

Chapter 22

Alpha Carbon Chemistry: Enols and Enolates

Review of Concepts

Fill in the blanks below. To verify that your answers are correct, look in your textbook at the end of Chapter 22. Each of the sentences below appears verbatim in the section entitled *Review of Concepts and Vocabulary*.

- In the presence of catalytic acid or base, a ketone will exist in equilibrium with an _____. In general, the equilibrium position will significantly favor the _____.
- When treated with a strong base, the α position of a ketone is deprotonated to give an _____.
- _____ or _____ will irreversibly and completely convert an aldehyde or ketone into an enolate.
- In the **haloform reaction**, a _____ ketone is converted into a carboxylic acid upon treatment with excess base and excess halogen followed by acid workup.
- When an aldehyde is treated with sodium hydroxide, an **aldol addition reaction** occurs, and the product is a _____.
- For most simple aldehydes, the position of equilibrium favors the aldol product. For most ketones, the reverse process, called a _____-**aldol reaction** is favored.
- When an aldehyde is heated in aqueous sodium hydroxide, an **aldol** _____ **reaction** occurs, and the product is an _____. Elimination of water occurs via an _____ **mechanism**.
- **Crossed aldol**, or **mixed aldol reactions** are aldol reactions that occur between different partners, and are only efficient if one partner lacks _____ or if a **directed aldol addition** is performed.
- Intramolecular aldol reactions show a preference for formation of _____ and _____-membered rings.
- When an ester is treated with an alkoxide base, a **Claisen condensation reaction** occurs, and the product is a _____.
- The α position of a ketone can be alkylated by forming an enolate and treating it with an _____.
- For unsymmetrical ketones, reactions with _____ at low temperature favor formation of the kinetic enolate, while reactions with _____ at room temperature favor the thermodynamic enolate.
- When LDA is used with an unsymmetrical ketone, alkylation occurs at the _____ position.
- The _____ **synthesis** enables the conversion of an alkyl halide into a carboxylic acid with the introduction of two new carbon atoms.
- The _____ **synthesis** enables the conversion of an alkyl halide into a methyl ketone with the introduction of two new carbon atoms.
- Aldehydes and ketones that possess _____-unsaturation are susceptible to nucleophilic attack at the β position. This reaction is called a _____ **addition**, **1,4-addition**, or a **Michael reaction**.

Review of Skills

Fill in the blanks and empty boxes below. To verify that your answers are correct, look in your textbook at the end of Chapter 22. The answers appear in the section entitled *SkillBuilder Review*.

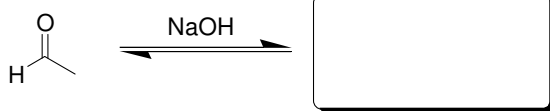
22.1 Drawing Enolates

DRAW THE RESONANCE STRUCTURES OF THE ENOLATE THAT IS FORMED WHEN THE KETONE BELOW IS TREATED WITH A STRONG BASE:



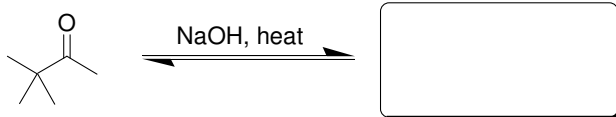
22.2 Predicting the Products of an Aldol Addition Reaction

PREDICT THE PRODUCT OF THE ALDOL ADDITION REACTION THAT OCCURS WHEN THE FOLLOWING ALDEHYDE IS TREATED WITH SODIUM HYDROXIDE:



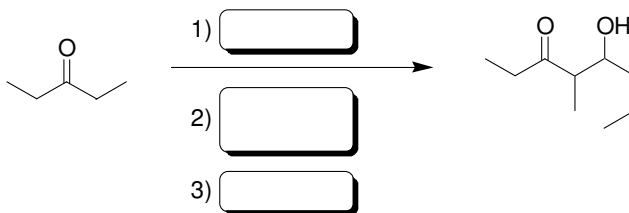
22.3 Drawing the Product of an Aldol Condensation

DRAW THE PRODUCT OF THE ALDOL CONDENSATION REACTION THAT OCCURS WHEN THE FOLLOWING COMPOUND IS HEATED WITH SODIUM HYDROXIDE:



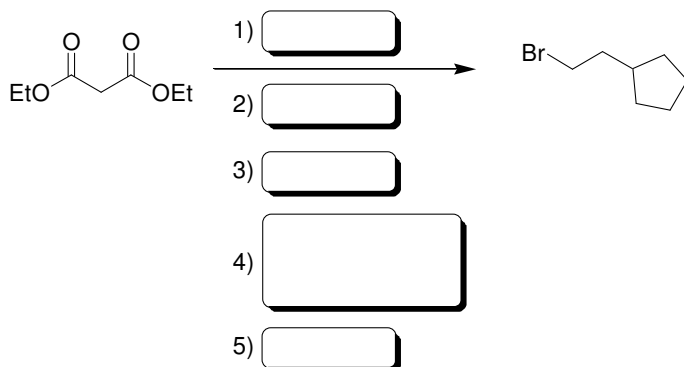
22.4 Identifying the Reagents Necessary for a Crossed Aldol Reaction

IDENTIFY REAGENTS THAT WILL ACHIEVE THE FOLLOWING TRANSFORMATION:



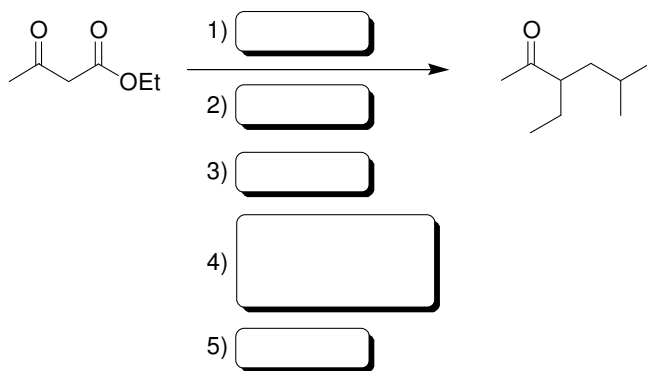
22.5 Using the Malonic Ester Synthesis

IDENTIFY REAGENTS THAT WILL ACHIEVE THE FOLLOWING TRANSFORMATION:



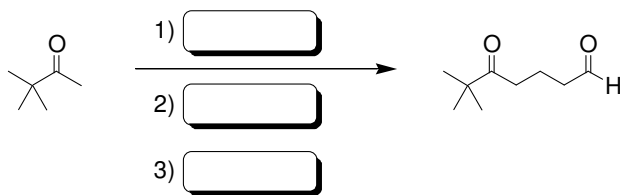
22.6 Using the Acetoacetic Ester Synthesis

IDENTIFY REAGENTS THAT WILL ACHIEVE THE FOLLOWING TRANSFORMATION:



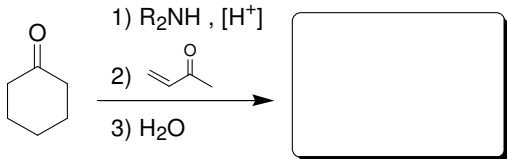
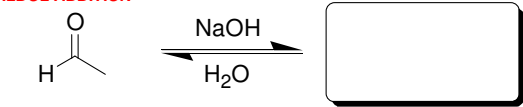
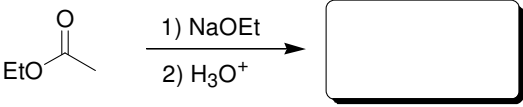
22.7 Determining When to Use a Stork Enamine Synthesis

IDENTIFY REAGENTS THAT WILL ACHIEVE THE FOLLOWING TRANSFORMATION:



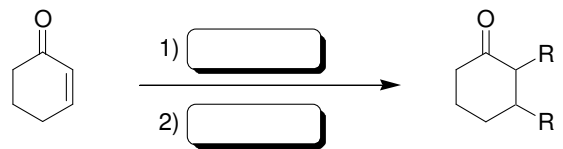
22.8 Determining which Addition or Condensation Reaction to Use

PREDICT THE MAJOR PRODUCT OF EACH REACTION BELOW:

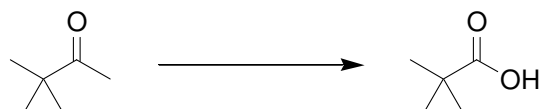
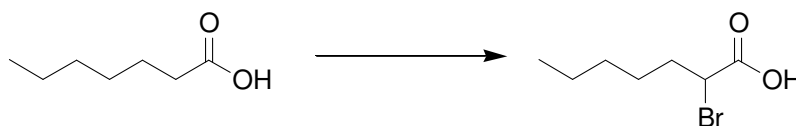
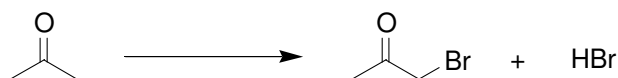
1,5-DIFUNCTIONALIZED COMPOUNDS	1,3-DIFUNCTIONALIZED COMPOUNDS
<p>STORK ENAMINE SYNTHESIS</p> 	<p>ALDOL ADDITION</p>  <p>CLAISEN CONDENSATION</p> 

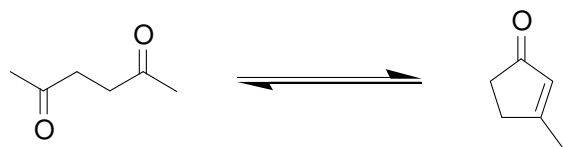
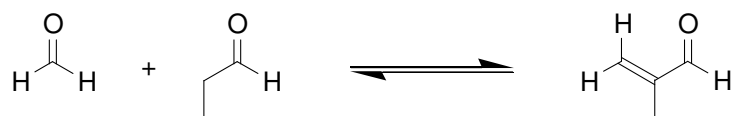
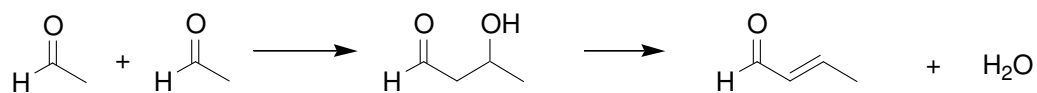
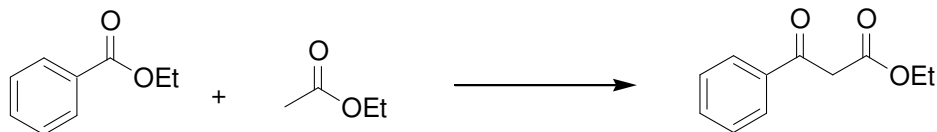
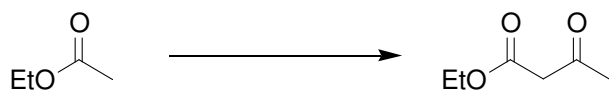
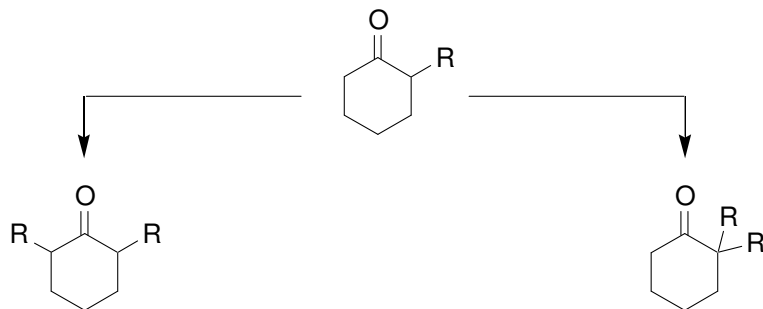
22.9 Alkylating the Alpha and Beta Positions

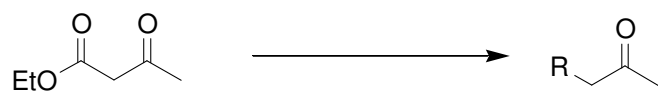
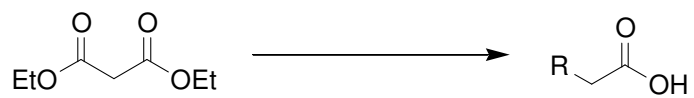
IDENTIFY REAGENTS THAT WILL ACHIEVE THE FOLLOWING TRANSFORMATION:


Review of Reactions

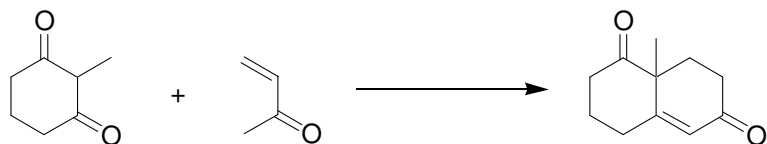
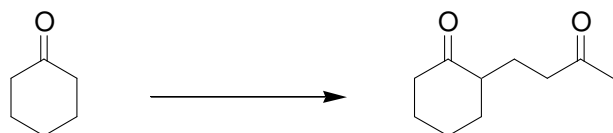
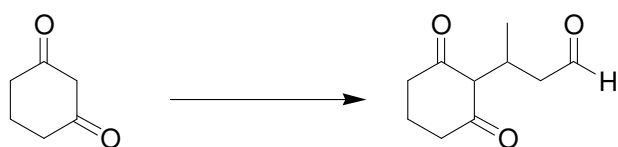
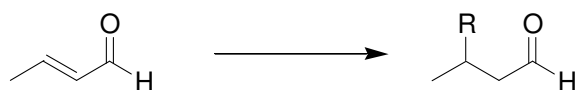
Identify the reagents necessary to achieve each of the following transformations. To verify that your answers are correct, look in your textbook at the end of Chapter 22. The answers appear in the section entitled *Review of Reactions*.

Alpha Halogenation

Aldol Reactions**Claisen Condensation****Alkylation**

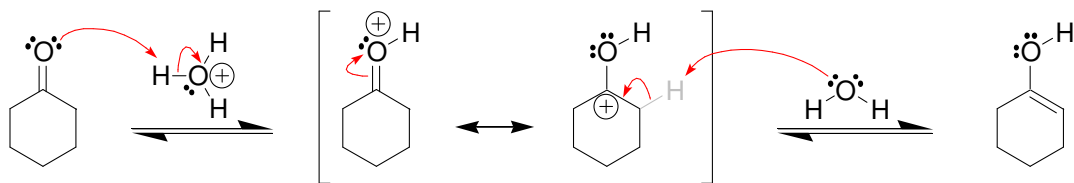


Michael Additions

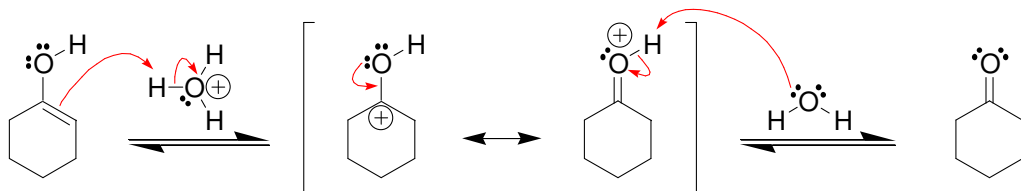


Solutions

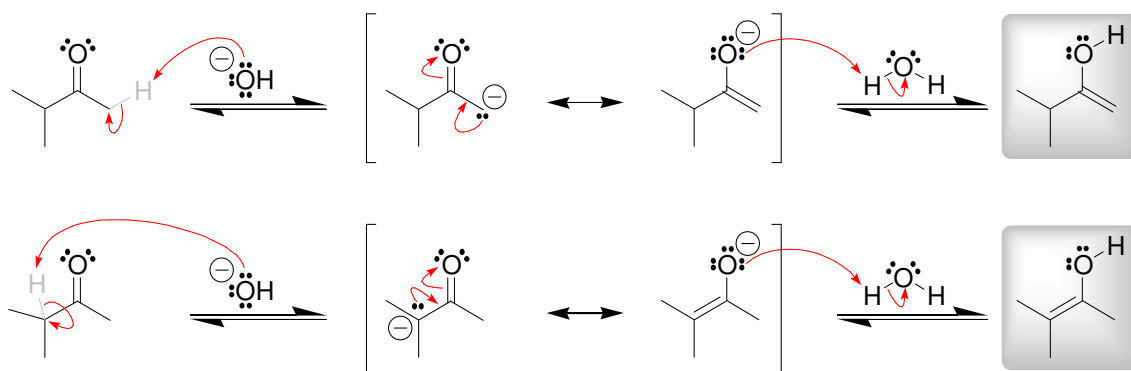
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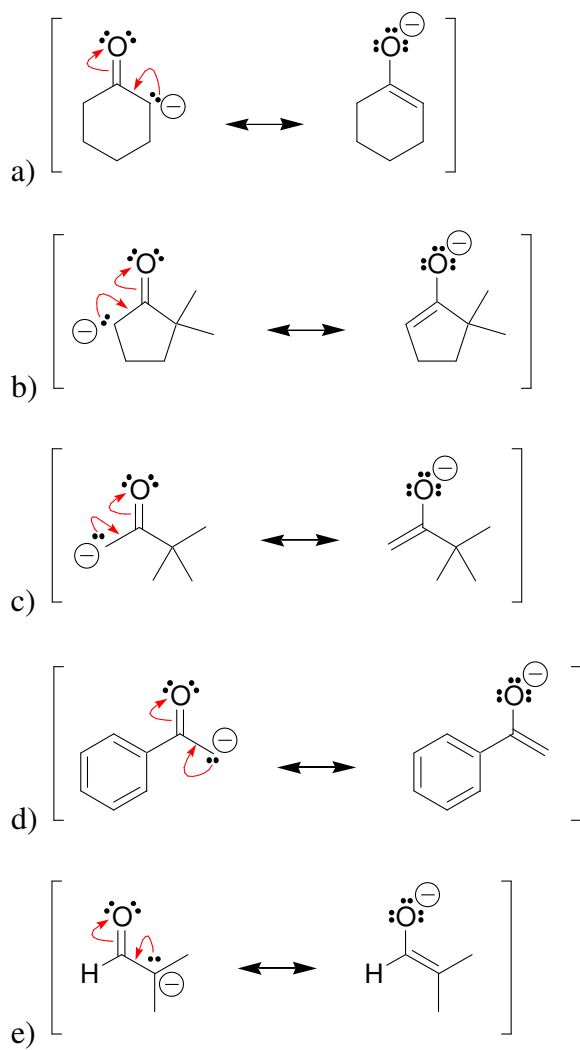
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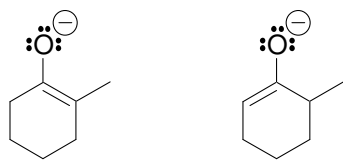
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22.4.

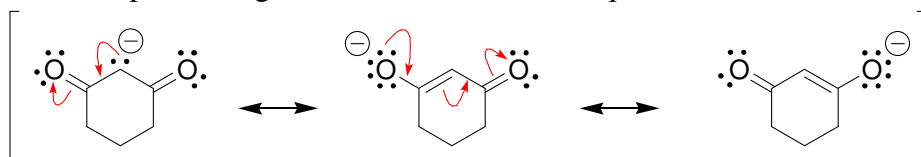


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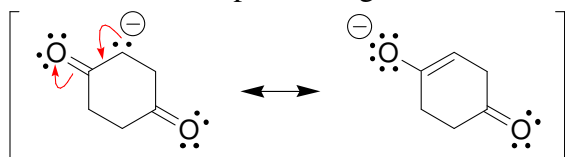


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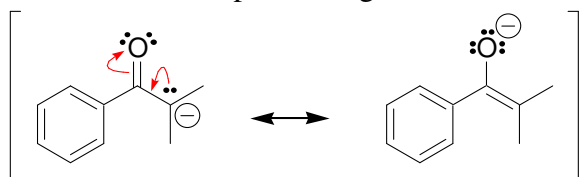
a) This anion is a doubly stabilized enolate ion, so there will not be a substantial amount of ketone present together with the enolate at equilibrium:



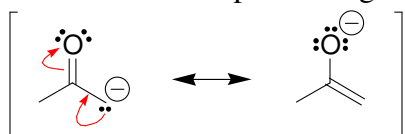
b) This anion is a regular enolate ion (not doubly stabilized), so there will be a substantial amount of ketone present together with the enolate at equilibrium:



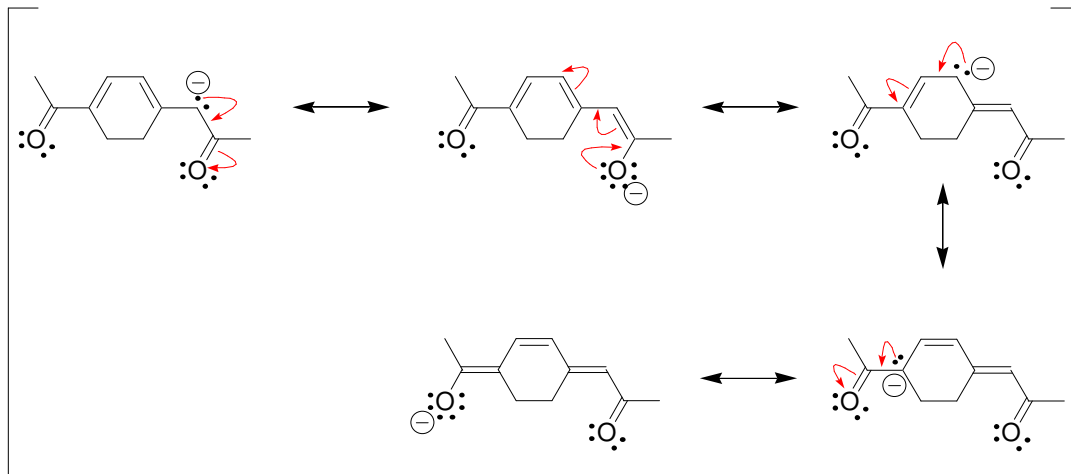
c) This anion is a regular enolate ion (not doubly stabilized), so there will be a substantial amount of ketone present together with the enolate at equilibrium:



d) This anion is a regular enolate ion (not doubly stabilized), so there will be a substantial amount of ketone present together with the enolate at equilibrium:



22.7. This anion is highly stabilized by resonance. The negative charge is spread over two oxygen atoms (just like a doubly stabilized enolate) and three carbon atoms:



22.8.

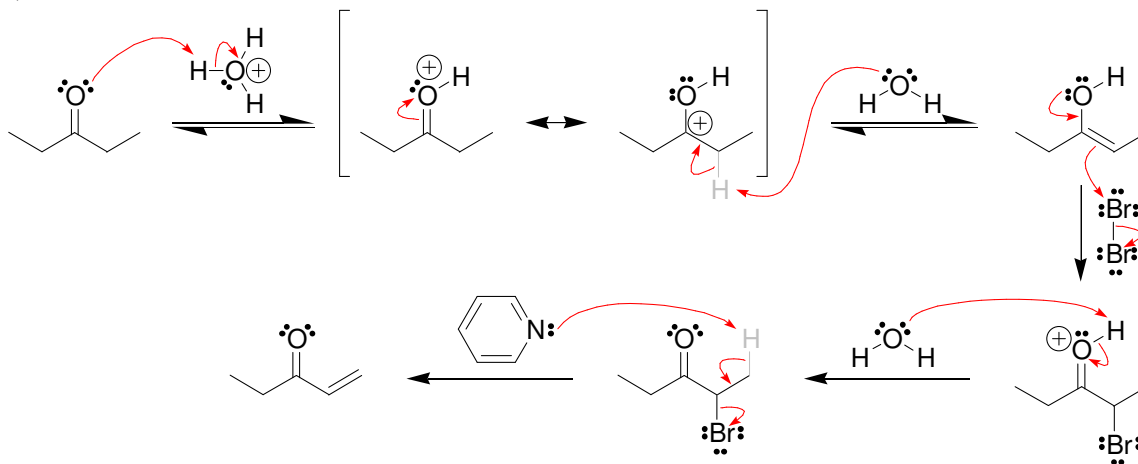
a) 2,4-dimethyl-3,5-heptanedione is more acidic because its conjugate base is a doubly stabilized enolate. The other compound (4,4-dimethyl-3,5-heptanedione) cannot form a doubly stabilized enolate because there are no protons connected to the carbon atom that is in between both carbonyl groups.

b) 1,3-cyclopentanedione is more acidic because its conjugate base is a doubly stabilized enolate. The other compound (1,2-cyclopentanedione) cannot form a doubly stabilized enolate because the carbonyl groups are adjacent to each other.

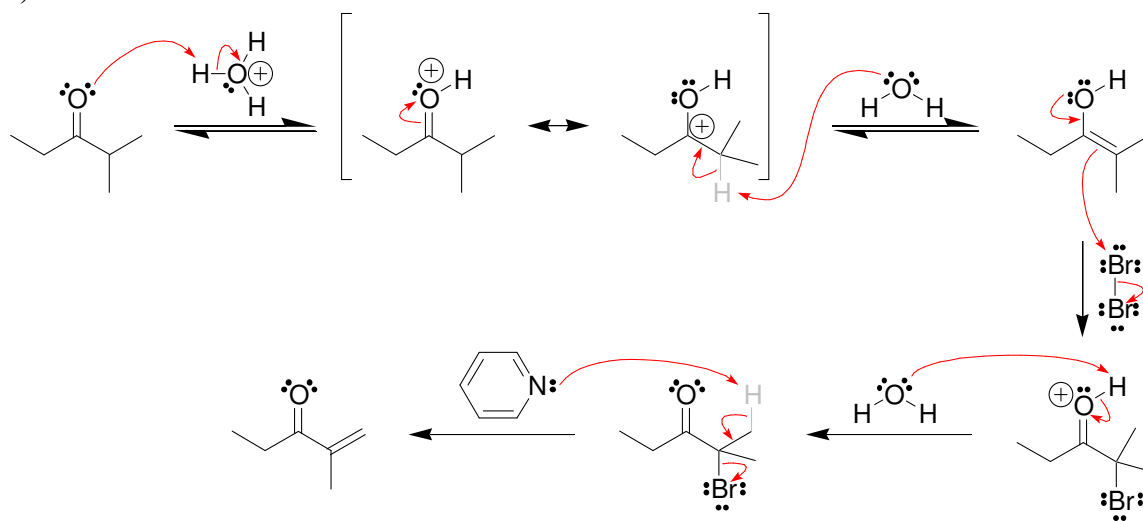
c) Acetophenone is more acidic than benzaldehyde because the former has alpha protons and the latter does not.

22.9.

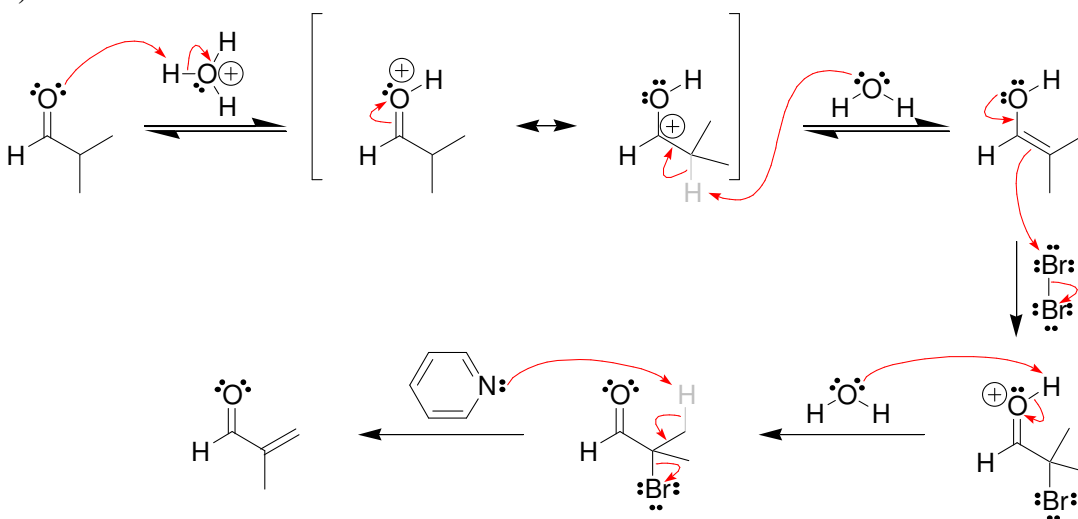
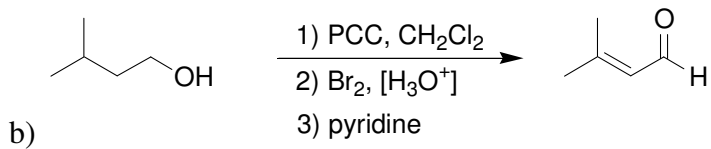
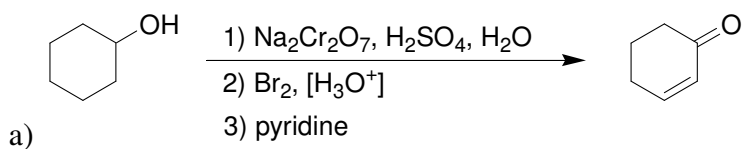
a)



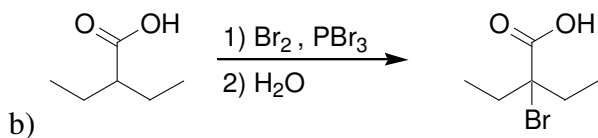
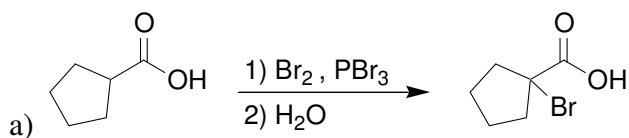
b)



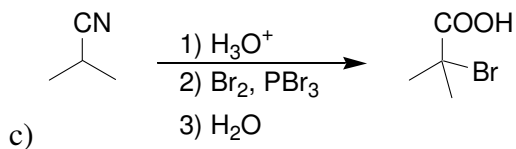
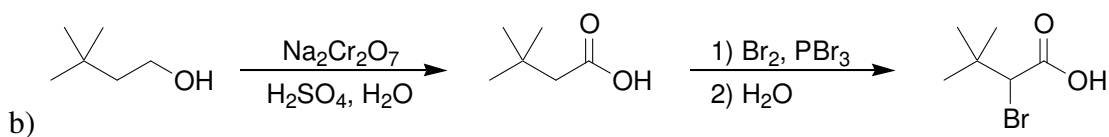
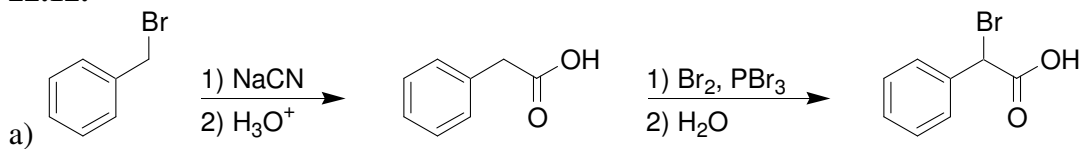
c)

**22.10.**

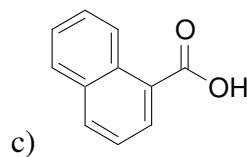
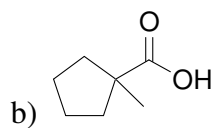
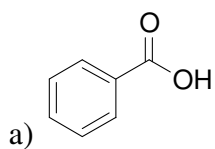
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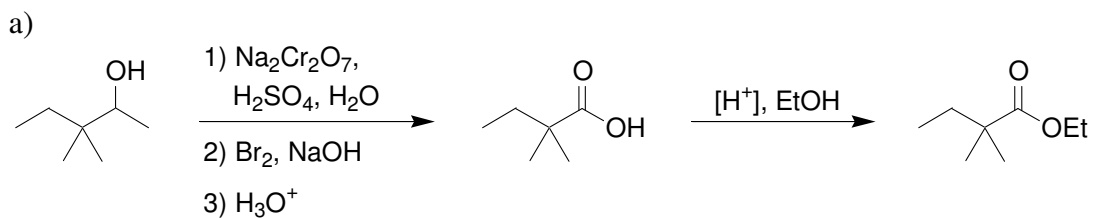
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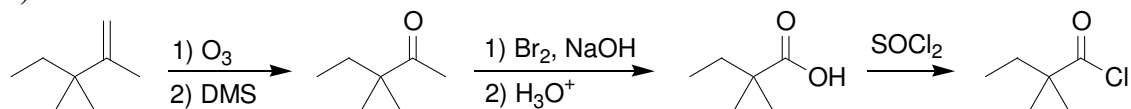
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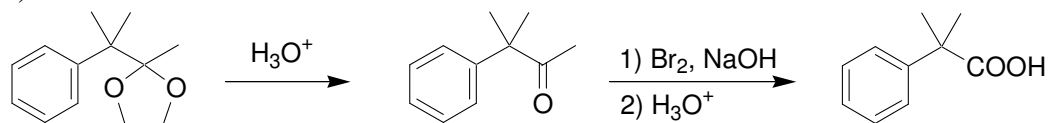
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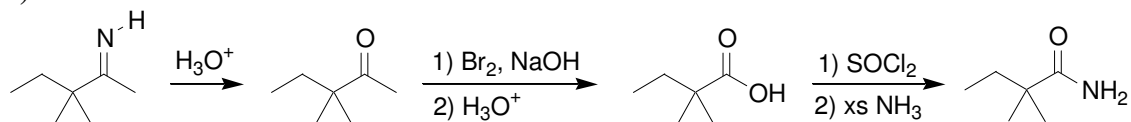
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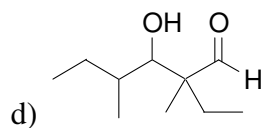
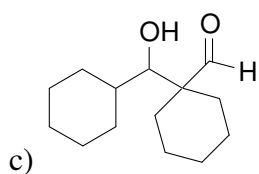
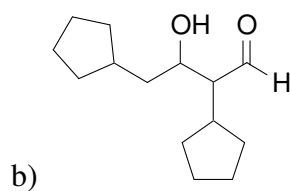
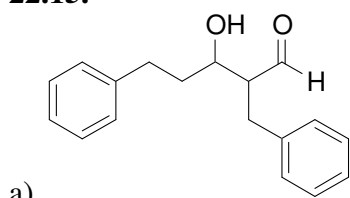
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d)

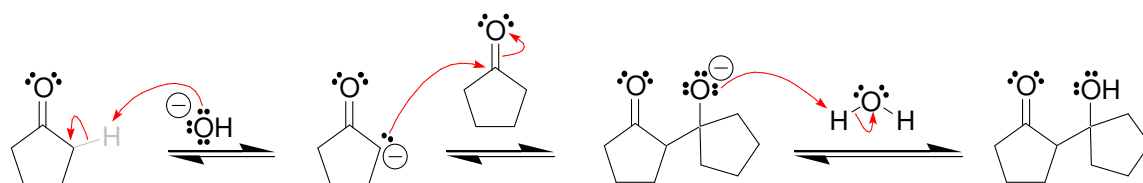


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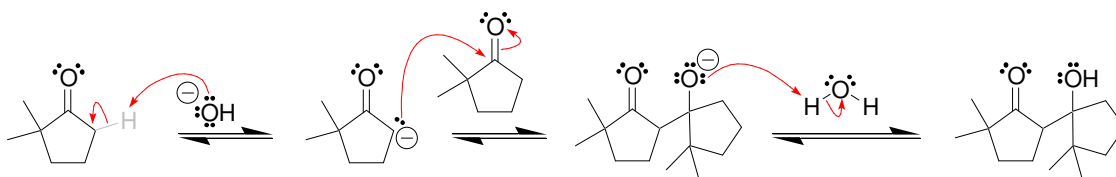


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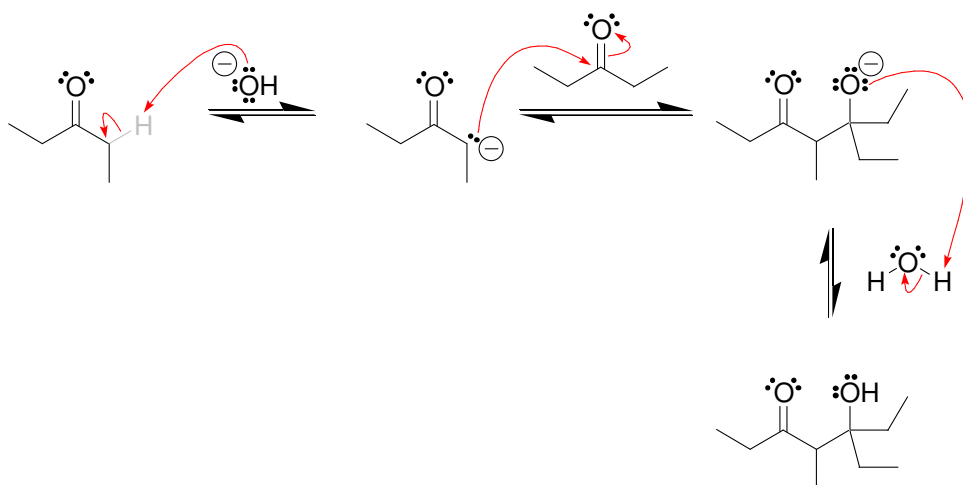
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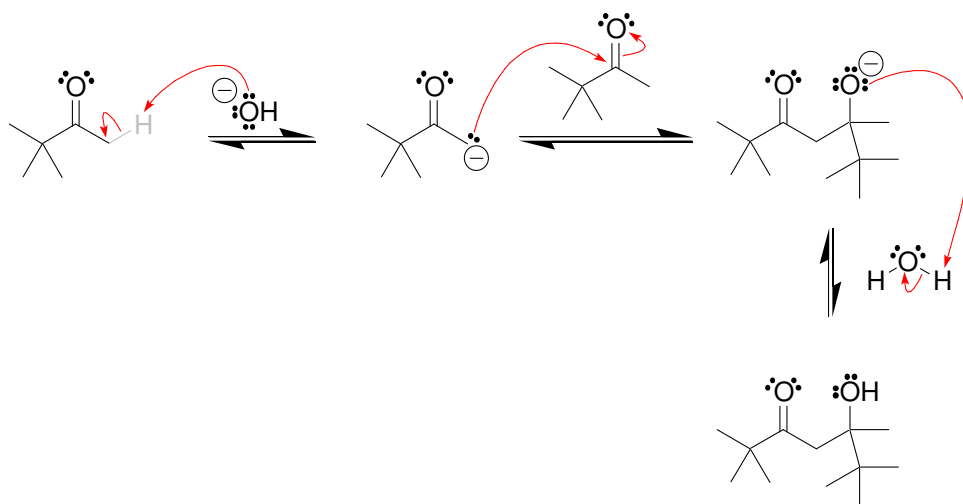
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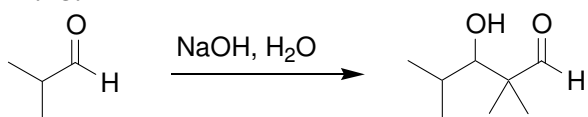


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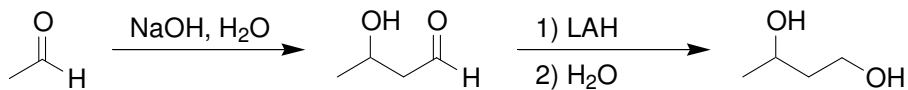


22.17. The first step of an aldol addition reaction is deprotonation at the alpha position, but this compound has no alpha protons.

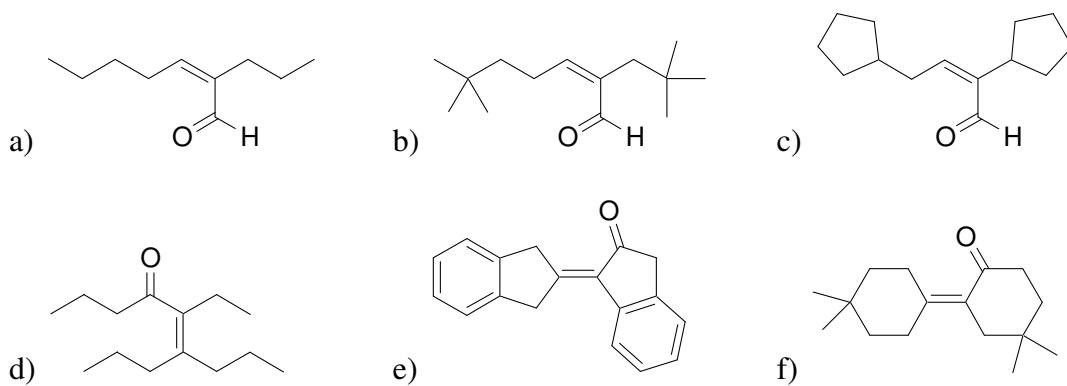
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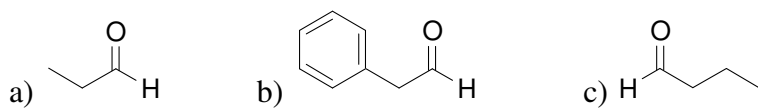
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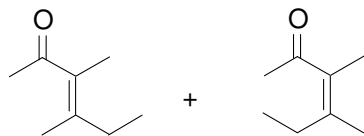
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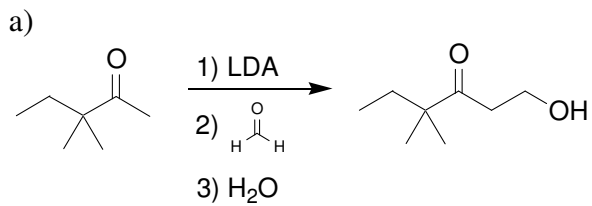
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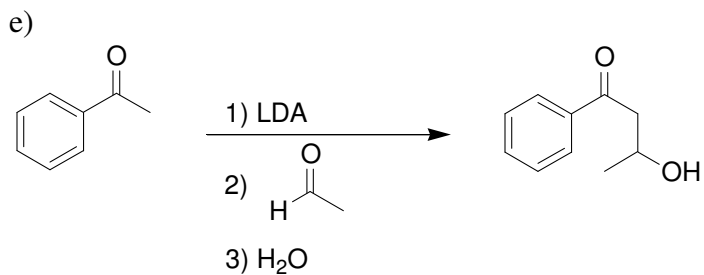
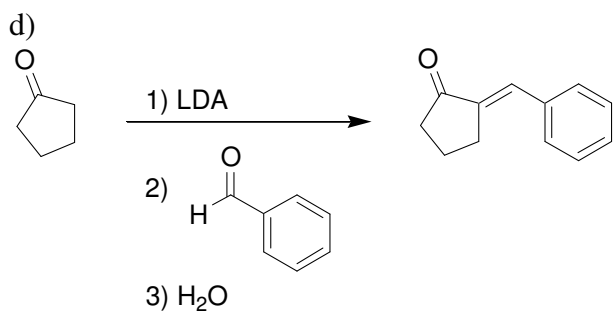
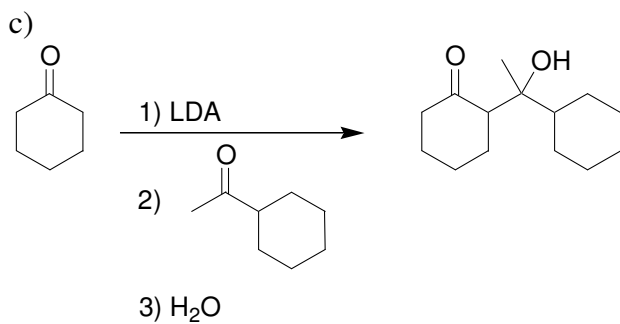
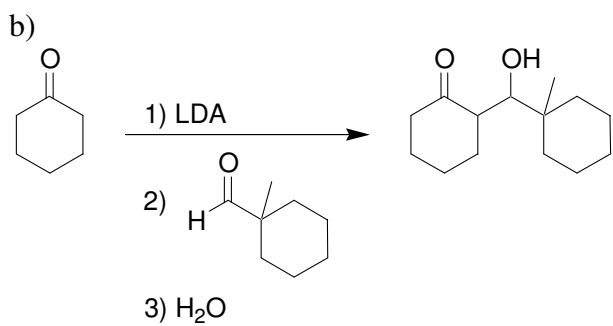
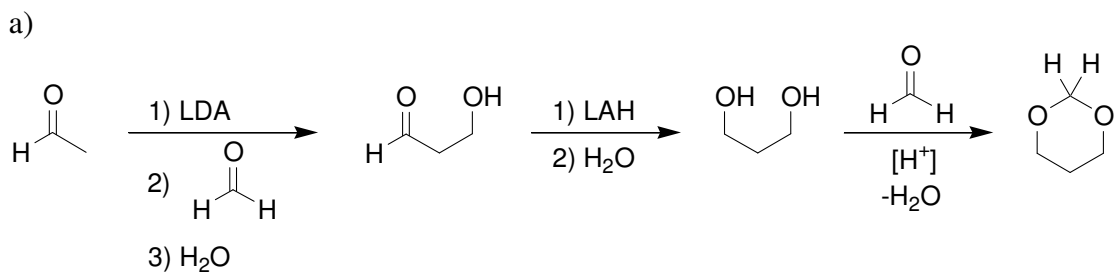


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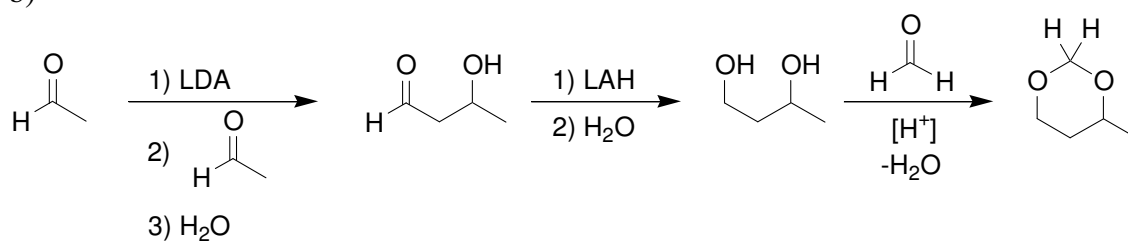


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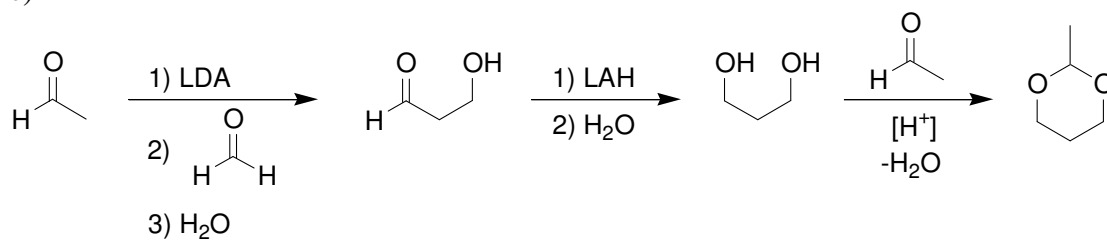


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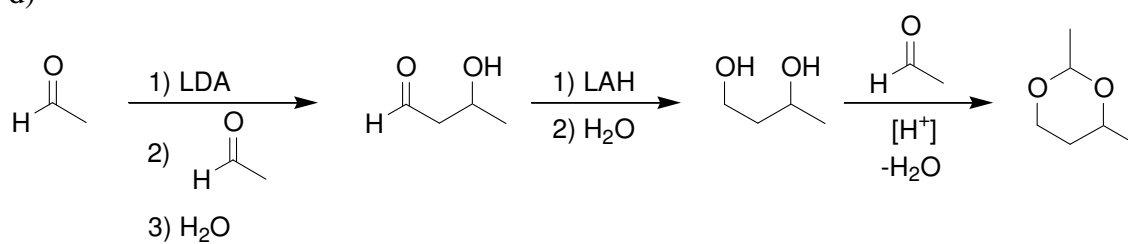
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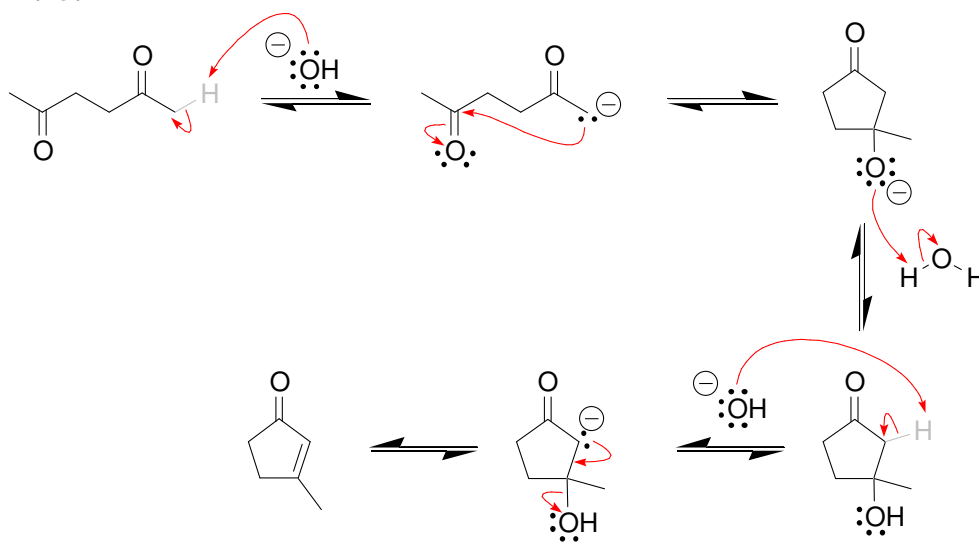
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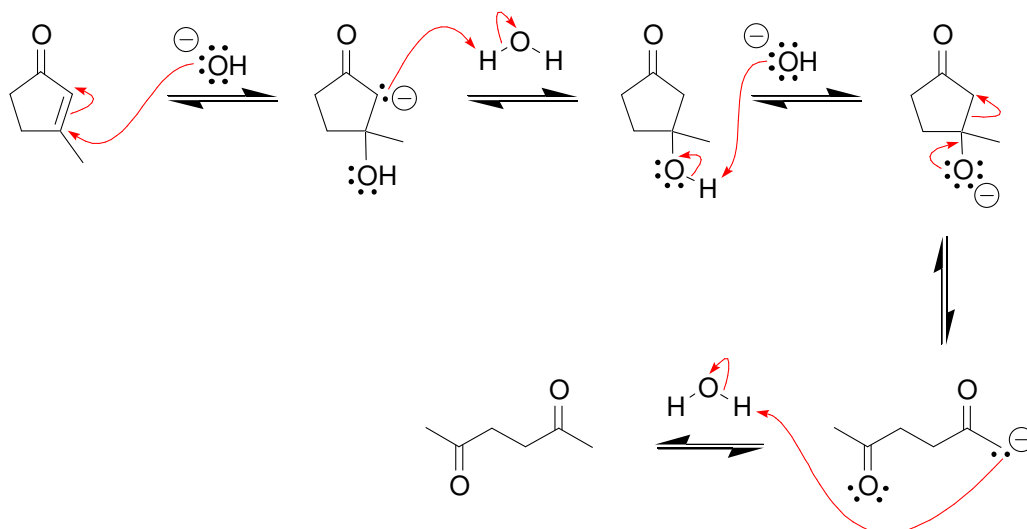
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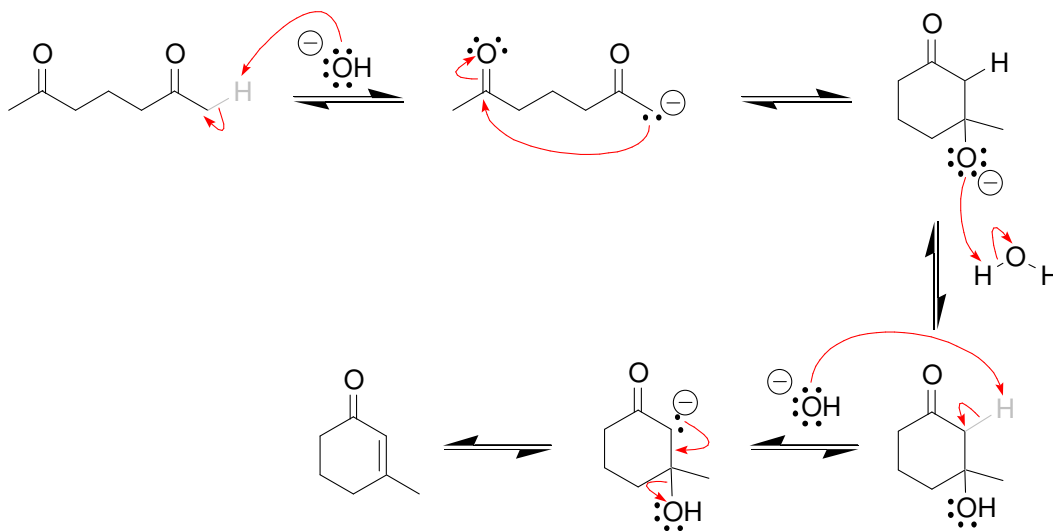
22.25.



22.26.



22.27.

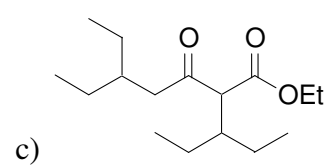
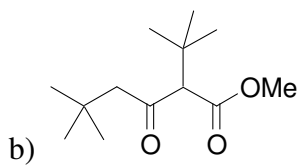
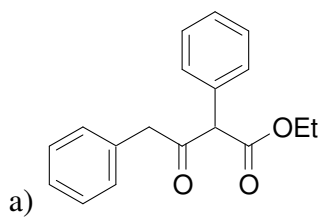


22.28.

a) NaOEt

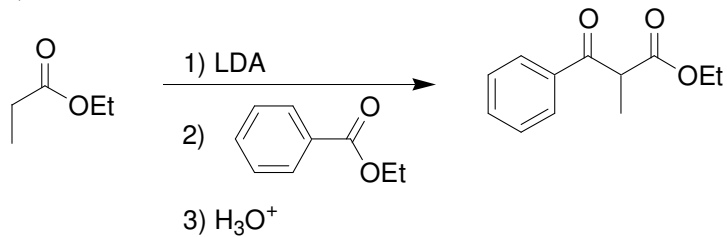
b) *t*-BuOK

22.29.

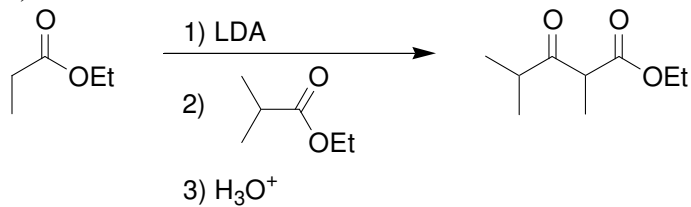


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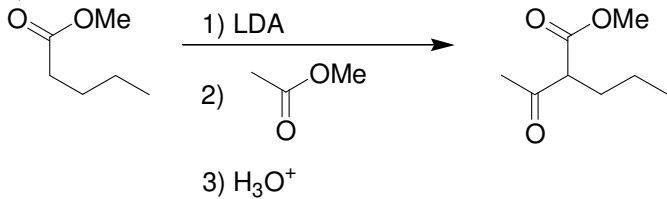
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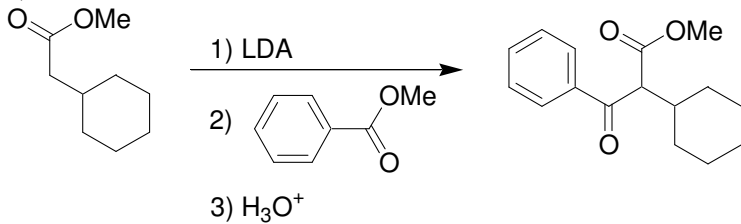
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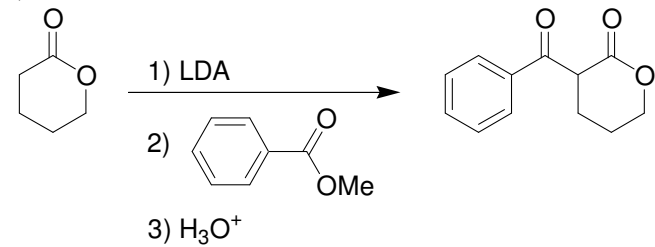
c)



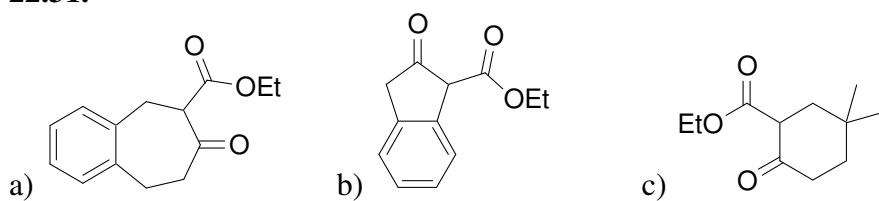
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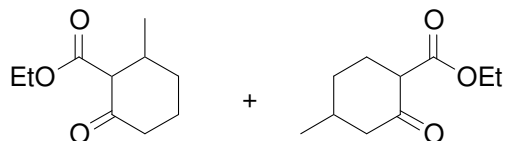
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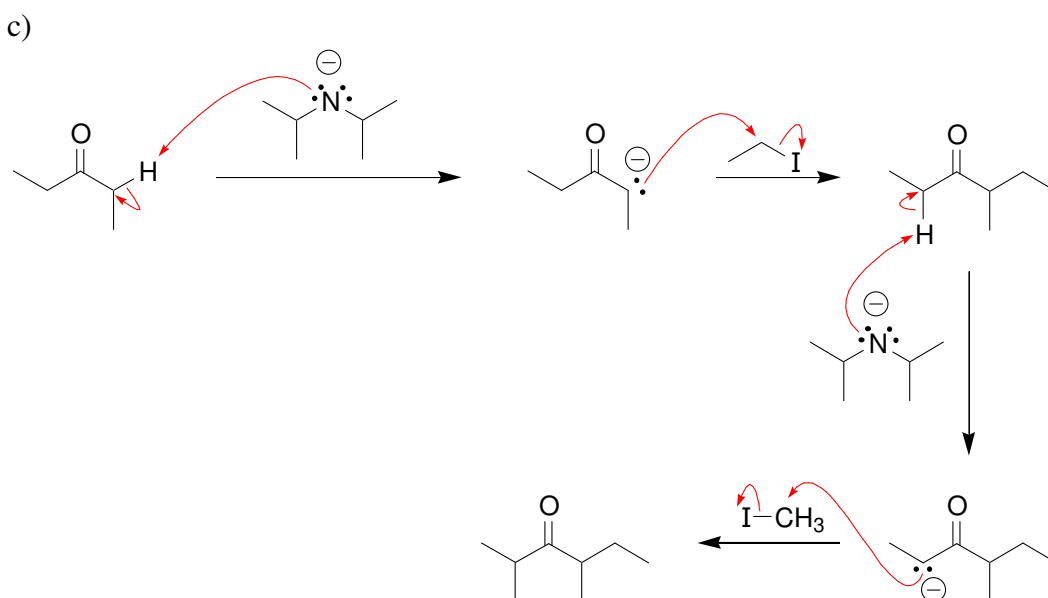
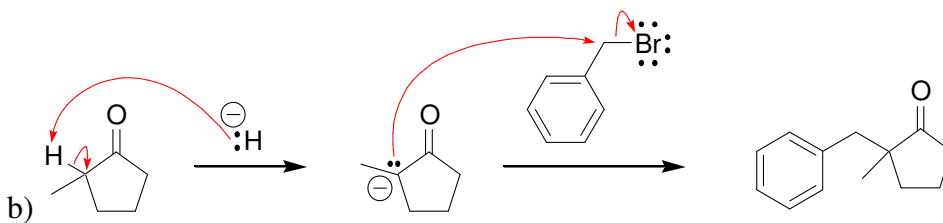
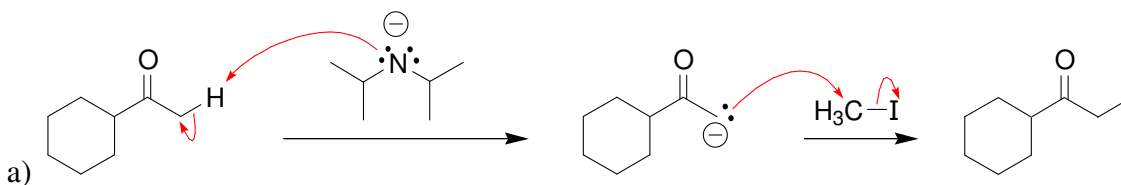
22.31.



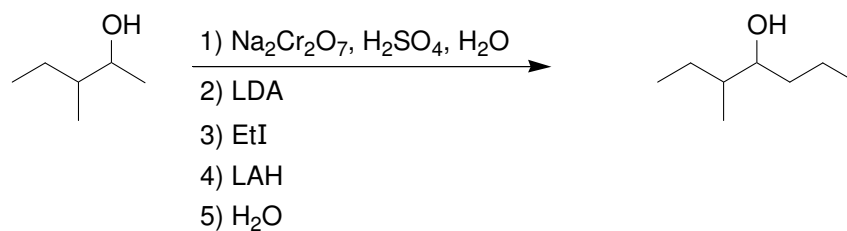
22.32.



22.33.

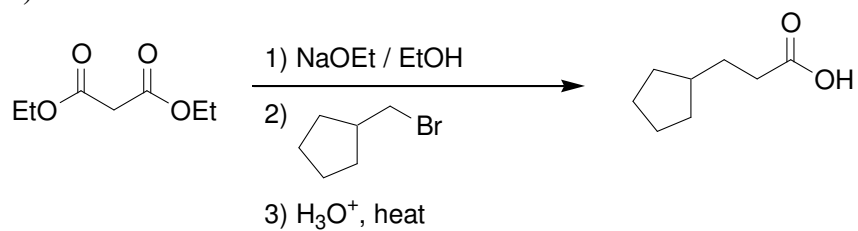


22.34.

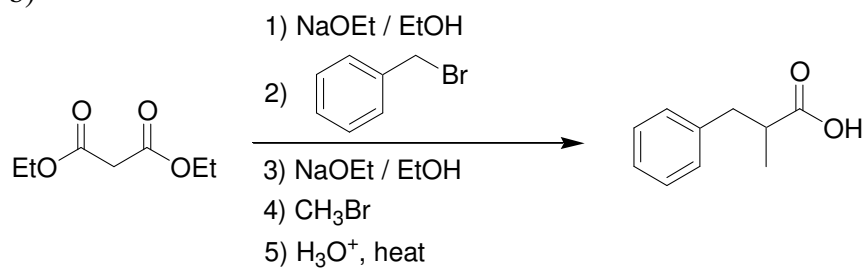


22.35.

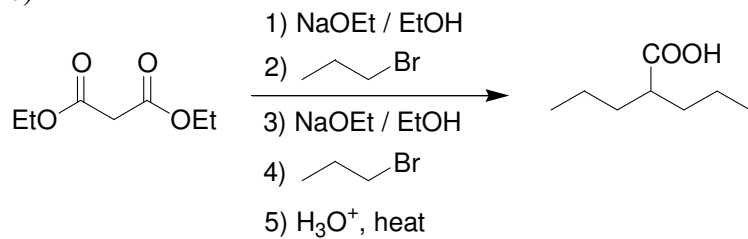
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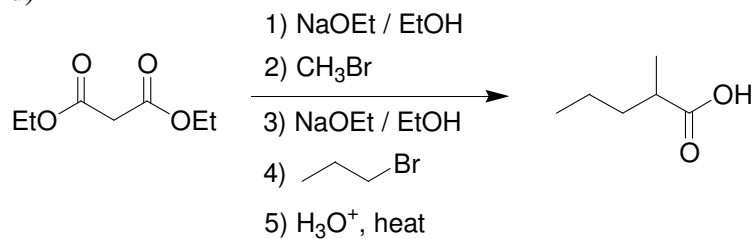
b)

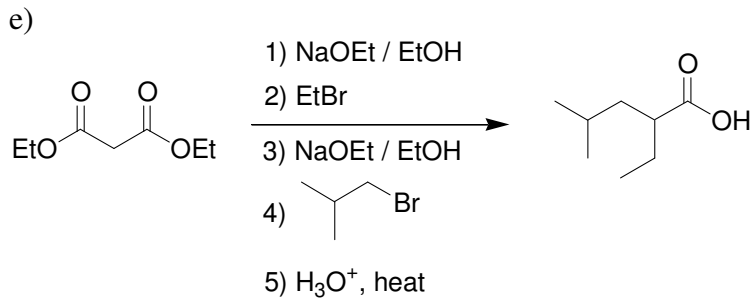
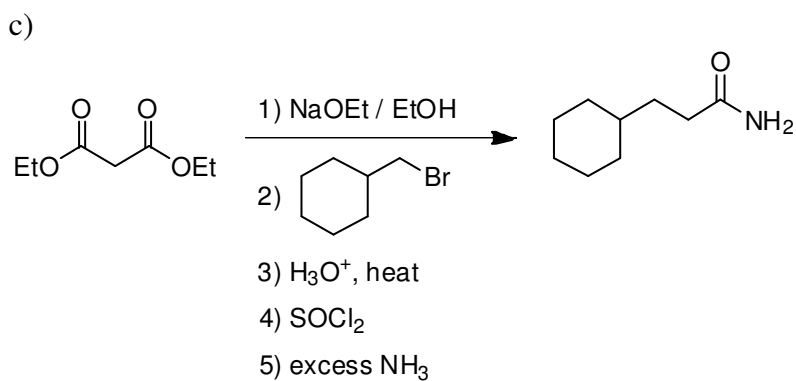
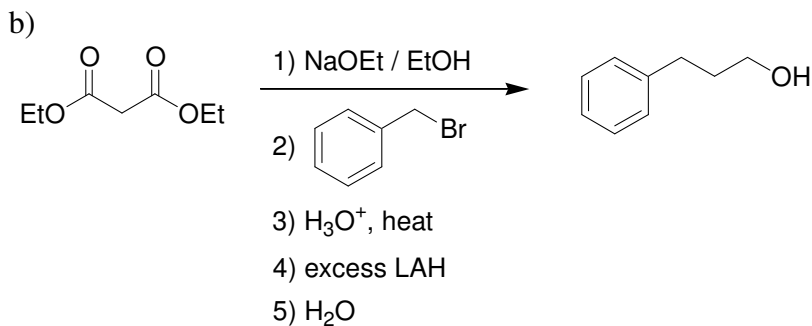
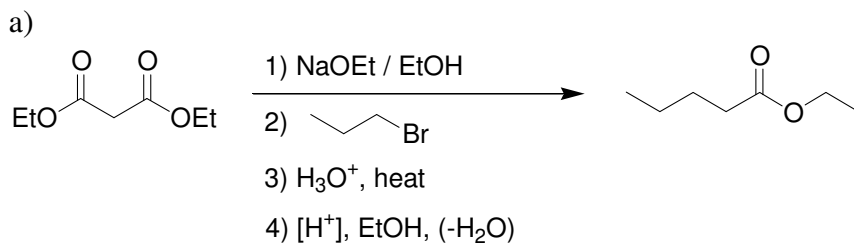


c)

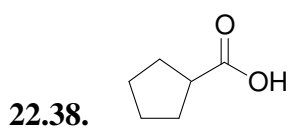


d)



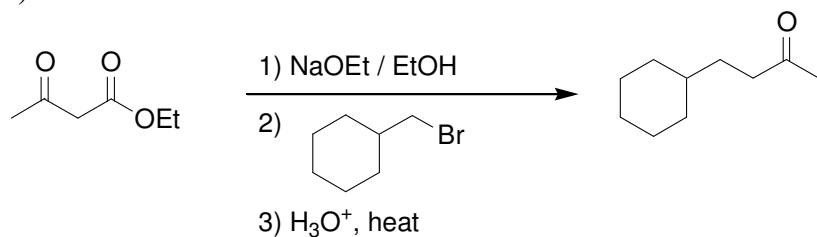
**22.36.**

22.37. Preparation of the desired compound requires the installation of three alkyl groups at the alpha position. The malonic ester synthesis can only be used to install two alkyl groups because the starting material (diethyl malonate) has only two alpha protons.

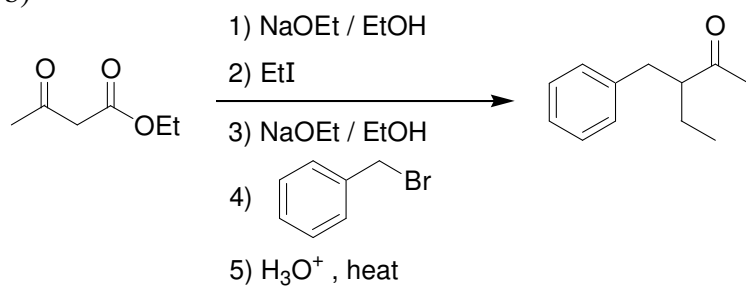


22.39.

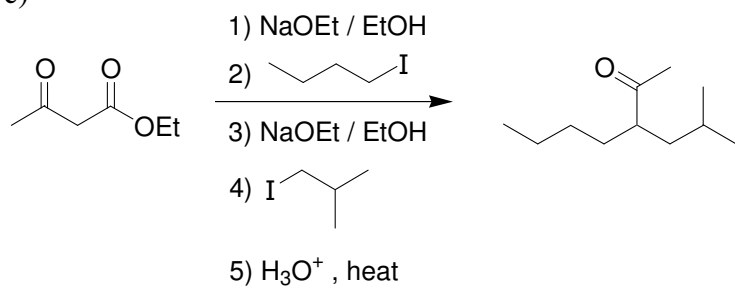
a)



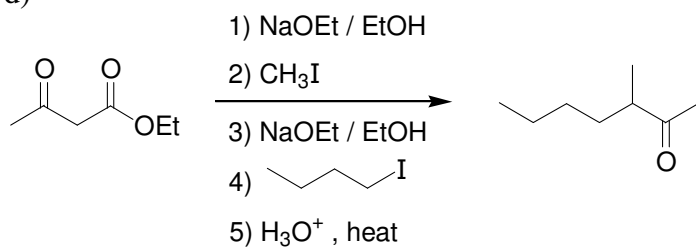
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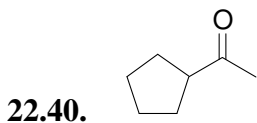


c)

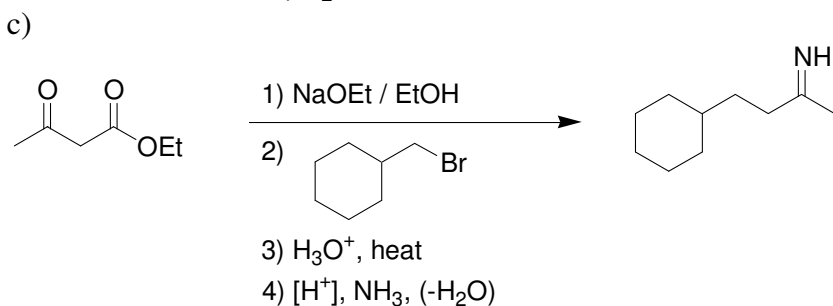
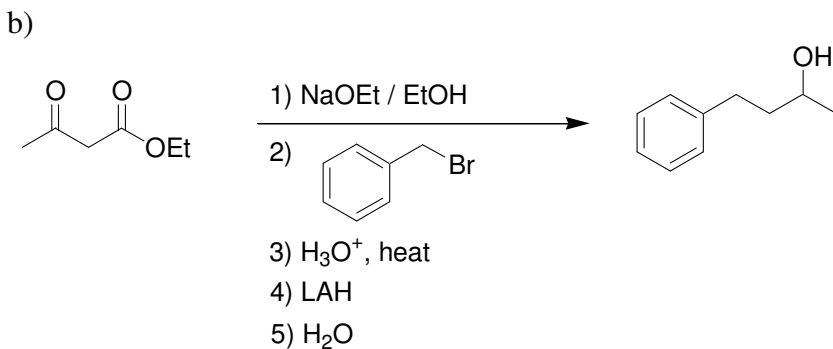
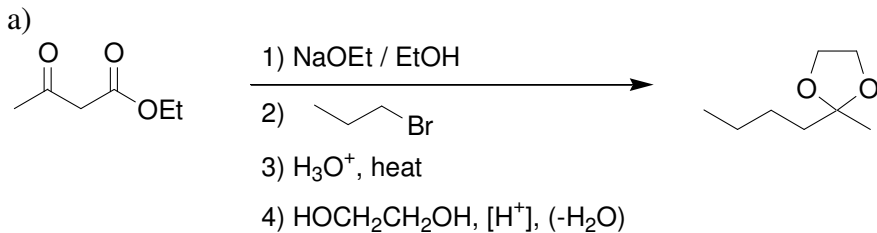


d)



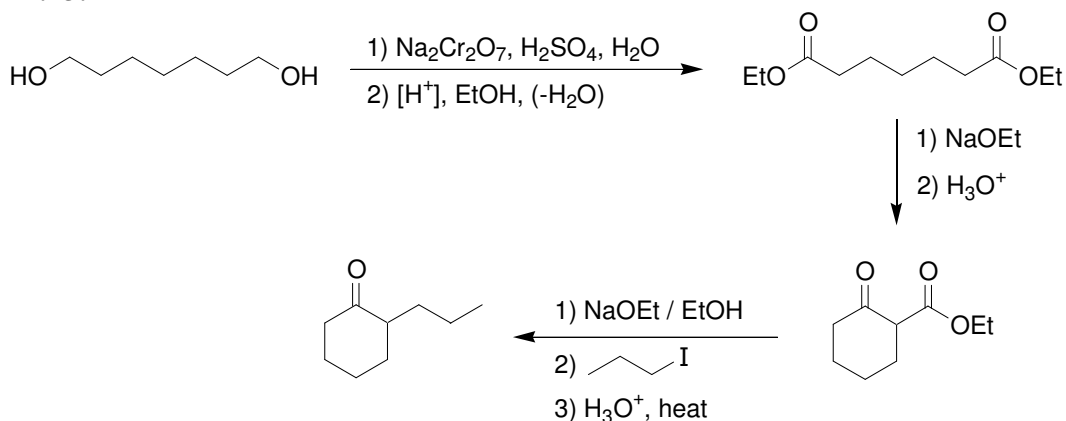


22.41.

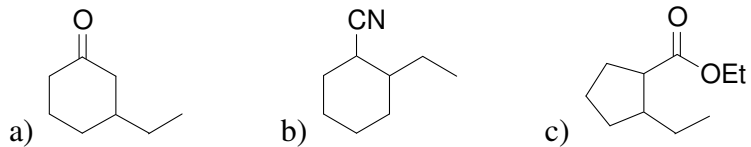


22.42. Preparation of the desired compound requires the installation of three alkyl groups at the alpha position. The acetoacetic ester synthesis can only be used to install two alkyl groups because the starting material (diethyl malonate) has only two alpha protons.

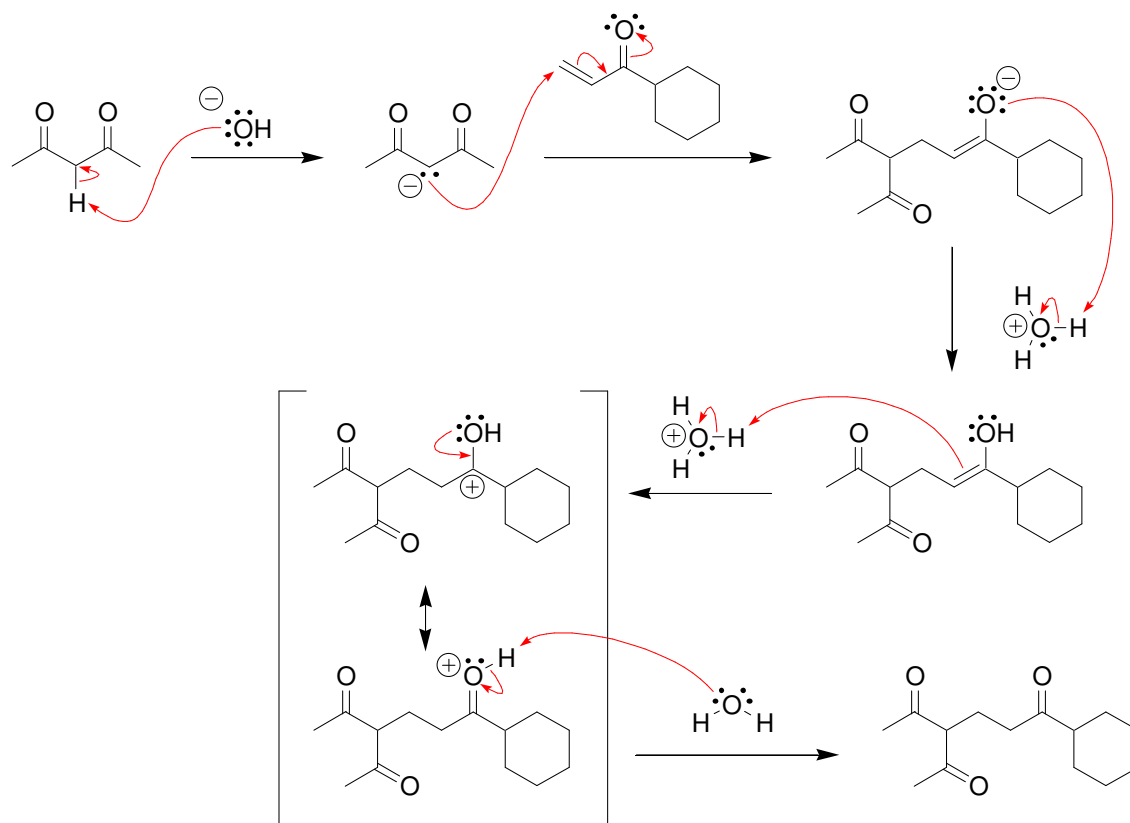
22.43.



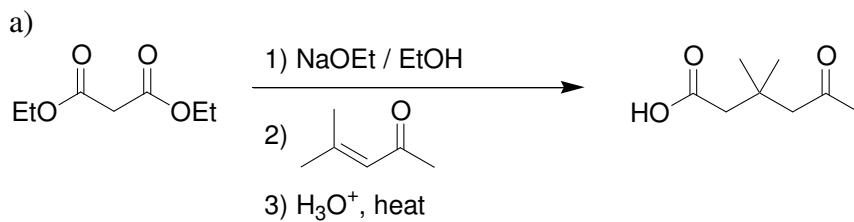
22.44.

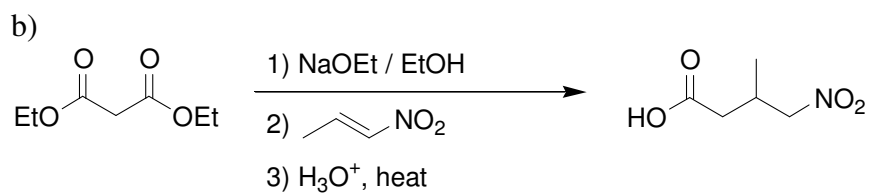
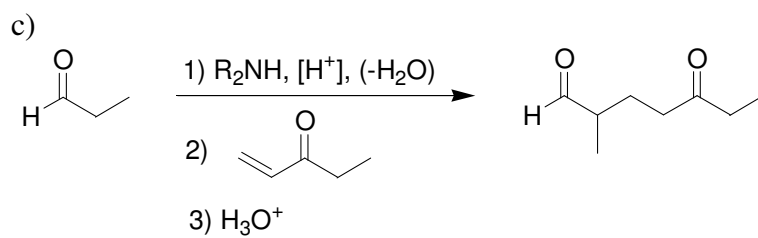
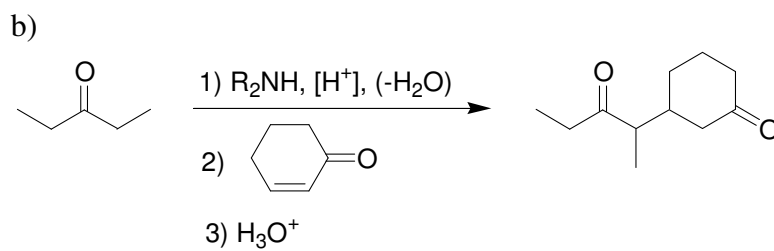
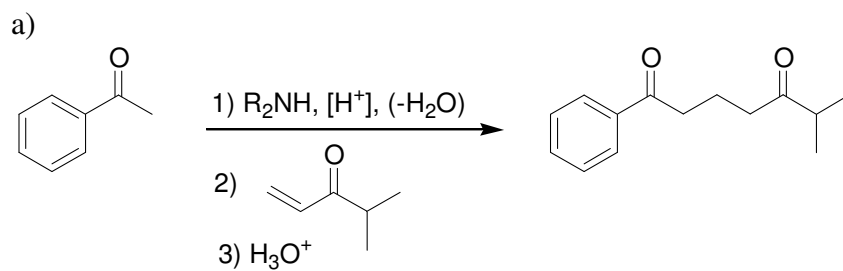


22.45.

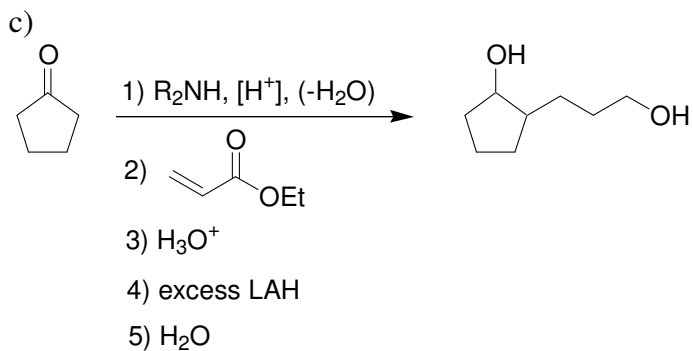
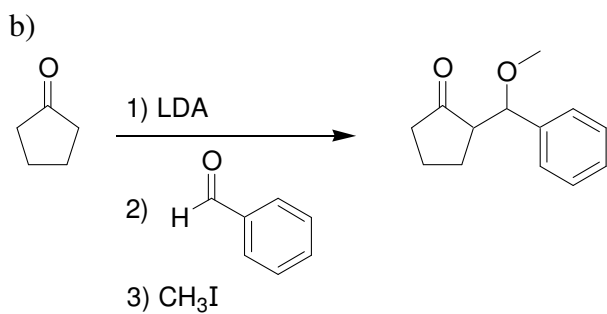
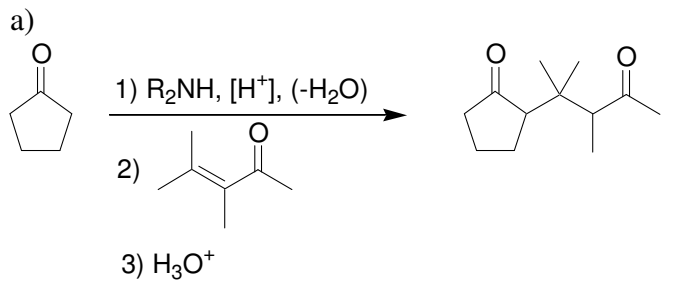


22.46.

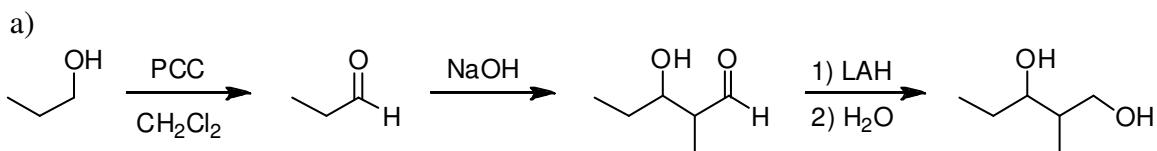


**22.47.**

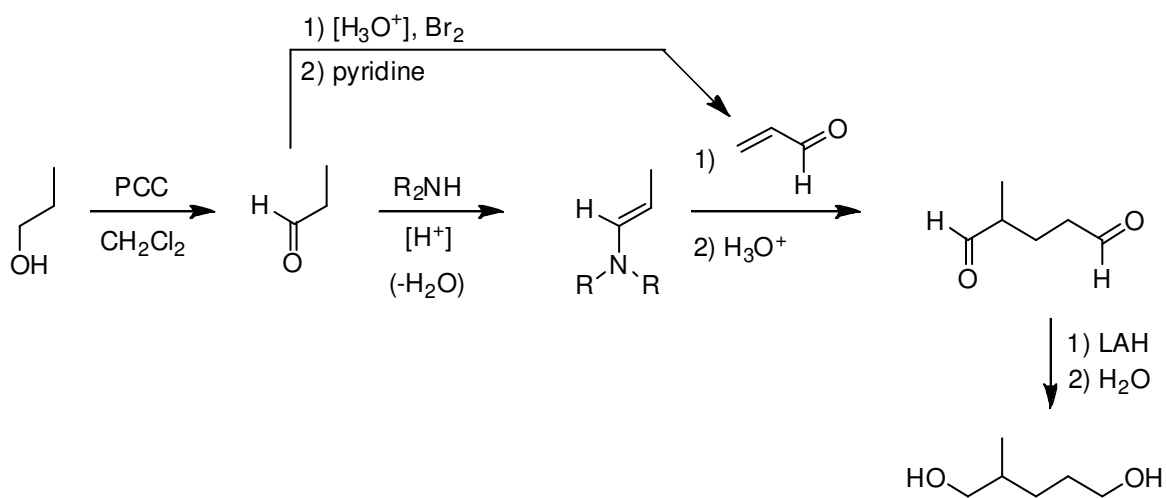
22.51.



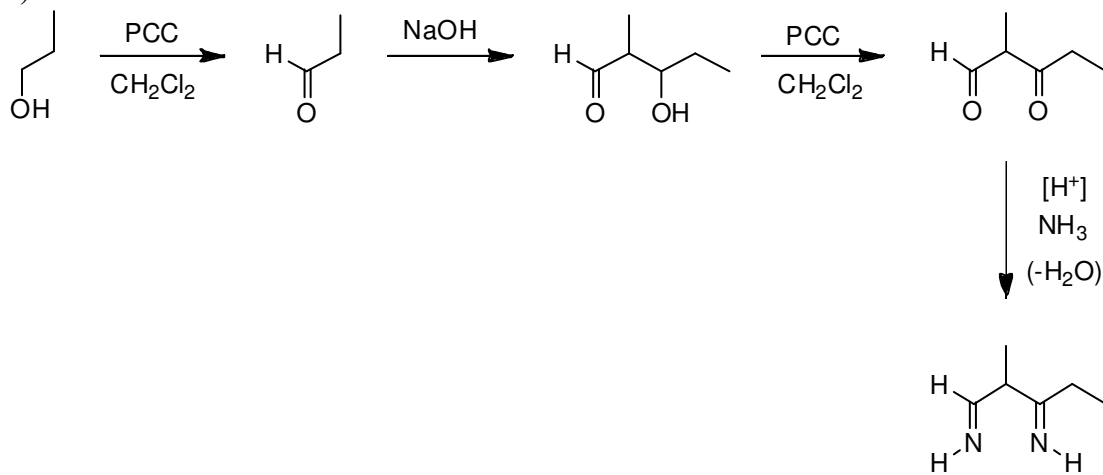
22.52.



b)

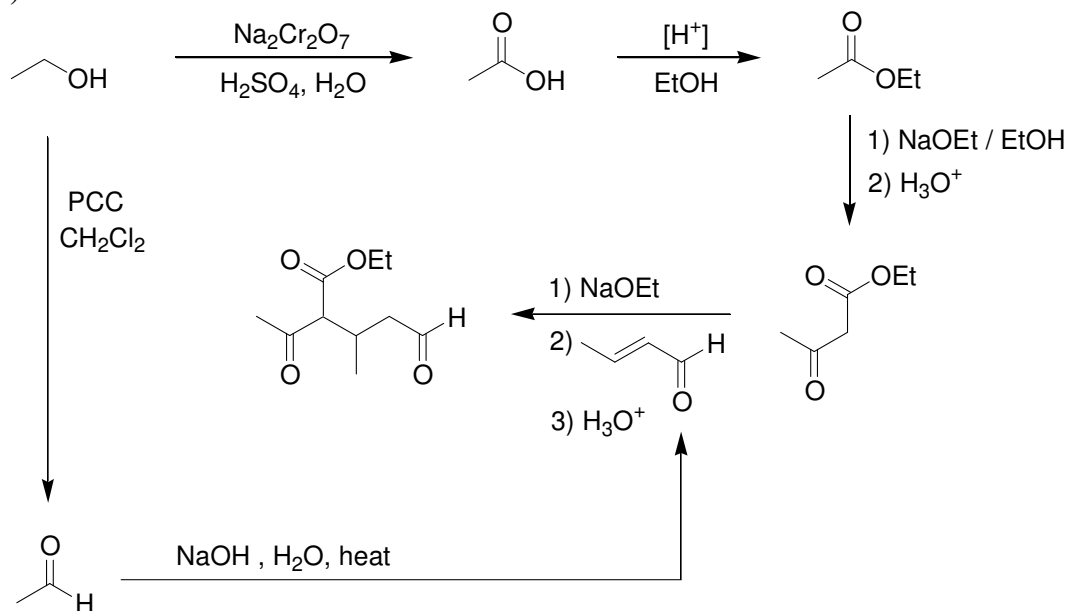


c)

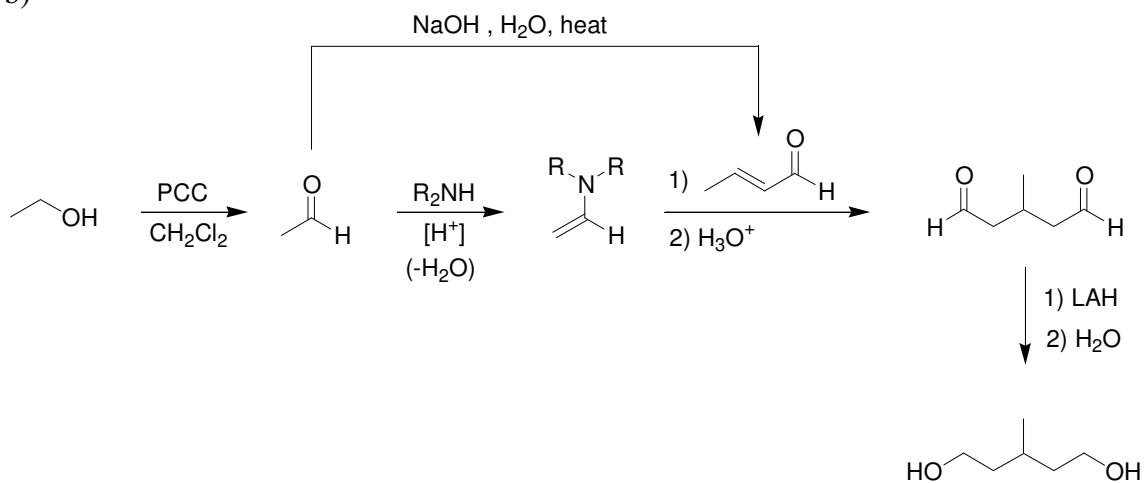


22.53.

a)

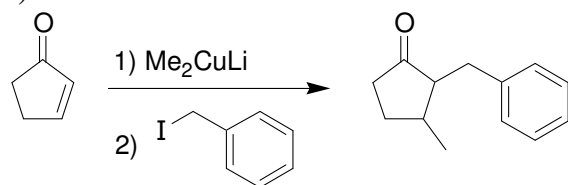


b)

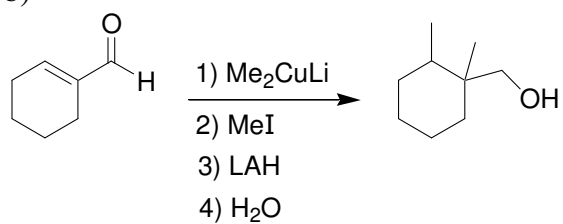


22.54.

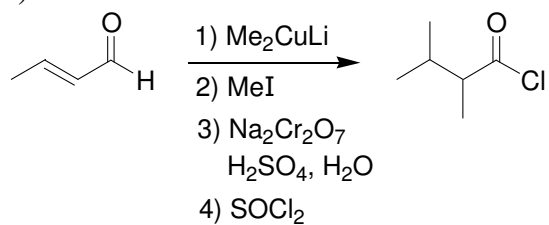
a)



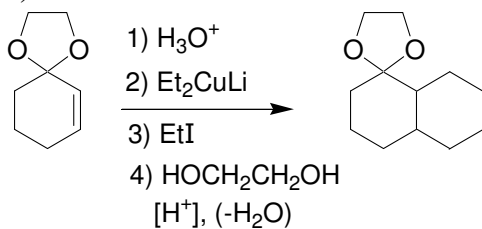
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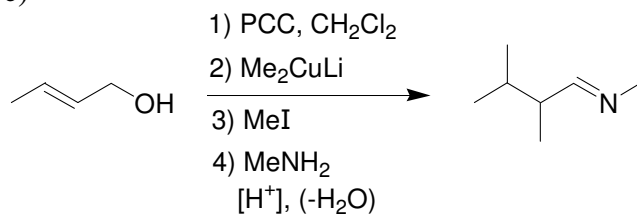
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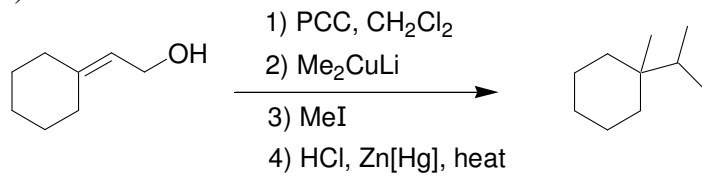
d)



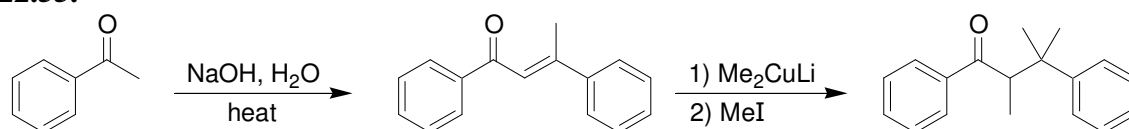
e)



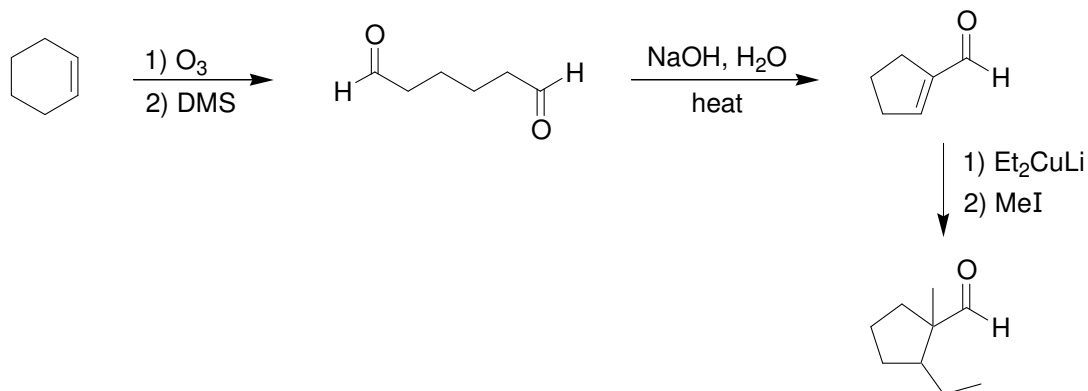
f)



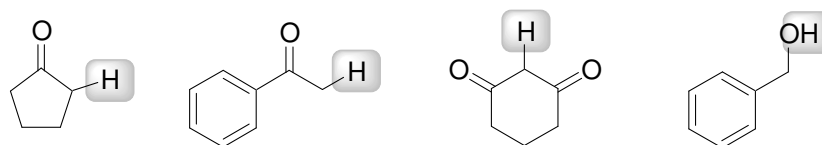
22.55.



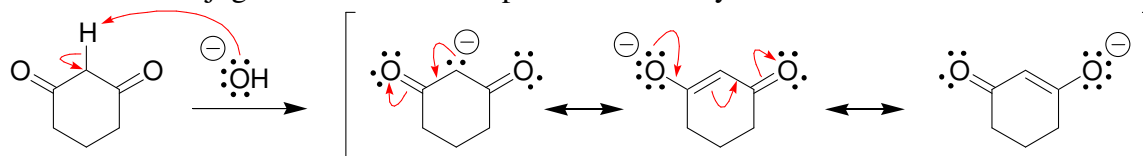
22.56.



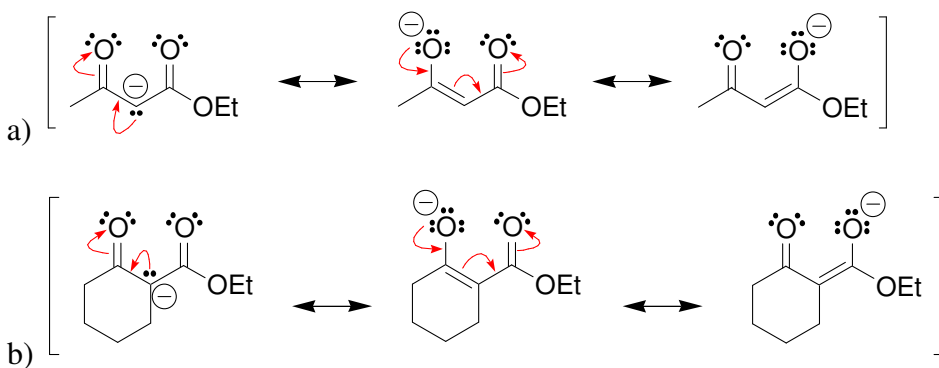
22.57.

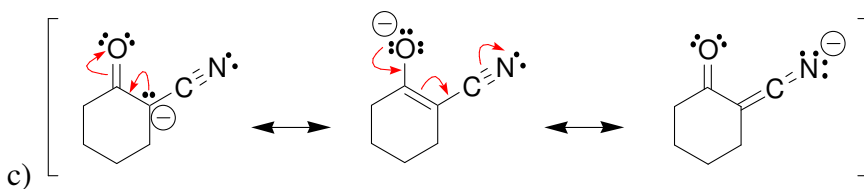


22.58. The conjugate base of this compound is a doubly stabilized enolate.

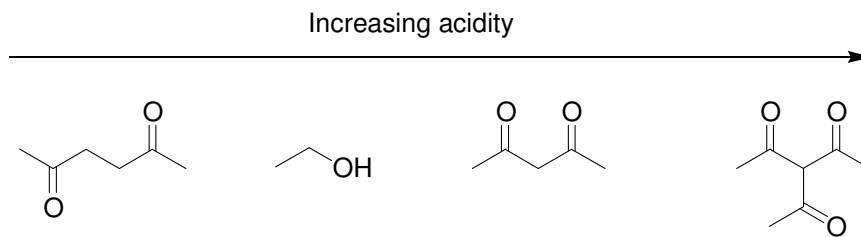


22.59.

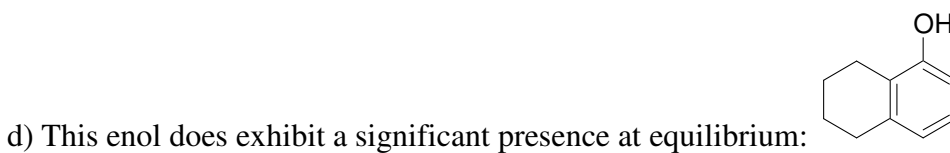
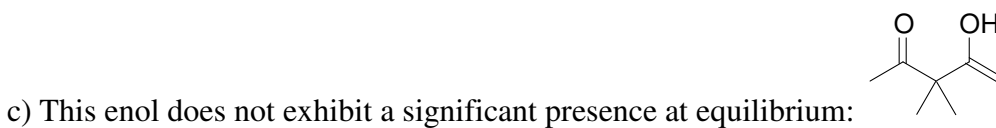
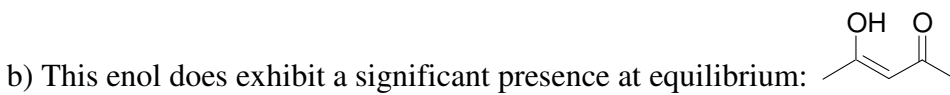
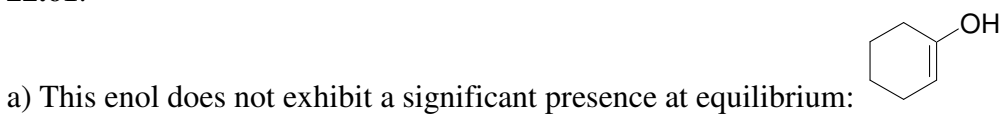




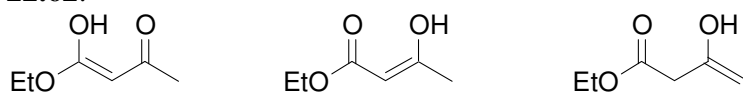
22.60.



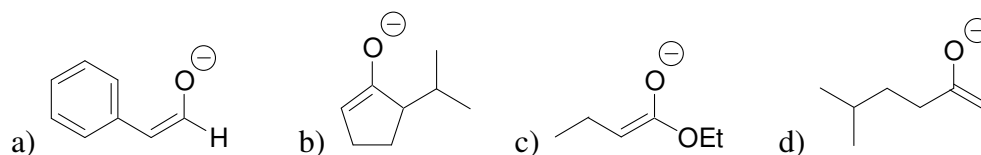
22.61.



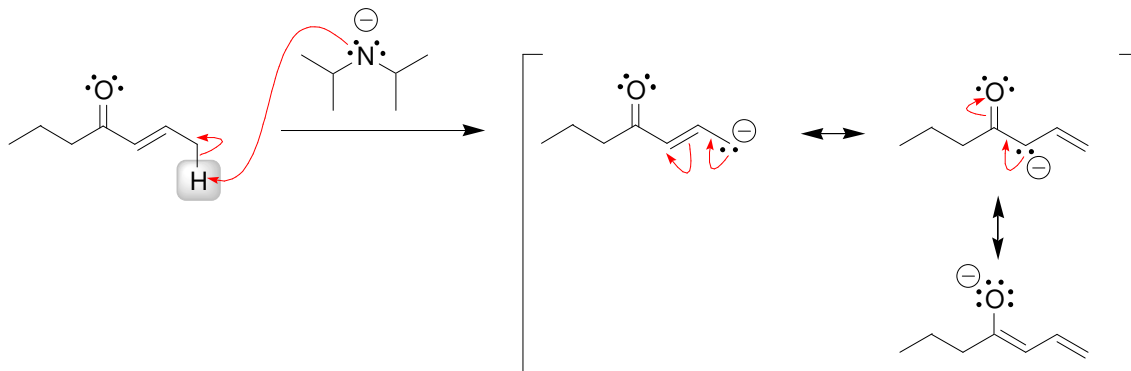
22.62.



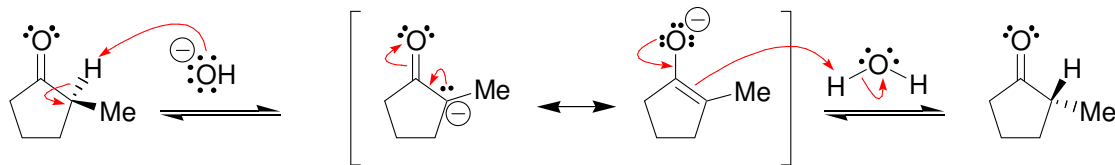
22.63.



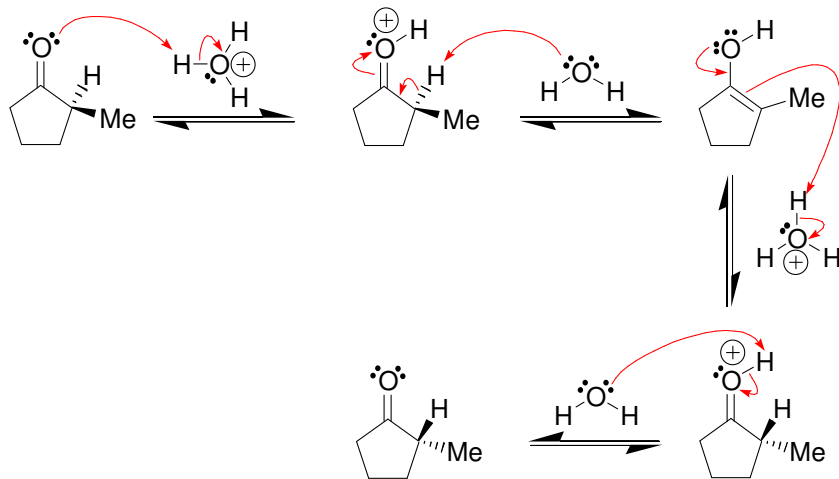
22.64. Deprotonation at the following γ -position results in an anion that has three resonance structures. The negative charge is spread over one oxygen atom and two carbon atoms:



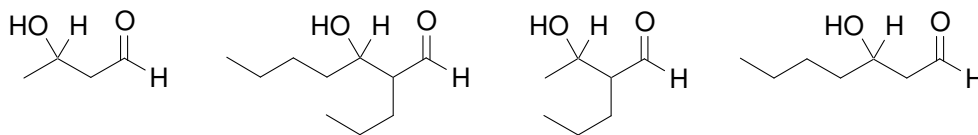
22.65. Deprotonation at the α carbon changes the hybridization state of the α carbon from sp^3 (tetrahedral) to sp^2 (planar). When the α position is protonated once again, the proton can be placed on either side of the planar α carbon, resulting in racemization:



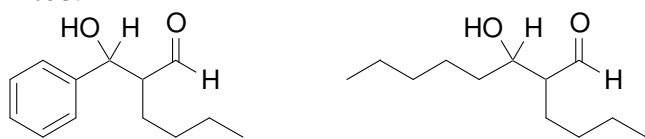
22.66.



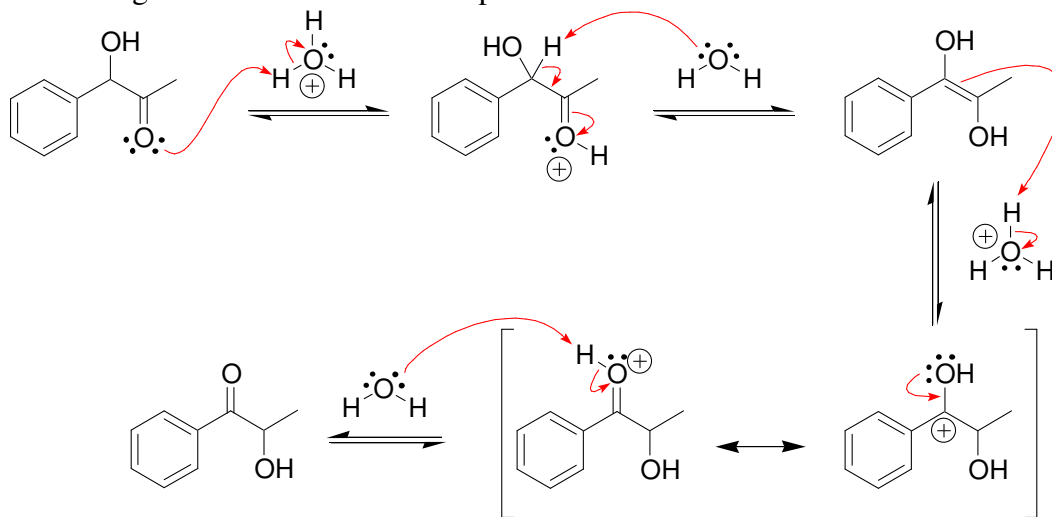
22.67.



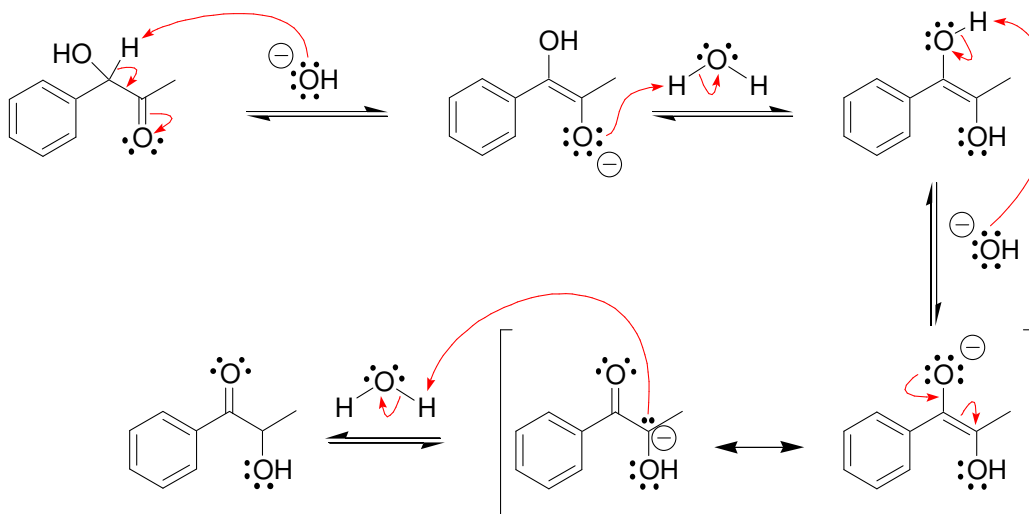
22.68.



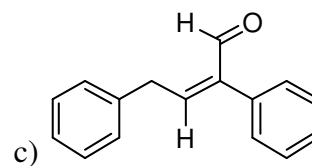
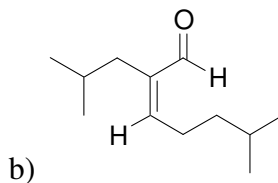
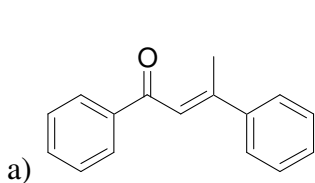
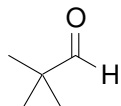
22.69. The carbonyl group and the aromatic ring are conjugated in the product, but are not conjugated in the starting material. Formation of conjugation serves as a driving force in formation of the product.



22.70.

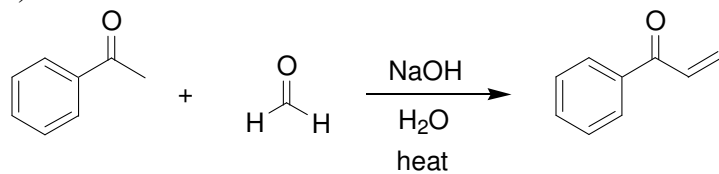


22.71.

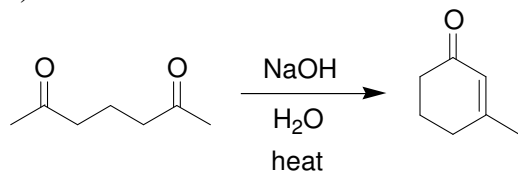
22.72. Trimethylacetaldehyde does not have any α protons.

22.73.

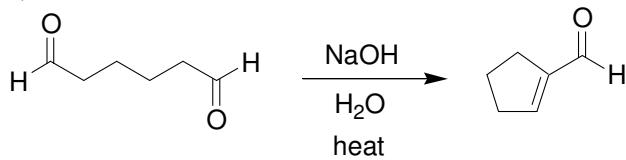
a)



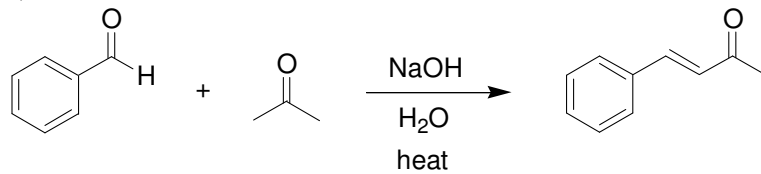
b)



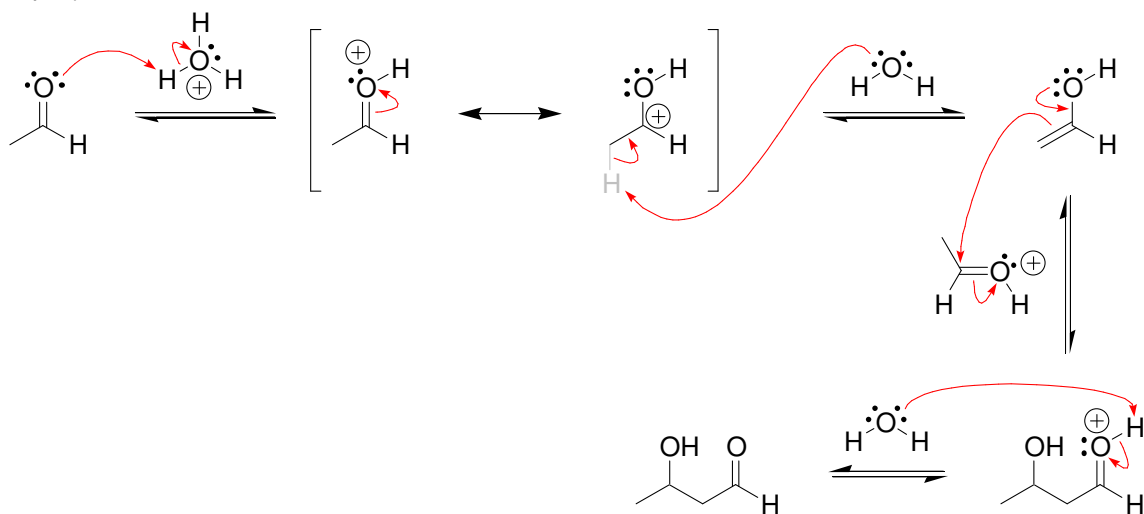
c)



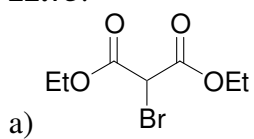
d)



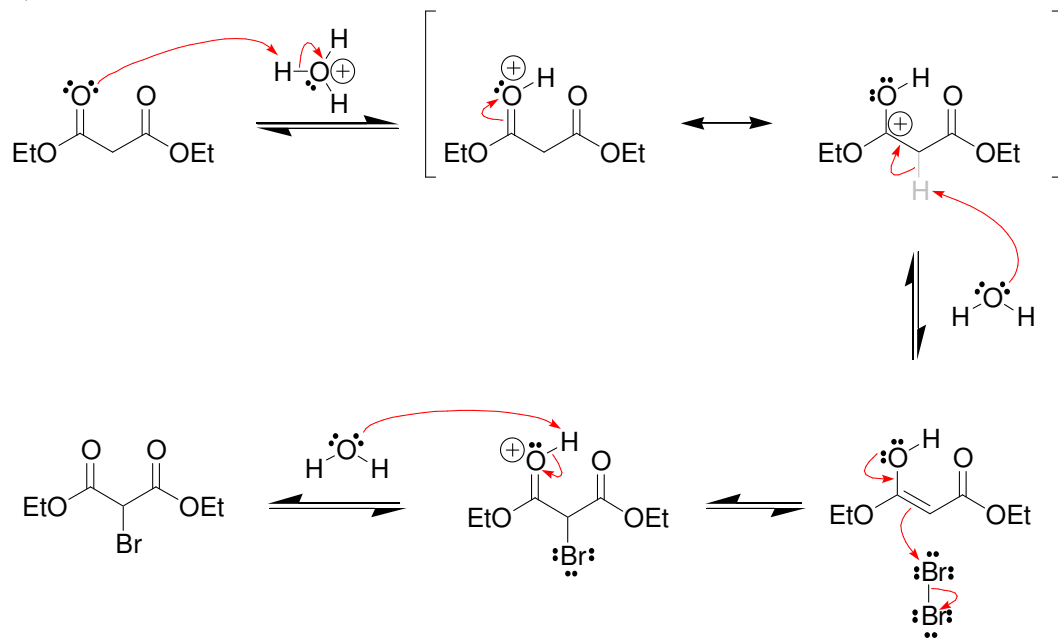
22.74.



22.75.

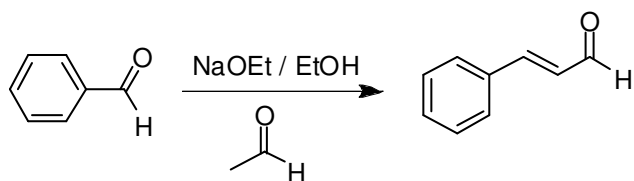


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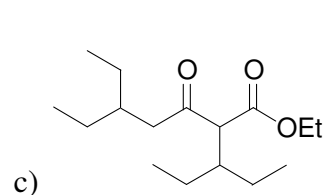
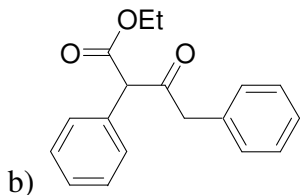
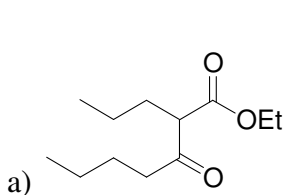


c) The product should be more acidic than diethyl malonate because of the inductive effect of the bromine atom.

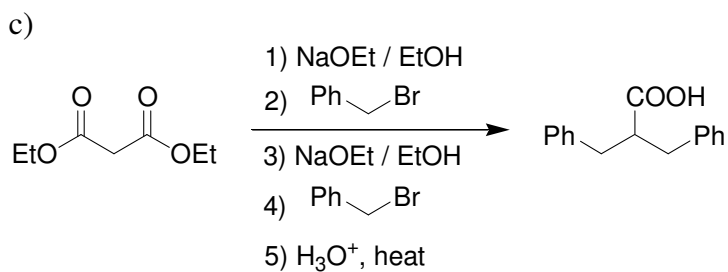
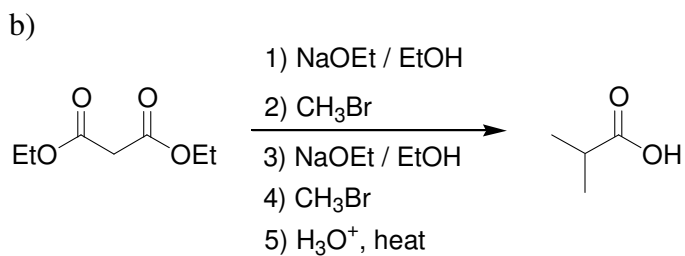
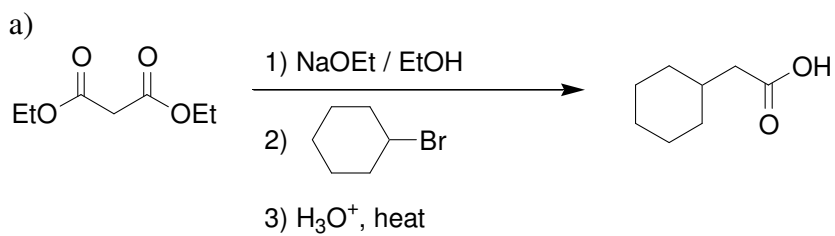
22.76.



22.77.

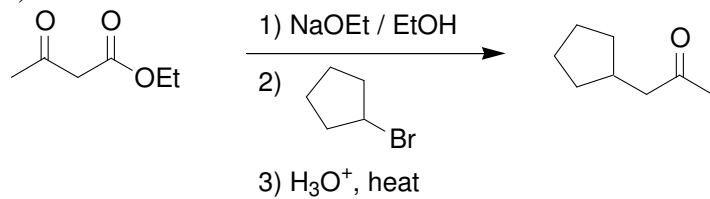


22.78.

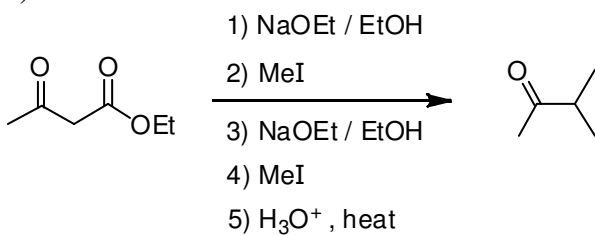


22.79.

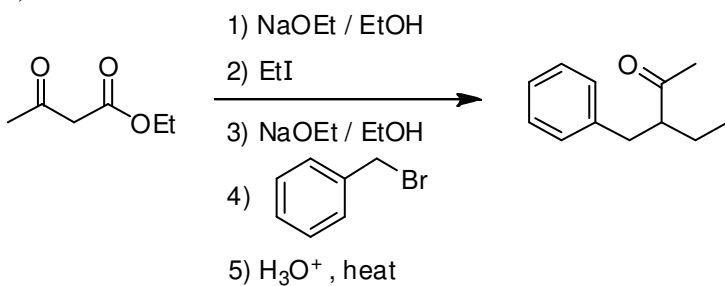
a)



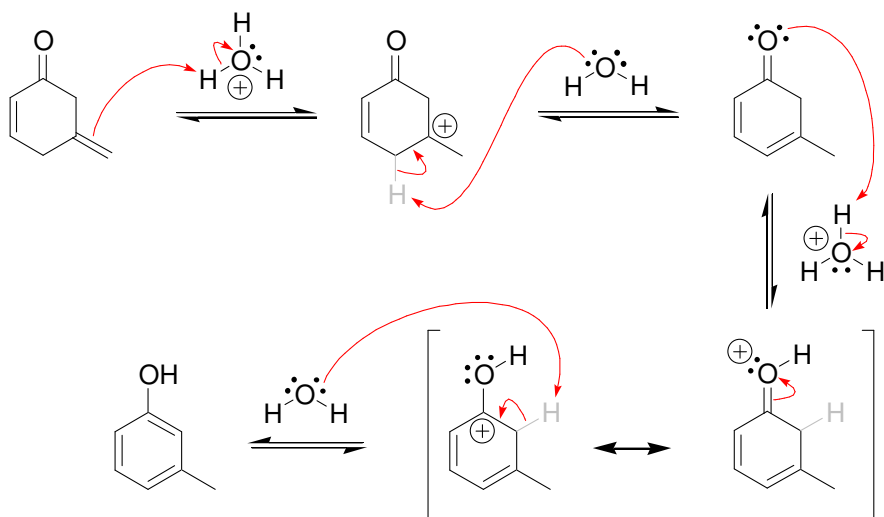
b)



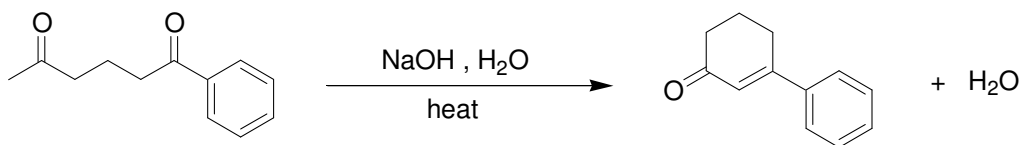
c)



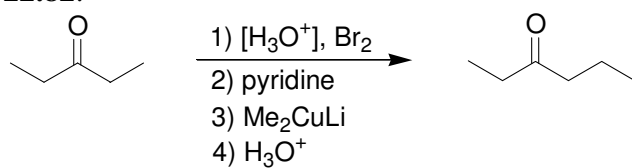
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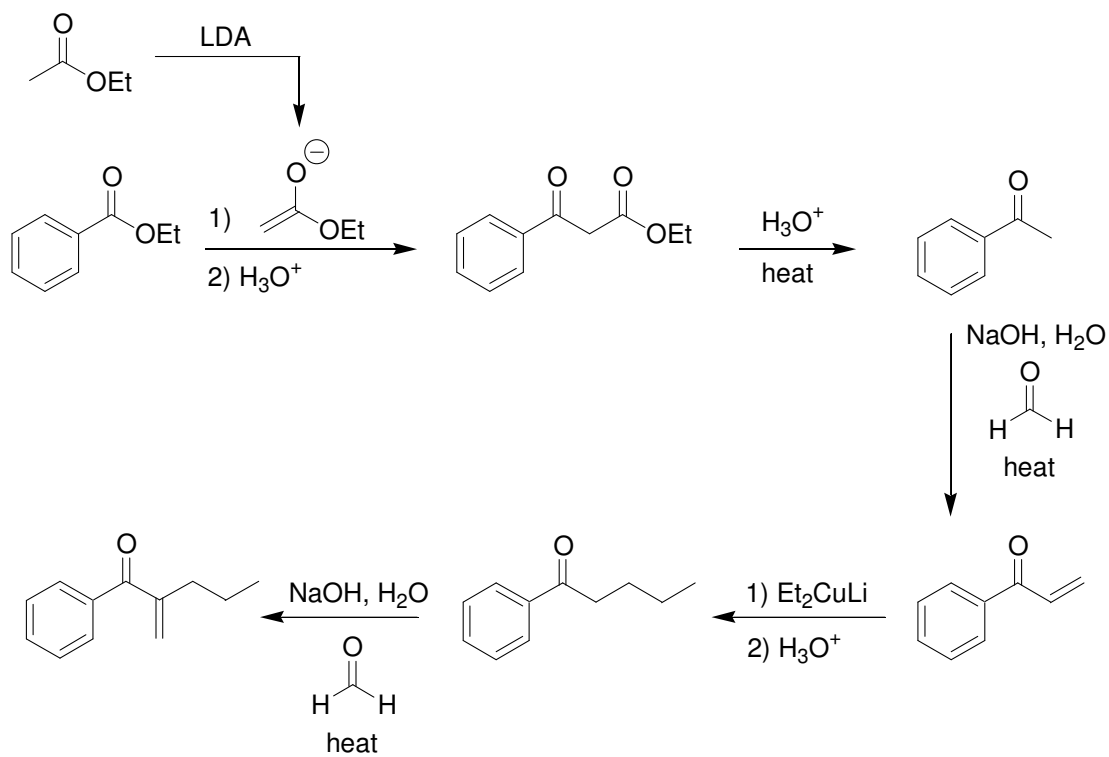
22.81.



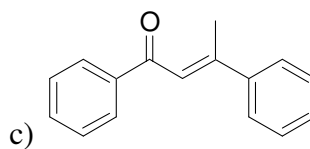
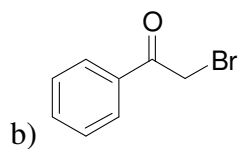
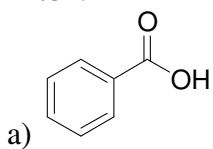
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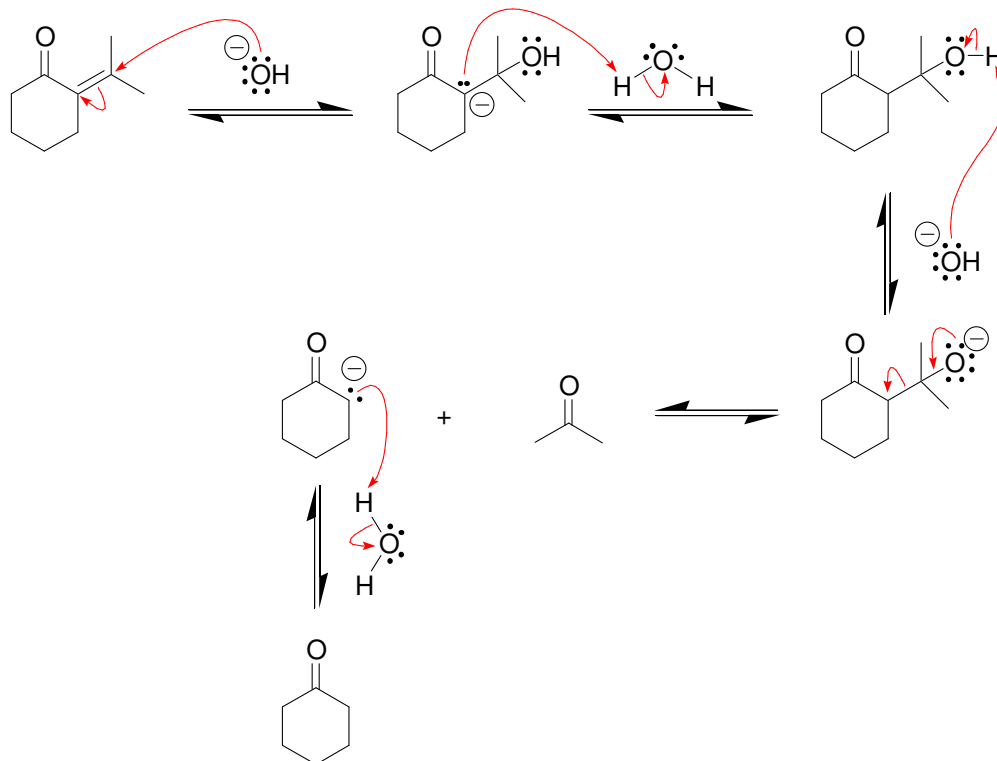
22.83.



22.84.

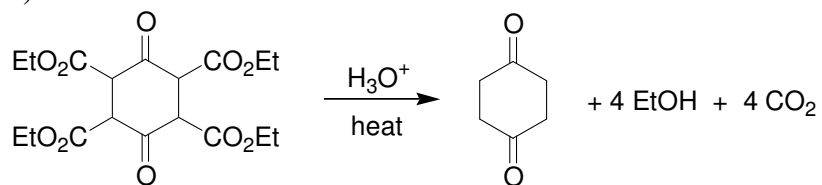


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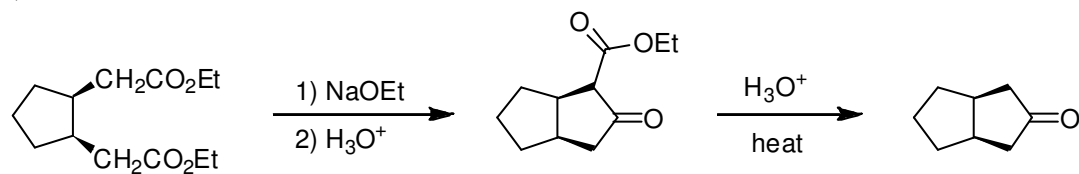


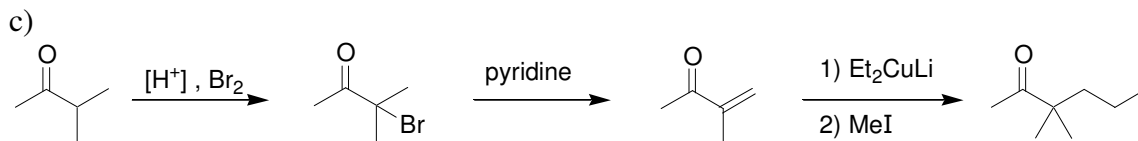
22.86.

a)

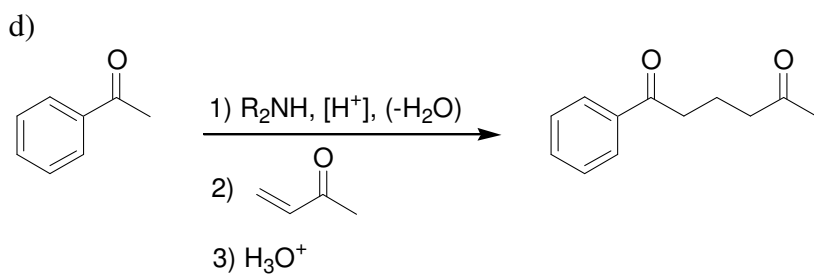
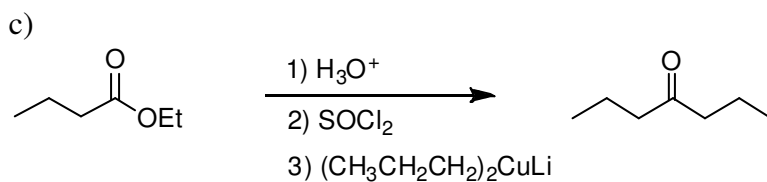
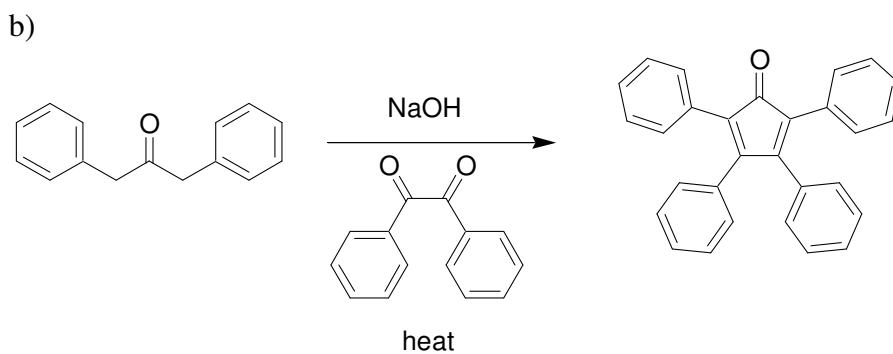
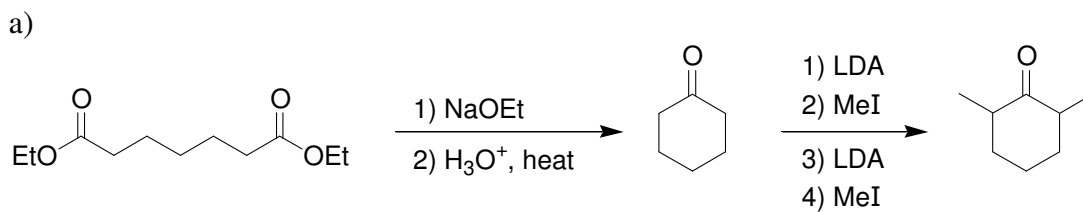


b)

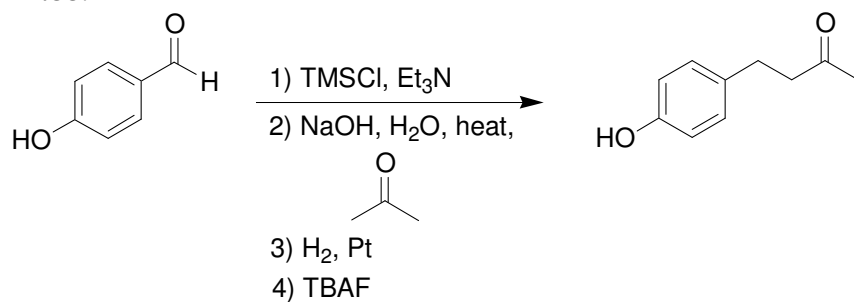




22.87.

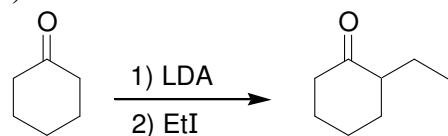


22.88.

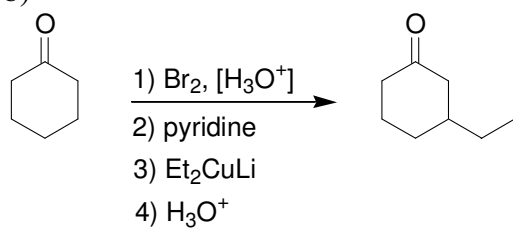


22.89.

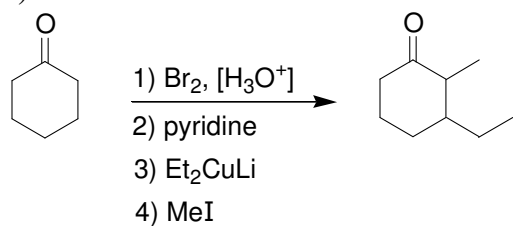
a)



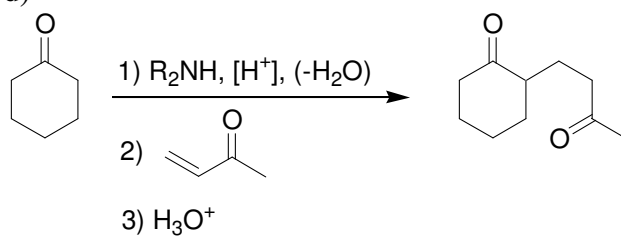
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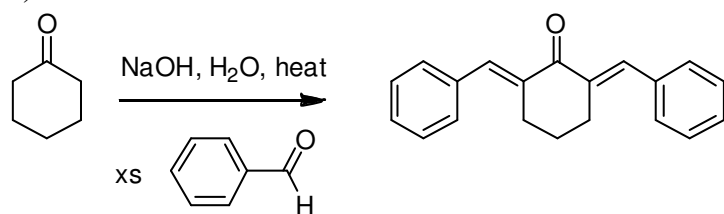
c)

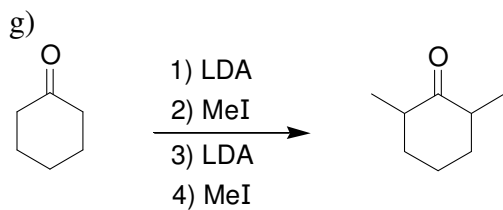
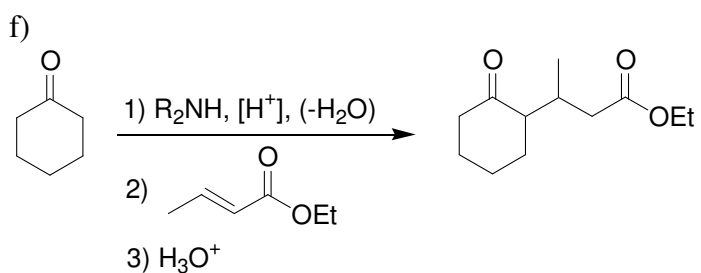


d)

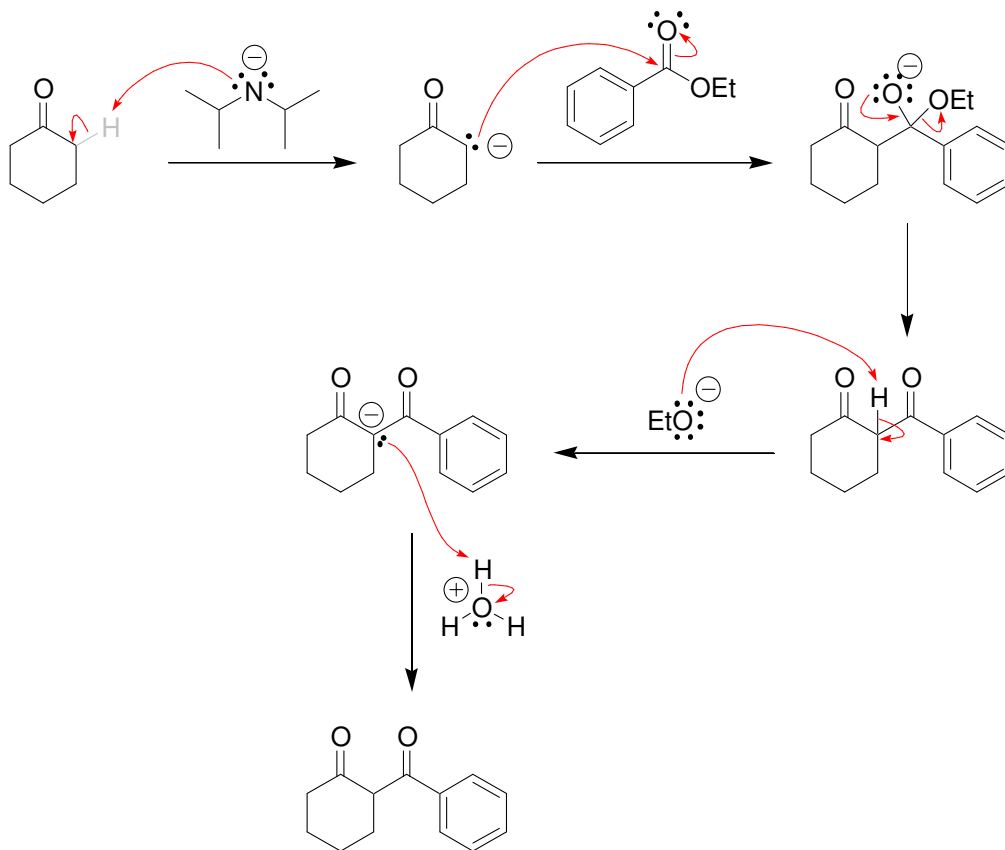


e)

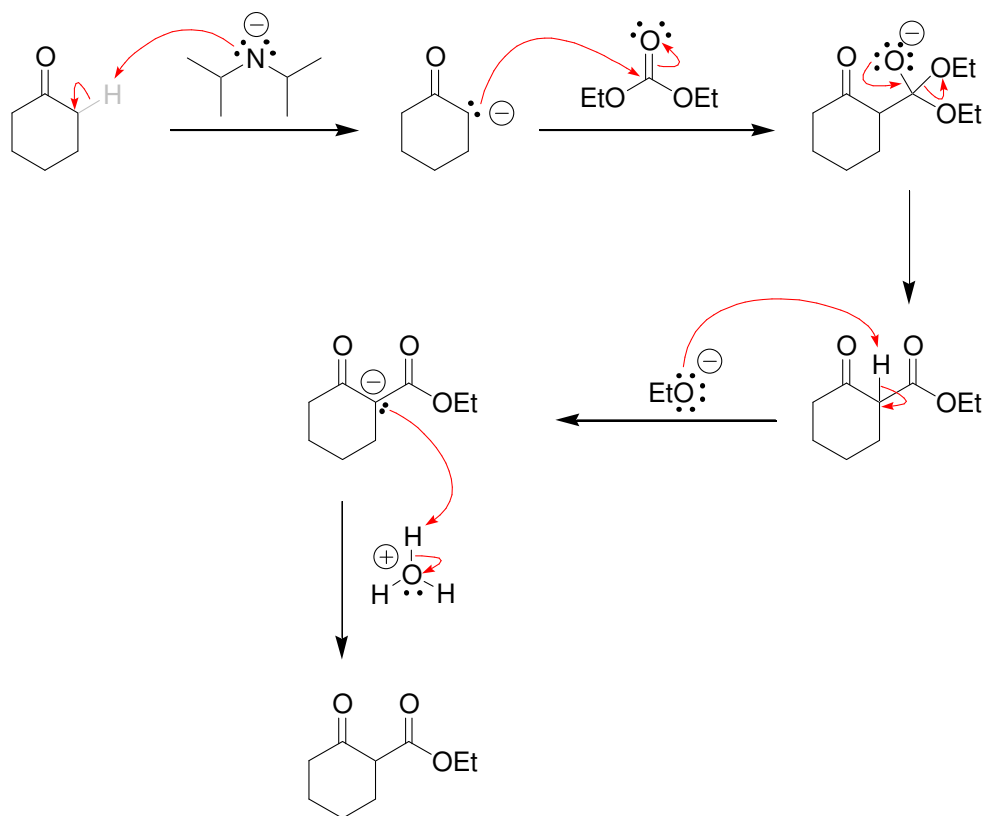




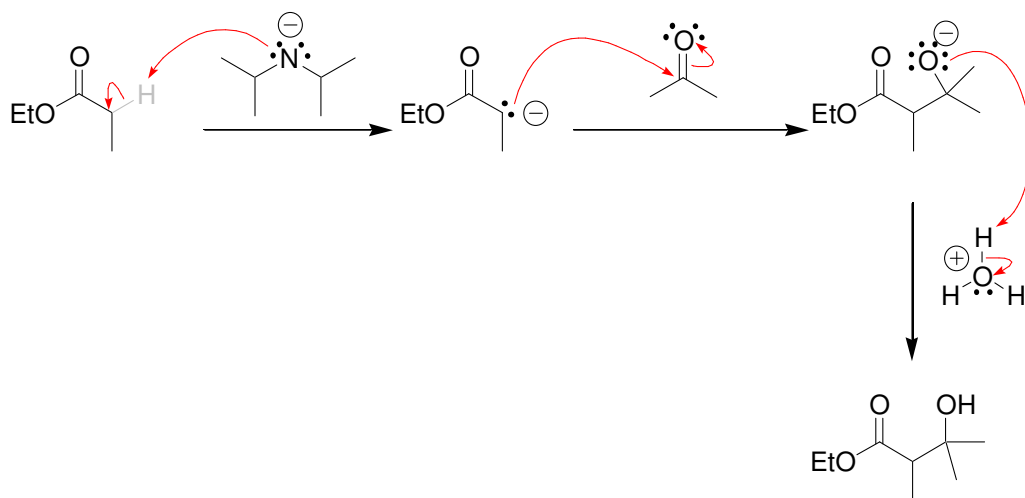
22.90. The driving force for this reaction is formation of a doubly stabilized enolate. After the reaction is complete, an acid is required to protonate this anion.



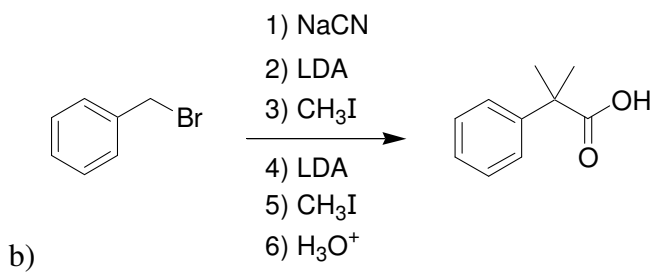
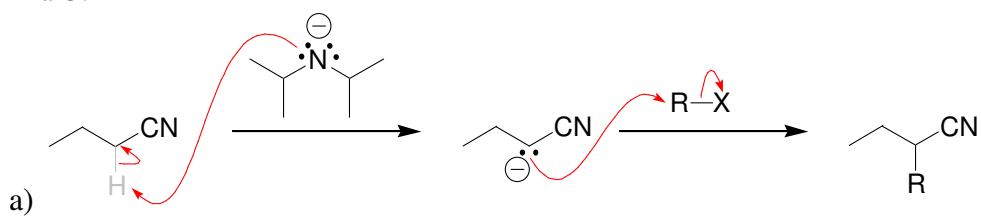
22.91.



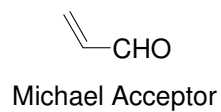
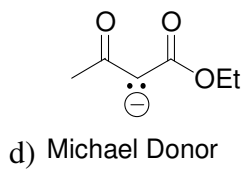
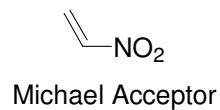
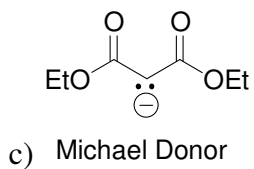
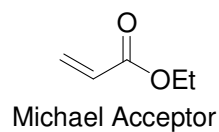
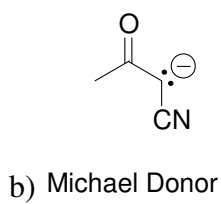
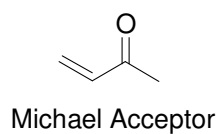
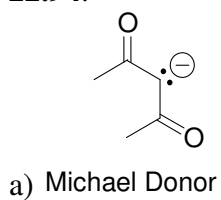
22.92.

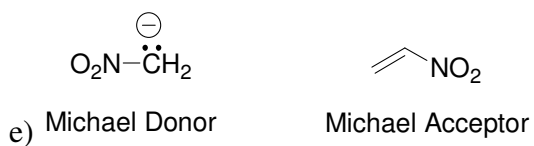


22.93.

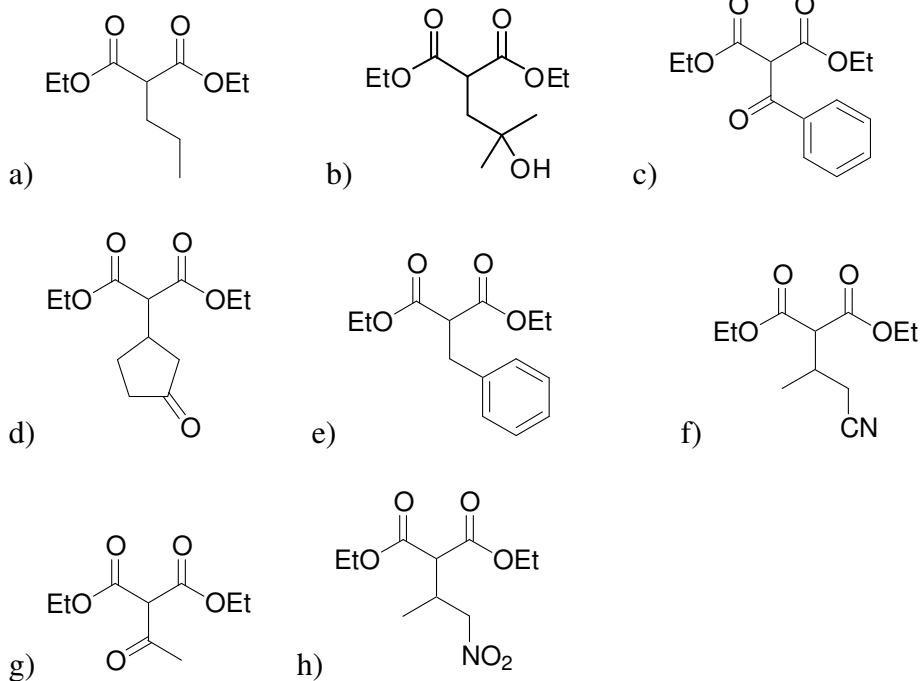


22.94.

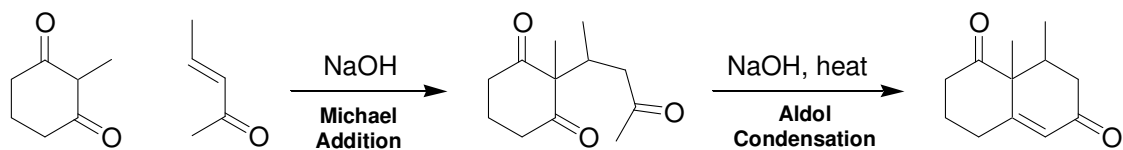




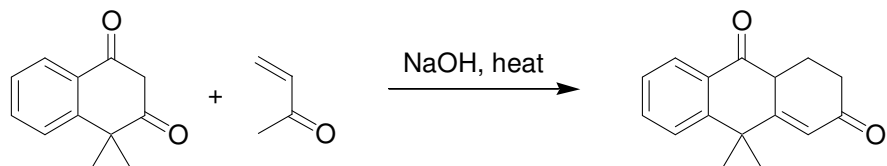
22.95.



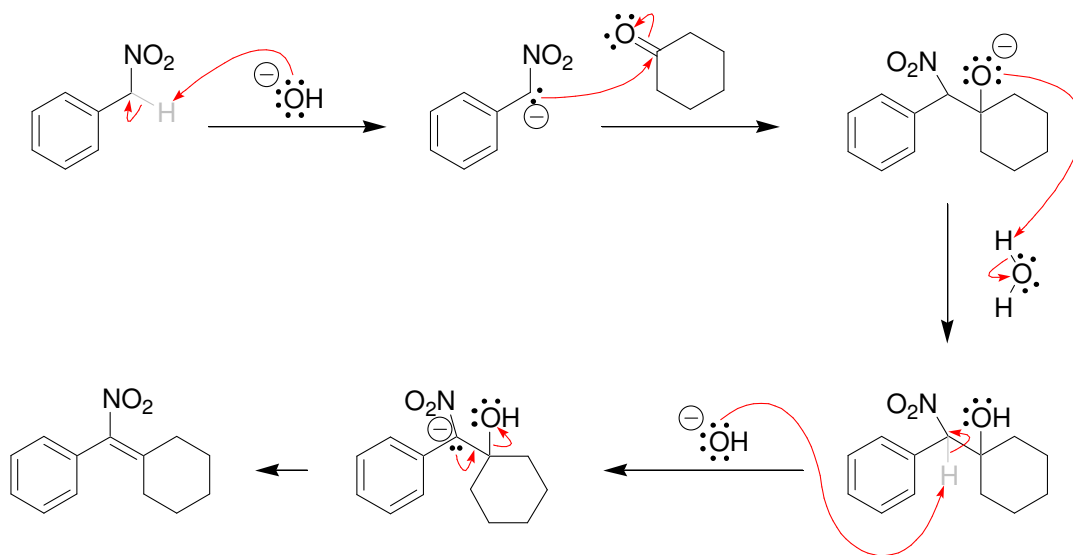
22.96.



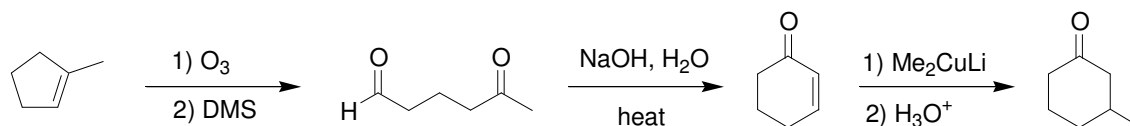
22.97.



22.98.

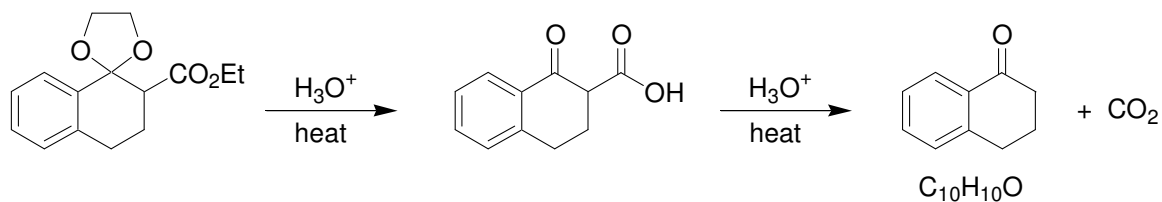


22.99.



22.100. A ketone generally produces a strong signal at approximately 1720 cm^{-1} ($\text{C}=\text{O}$ stretching), while an alcohol produces a broad signal between 3200 and 3600 cm^{-1} ($\text{O}-\text{H}$ stretching). These regions of an IR spectrum can be inspected to determine whether the ketone or the enol predominates.

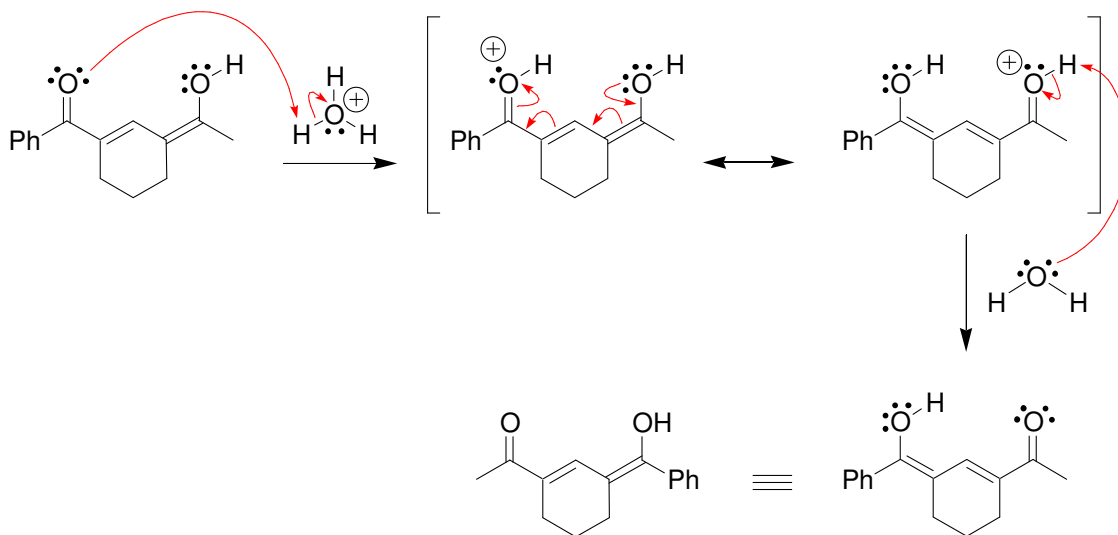
22.104.



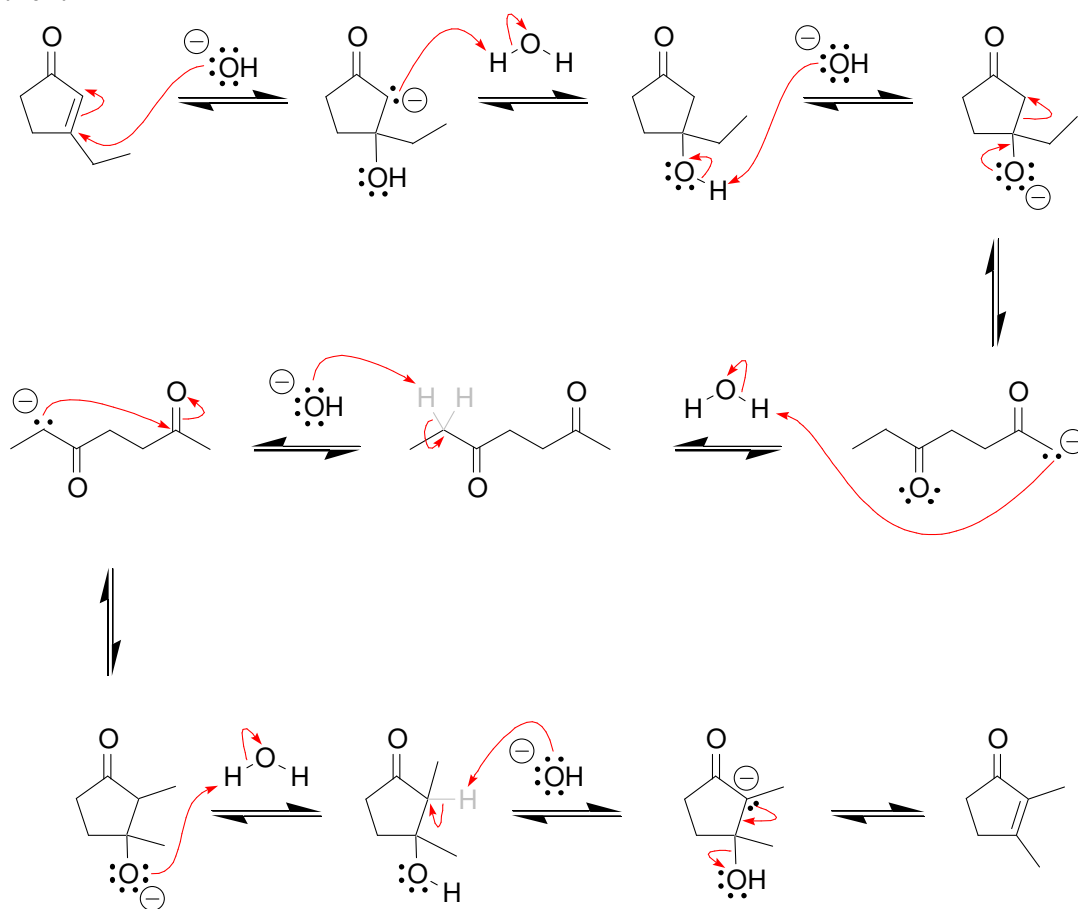
22.105.

When treated with aqueous acid, both compound A and compound B undergo racemization at the α position (via the enol as an intermediate, see problem 22.65). Each of these compounds establishes an equilibrium between *cis* and *trans* isomers. But the position of equilibrium is very different for compound A than it is for compound B. The equilibrium for compound A favors a *cis* configuration, because that is the configuration for which the compound can adopt a chair conformation in which both groups occupy equatorial positions. The equilibrium for compound B favors a *trans* configuration, because that is the configuration for which that compound can adopt a chair conformation in which both groups occupy equatorial positions.

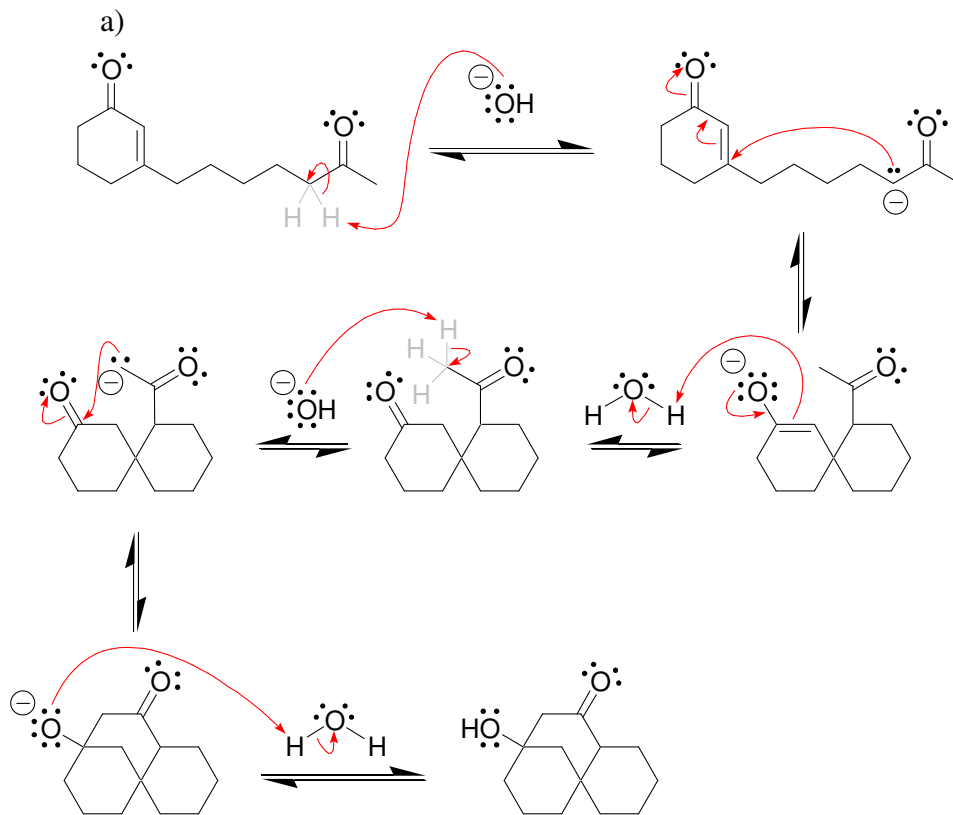
22.106.

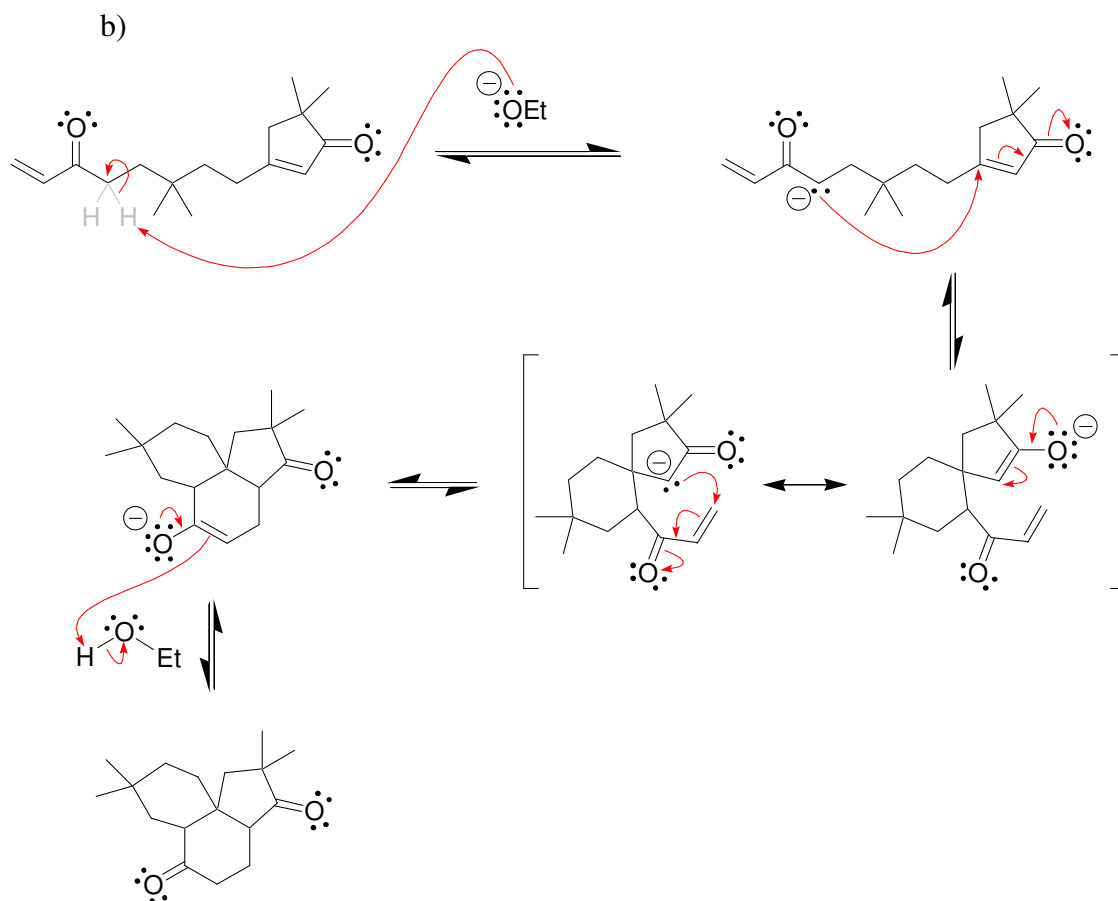


22.107.



22.108.





22.109. Direct alkylation would require performing an $\text{S}_{\text{N}}2$ reaction on a tertiary substrate, which will not occur. Instead the enolate would function as a base and $\text{E}2$ elimination would be observed instead of $\text{S}_{\text{N}}2$. The desired transformation can be achieved via a crossed aldol condensation, followed by a Michael addition:

