **(C)**), which then attack the carbonyl group of another ester molecule. Neither carbanion can be generated when sodium ethoxide is the base. Choice **(D)** is illogical because it is the reduction product of choice **(B)**, but there is no reducing agent indicated.

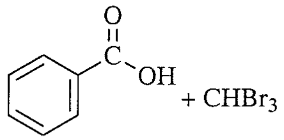
EE-8. What is the expected product of this reaction?



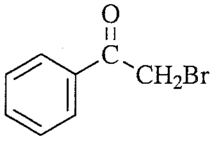
(A)



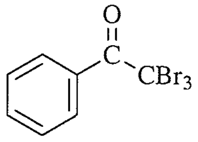
(B)



(C)



(D)

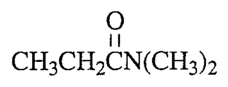


Knowledge Required: (1) Acid-catalyzed enolization of ketones. (2) Mechanism of acid-catalyzed α–halogenation of ketones.

Thinking it Through: Ketones will undergo α–bromination with bromine in the presence of either an acid or a base. Choice **(A)** would be the result of an electrophilic aromatic substitution, which requires the presence of a Lewis acid catalyst, such as $FeBr_3$, and is eliminated. Choices **(B)**, **(C)** and **(D)** all involve α–bromination. However, choices **(B)** and **(D)** are products that would form under base-catalyzed α–bromination, which proceeds through an enolate ion. The acid-catalyzed reaction proceeds through the enol tautomer, so choices **(B)** and **(D)** are eliminated. Once the ketone has been mono–α–brominated, it resists further tautomerization to the enol, and the monobrominated ketone can be prepared in high yield. Under basic conditions, each successive bromination increases the acidity of the remaining α–hydrogen atoms, and the rate at which the ketone forms the enolate ion. Consequently, it is difficult to stop the reaction at the monobromination stage. Thus, choice **(C)** is the correct answer.

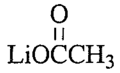
Practice Questions

1. Which base should be used to quantitatively convert this *N,N*-dimethylamide into its enolate ion?



$CH_3CH_2\overset{O}{\overset{\|}{C}}N(CH_3)_2$

(A)



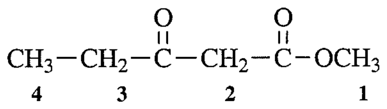
$LiO\overset{O}{\overset{\|}{C}}CH_3$

(B) $LiOCH_2CH_3$

(C) $LiN[CH(CH_3)_2]_2$

(D) $LiOH$

2. Which sets of hydrogen atoms in this compound will undergo deuterium exchange with CH_3OD in the presence of CH_3ONa?



$\underset{4}{CH_3}-\underset{3}{CH_2}-\overset{O}{\overset{\|}{C}}-\underset{2}{CH_2}-\overset{O}{\overset{\|}{C}}-\underset{1}{OCH_3}$

(A) 2 and 3 only

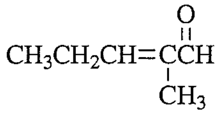
(B) 1, 2, and 3 only

(C) 2, 3, and 4 only

(D) 1 and 4 only

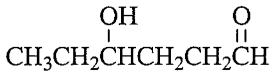
3. Which compound is the product of an aldol condensation?

(A)



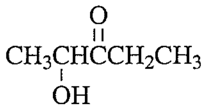
$CH_3CH_2CH{=}\underset{CH_3}{\underset{|}{\overset{O}{\overset{\|}{C}}}}H$

(B)



$CH_3CH_2\overset{OH}{\overset{|}{C}}HCH_2CH_2\overset{O}{\overset{\|}{C}}H$

(C)

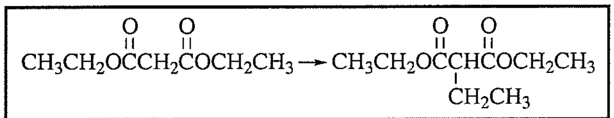


$CH_3\underset{OH}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}CH_2CH_3$

(D)

$CH_3\overset{O}{\overset{\|}{C}}CH_2CH=CH_2$

4. Which set of the reagents would accomplish this conversion?



$CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \longrightarrow CH_3CH_2O\overset{O}{\overset{\|}{C}}\underset{CH_2CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_2CH_3$

(A) NaH followed by CH_3CH_2OH

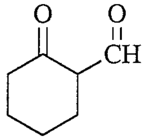
(B) CH_3CH_2ONa followed by CH_3CH_2Br

(C) NaH followed by $CH_2{=}CH_2$

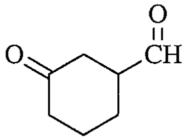
(D) CH_3CH_2OH with H^+ as a catalyst

5. Which compound forms the greatest equilibrium concentration of the enol tautomer?

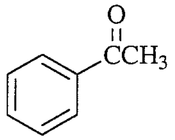
(A)



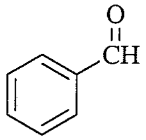
(B)



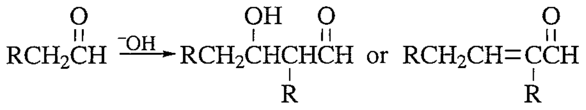
(C)



(D)



6. An aldol reaction can produce an addition product or the dehydrated addition product (condensation product). What factor favors the formation of the dehydration product?



$RCH_2\overset{O}{\overset{\|}{C}}H \xrightarrow{^-OH} RCH_2\overset{OH}{\overset{|}{C}}H\underset{R}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}H$ or $RCH_2CH{=}\underset{R}{\underset{|}{C}}\overset{O}{\overset{\|}{C}}H$

addition product

dehydration product

(A) excess aldehyde

(B) excess base

(C) no α–hydrogen atoms

(D) stabilization by conjugation

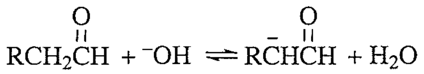
7. Which is ***not*** true of the aldol reaction?

(A) It accomplishes the formation of a new carbon–carbon bond.

(B) The key step in the mechanism is attack of the α–carbon atom of an enolate ion on a carbonyl carbon atom.

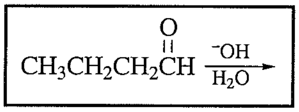
(C) Dehydration of the aldol product is often observed (an aldol condensation)

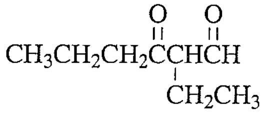
(D) The enolate is favored at equilibrium.



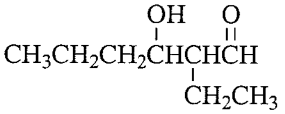
$RCH_2\overset{O}{\overset{\|}{C}}H + {}^-OH \rightleftharpoons R\overset{-}{C}H\overset{O}{\overset{\|}{C}}H + H_2O$

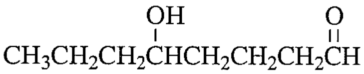
8. What would be the major product of this reaction?


$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}H \xrightarrow[H_2O]{^-OH}$

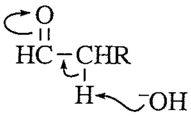
(A)

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

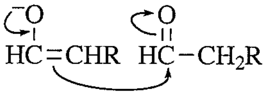
(B) $CH_3CH_2CH_2CH_2OH + CH_3CH_2CH_2COO_2^-$

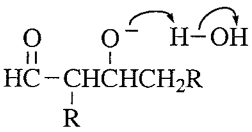
(C)

$CH_3CH_2CH_2\overset{\overset{OH}{|}}{C}H\underset{\underset{CH_2CH_3}{|}}{C}H\overset{\overset{O}{\|}}{C}H$

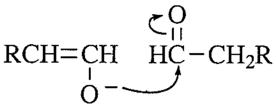
(D)

$CH_3CH_2CH_2\overset{\overset{OH}{|}}{C}HCH_2CH_2CH_2\overset{\overset{O}{\|}}{C}H$

9. Which of these is ***not*** a step in the mechanism of the aldol reaction?

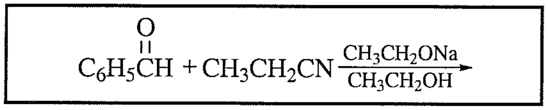
(A)


(B)


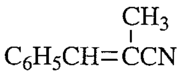
(C)


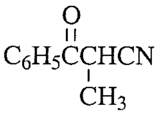
(D)


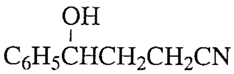
10. What would be the product of this reaction?


$C_6H_5\overset{\overset{O}{\|}}{C}H + CH_3CH_2CN \xrightarrow[CH_3CH_2OH]{CH_3CH_2ONa}$

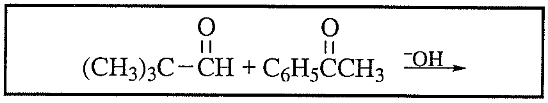
(A) $C_6H_5CH{=}CHCH_2CN$

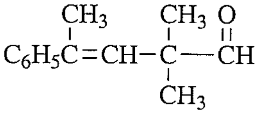
(B)

$C_6H_5CH{=}\overset{\overset{CH_3}{|}}{C}CN$

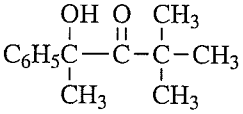
(C)

$C_6H_5\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{C}HCN$

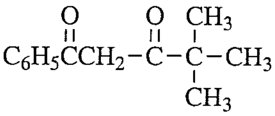
(D)

$C_6H_5\overset{\overset{OH}{|}}{C}HCH_2CH_2CN$

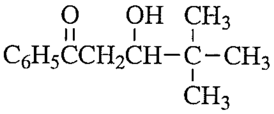
11. What would be the major organic product of this base-catalyzed reaction?


$(CH_3)_3C-\overset{\overset{O}{\|}}{C}H + C_6H_5\overset{\overset{O}{\|}}{C}CH_3 \xrightarrow{^-OH}$

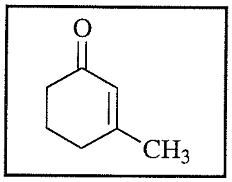
(A)

$C_6H_5\overset{\overset{CH_3}{|}}{C}{=}CH-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-\overset{\overset{O}{\|}}{C}H$

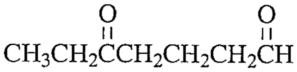
(B)

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

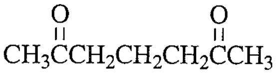
(C)

$C_6H_5\overset{\overset{O}{\|}}{C}CH_2-\overset{\overset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-CH_3$

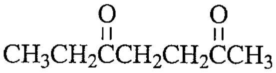
(D)

$C_6H_5\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{OH}{|}}{C}H-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-CH_3$

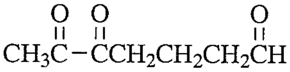
12. Which of these reactants can be used to make the compound shown by an intramolecular aldol reaction?



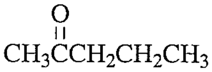
(A)

$CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}H$

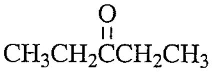
(B)

$CH_3\overset{\overset{O}{\|}}{C}CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}CH_3$

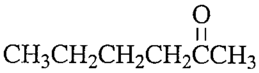
(C)

$CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2\overset{\overset{O}{\|}}{C}CH_3$

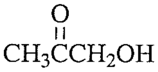
(D)

$CH_3\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}H$

13. Which compound would ***not*** react in the iodoform test to produce a yellow precipitate?

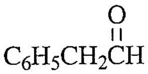
(A)

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

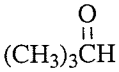
(B)

$CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_3$

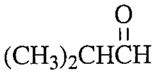
(C)

$CH_3CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}CH_3$

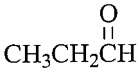
(D)

$CH_3\overset{\overset{O}{\|}}{C}CH_2OH$

14. Which of these compounds *cannot* undergo an aldol reaction in the presence of dilute base?

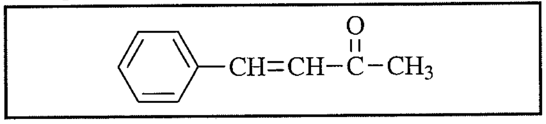
(A) 
$C_6H_5CH_2\overset{\overset{O}{\|}}{C}H$

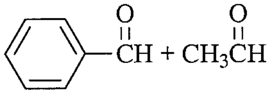
(B) 
$(CH_3)_3\overset{\overset{O}{\|}}{C}H$

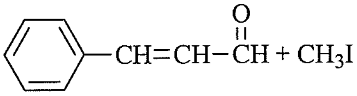
(C) 
$(CH_3)_2CH\overset{\overset{O}{\|}}{C}H$

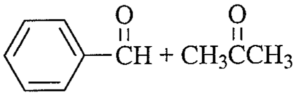
(D) 
$CH_3CH_2\overset{\overset{O}{\|}}{C}H$

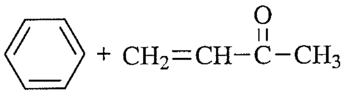
15. Which set of reactants, in the presence of a basic catalyst, could be used to prepare this compound?



(A) 

(B) 

(C) 

(D) 

16. The first two steps in the base-catalyzed condensation of acetaldehyde would be described as

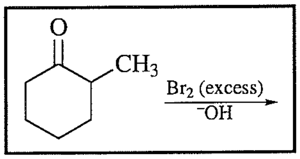
(A) attack of $^-$OH on the carbonyl carbon atom, then loss of water.

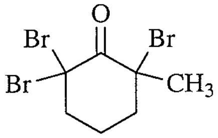
(B) attack of $^-$OH on the carbonyl carbon atom, then the resultant anion attacks the carbonyl carbon atom on a second molecule of acetaldehyde.

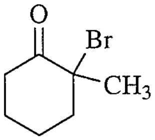
(C) $^-$OH abstracts an α–hydrogen atom, then the resultant anion attacks the carbonyl carbon atom on a second molecule of acetaldehyde.

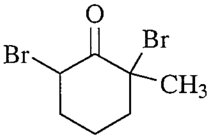
(D) $^-$OH abstracts the hydrogen atom from the carbonyl carbon atom, then the resultant anion attacks the carbonyl carbon atom on a second molecule of acetaldehyde.

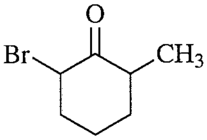
17. What is the product of this reaction?



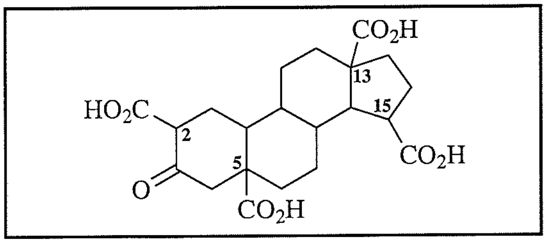
(A) 

(B) 

(C) 

(D) 

18. If this steroid tetracarboxylic acid is heated, which carboxyl group will be readily lost as carbon dioxide?

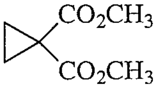


(A) CO_2H at C–15 **(B)** CO_2H at C–13

(C) CO_2H at C–5 **(D)** CO_2H at C–2

19. What product is expected from this reaction sequence?

$$CH_2(CO_2CH_3)_2 \xrightarrow{CH_3ONa} \xrightarrow[\text{1 molar equiv.}]{BrCH_2CH_2Br} \xrightarrow{CH_3ONa}$$

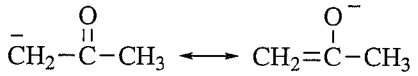
(A) 

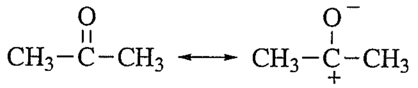
(B) $(CH_3O_2C)_2CHCH_2CH_2CH(CO_2CH_3)_2$

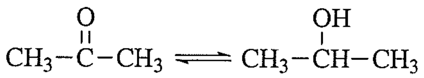
(C) $CH_3OCH_2CH_2CH(CO_2CH_3)_2$

(D) $CH_2{=}CHCH(CO_2CH_3)_2$

20. Which represents a keto–enol tautomerization?

(A)

$\overset{-}{C}H_2-\overset{O}{\overset{\|}{C}}-CH_3 \longleftrightarrow CH_2=\overset{O^-}{\overset{|}{C}}-CH_3$

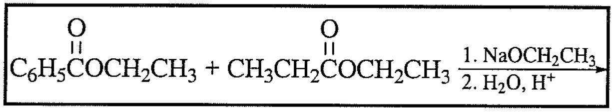
(B)

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

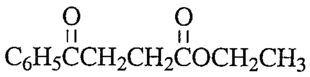
(C)

$CH_3-\overset{O}{\overset{\|}{C}}-CH_3 \rightleftharpoons CH_3-\overset{OH}{\overset{|}{C}}H-CH_3$

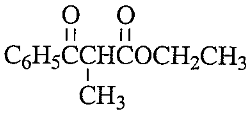
(D)

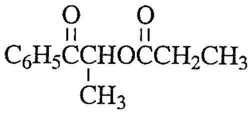
$CH_3-\overset{O}{\overset{\|}{C}}-CH_3 \rightleftharpoons CH_2=\overset{OH}{\overset{|}{C}}-CH_3$

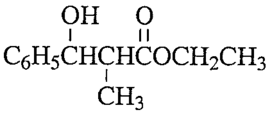
21. What would be the major product of this reaction sequence?


$C_6H_5\overset{O}{\overset{\|}{C}}OCH_2CH_3 + CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2.\ H_2O,\ H^+]{1.\ NaOCH_2CH_3}$

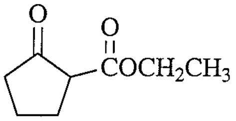
(A)

$C_6H_5\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$

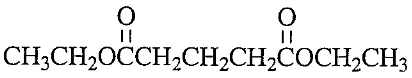
(B)

$C_6H_5\overset{O}{\overset{\|}{C}}\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_2CH_3$

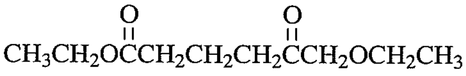
(C)

$C_6H_5\overset{O}{\overset{\|}{C}}\underset{CH_3}{\underset{|}{C}}HO\overset{O}{\overset{\|}{C}}CH_2CH_3$

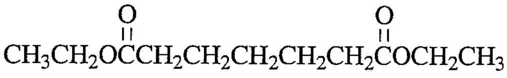
(D)

$C_6H_5\overset{OH}{\overset{|}{C}}H\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_2CH_3$

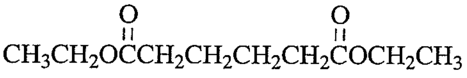
22. What is the starting material that will yield this compound upon treatment with CH_3CH_2ONa in CH_3CH_2OH?



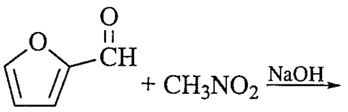
(A)

$CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$

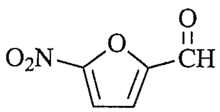
(B)

$CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}CH_2OCH_2CH_3$

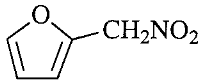
(C)

$CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$

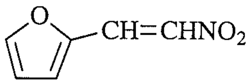
(D)

$CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$

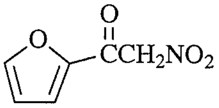
23. What is the product of this reaction?



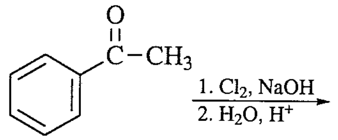
(A)


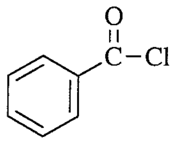
(B)


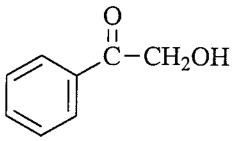
(C)


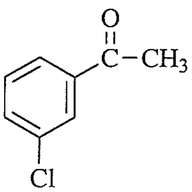
(D)


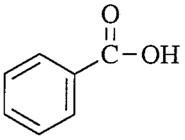
24. What is the product formed from this reaction?



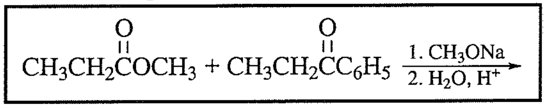
(A)


(B)


(C)


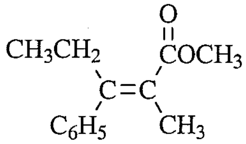
(D)


25. What is the product of this reaction?

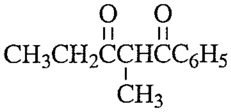


$$\mathrm{CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_3 + CH_3CH_2\overset{O}{\overset{\|}{C}}C_6H_5 \xrightarrow[2.\ H_2O,\ H^+]{1.\ CH_3ONa}}$$

(A)

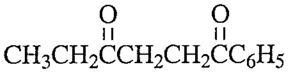


(B)



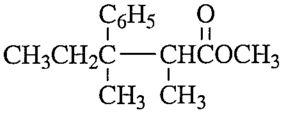
$\mathrm{CH_3CH_2\overset{O}{\overset{\|}{C}}\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}C_6H_5}$

(C)



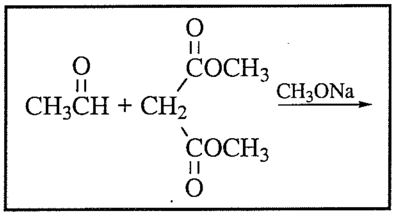
$\mathrm{CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}C_6H_5}$

(D)

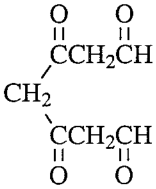


$\mathrm{CH_3CH_2\overset{C_6H_5}{\overset{|}{\underset{CH_3}{\underset{|}{C}}}}—\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_3}$

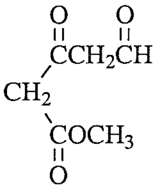
26. What is the expected product of this reaction?



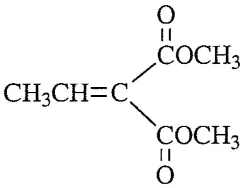
(A)



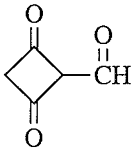
(B)



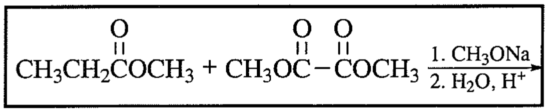
(C)



(D)

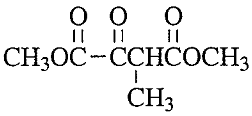


27. What compound will be produced by this reaction?



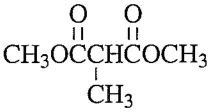
$$\mathrm{CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_3 + CH_3O\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[2.\ H_2O,\ H^+]{1.\ CH_3ONa}}$$

(A)



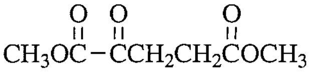
$\mathrm{CH_3O\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_3}$

(B)



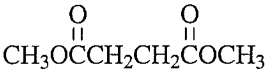
$\mathrm{CH_3O\overset{O}{\overset{\|}{C}}\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_3}$

(C)



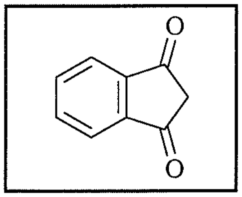
$\mathrm{CH_3O\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3}$

(D)

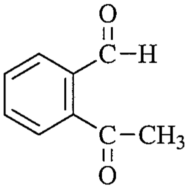


$\mathrm{CH_3O\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3}$

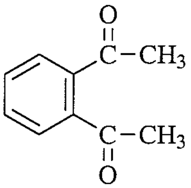
28. Which compound when treated with $NaOCH_3$ followed by neutralization with aqueous acid will produce this β–diketone?



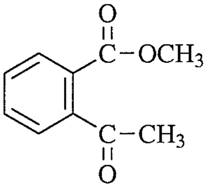
(A)



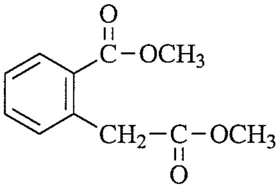
(B)



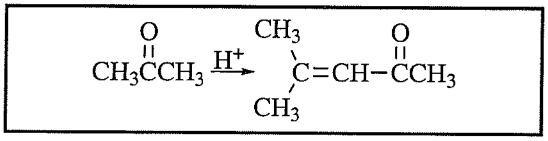
(C)



(D)

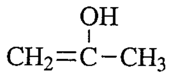


29. Aldol condensations, even with ketones, can occur under acid conditions where the active nucleophile is the enol, not the enolate ion. For the aldol condensation shown for acetone, what would be the structure of the electrophilic species that the enol attacks?



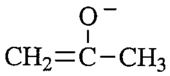
$$CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow{H^+} \underset{CH_3}{\overset{CH_3}{C}}=CH-\overset{O}{\overset{\|}{C}}CH_3$$

(A)



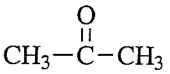
$CH_2=\overset{OH}{\overset{|}{C}}-CH_3$

(B)



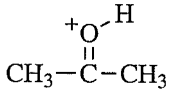
$CH_2=\overset{O^-}{\overset{|}{C}}-CH_3$

(C)



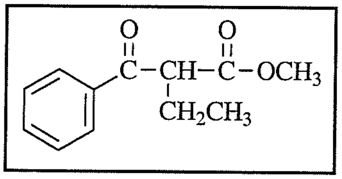
$CH_3-\overset{O}{\overset{\|}{C}}-CH_3$

(D)

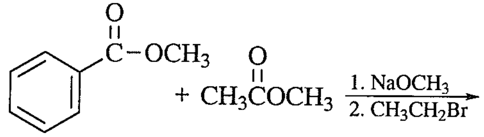


$CH_3-\overset{{}^{+}O-H}{\overset{\|}{C}}-CH_3$

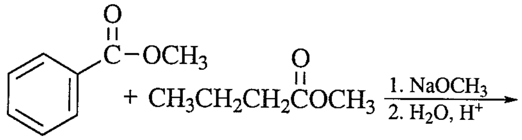
30. Which of these reactions could be used to prepare this β-keto ester?



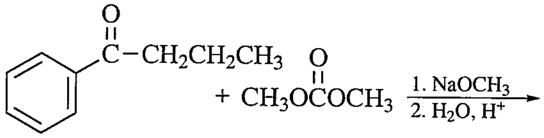
I



II



III



(A) I, II, and III **(B)** I and II only

(C) I and III only **(D)** II and III only

Answers to Study Questions

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

Answers to Practice Questions

1. C
2. A
3. A
4. B
5. A
6. D
7. D
8. C
9. D
10. B
11. D
12. B
13. B
14. B
15. C
16. C
17. A
18. D
19. A
20. D
21. B
22. D
23. C
24. D
25. B
26. C
27. A
28. C
29. D
30. A