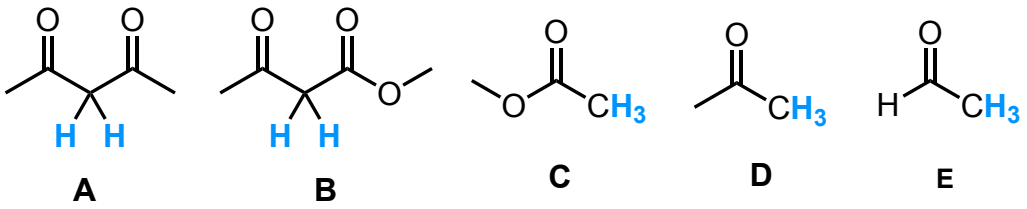
1. **Rank α C—H atoms** in each of the carbonyl compounds below **in order of increasing acidity**. Provide a brief explanation of your order.



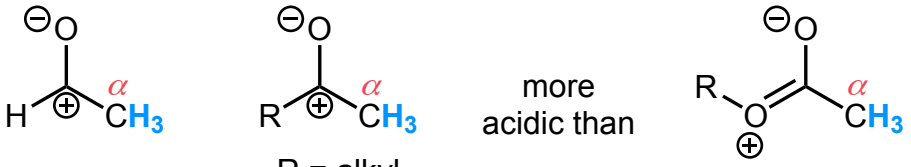
A **B** **C** **D** **E**

least acidic | **C** | **D** | **E** | **B** | **A** | **most acidic**

Explanation:

Aldehydes have more acidic α hydrogens than ketones which have more acidic α hydrogens than esters. This is due to a combination of inductive and resonance effects:

resonance structures of

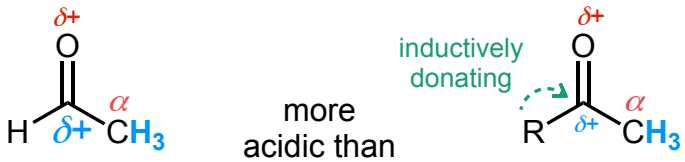


aldehyde (**E**) | ketone (**D**) | more acidic than | ester (**C**)

R = alkyl

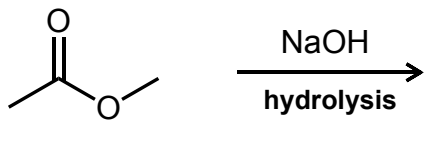
Since there is a full positive charge on the carbonyl carbon in the 2nd best resonance structures of the aldehyde (**E**) and the ketone (**D**), these species will have a more acidic α hydrogens than esters (**C**).

When comparing the acidity of an aldehyde (**E**) to a ketone (**D**), we conclude the α hydrogens of an aldehyde are more acidic than those of a ketone, because alkyl groups (in the ketone) are inductively donating, and reduce the size of the partial positive charge on the carbonyl carbon.



aldehyde (**E**) | ketone (**D**)

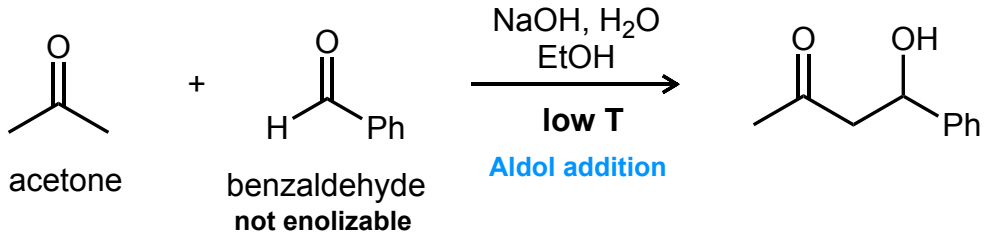
2. **In Claisen condensations**, the alkoxide base $^{1-}$OR is usually selected so that it is identical to the OR group of the ester. **What would be the product of the reaction below**, in which hydroxide is used instead of methoxide



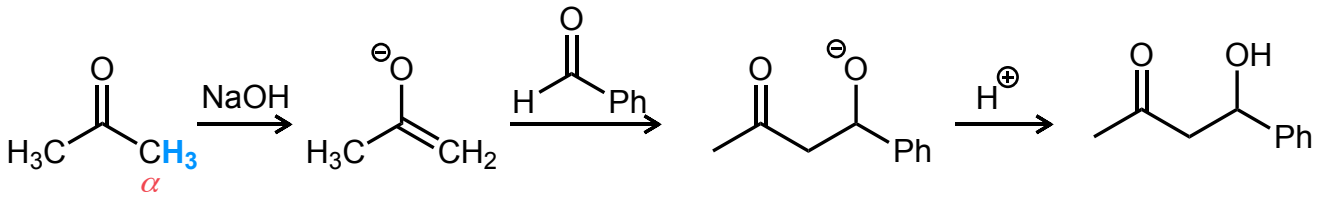
Note: under basic conditions, the carboxylic acid will be deprotonated to form the carboxylate

3. In each of the reactions below, two carbonyl compounds are present. However, **each reaction is selective for the formation of only one product**. **Describe why** we only observe one major product in each reaction.

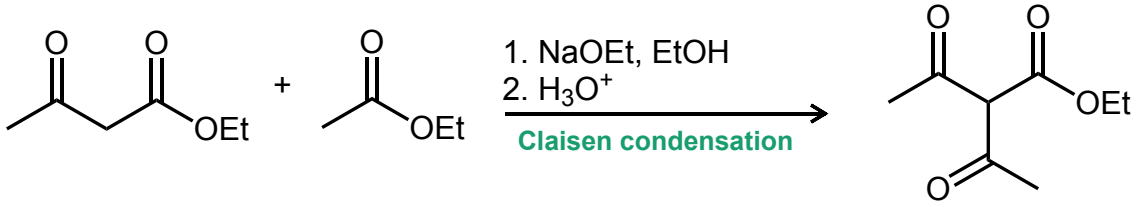
A.



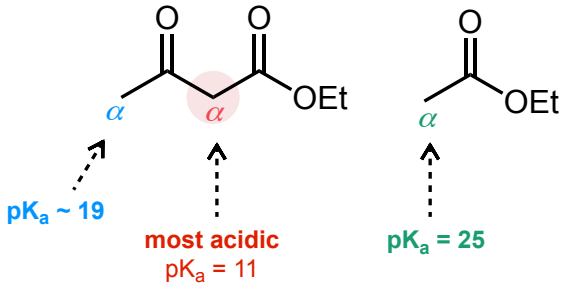
The reaction cannot product another addition product since only acetone is enolizable (has α hydrogens). Benzaldehyde contains no α hydrogens. Therefore, only acetone can form an enolate and be a nucleophile for the addition reaction to benzaldehyde as the electrophile.



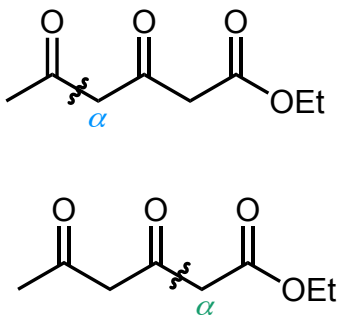
B.



Even though both the esters above are enolizable (have α hydrogens), we observe the formation of only one acylation product due to **the high acidity of the hydrogens that are α to both carbonyls**

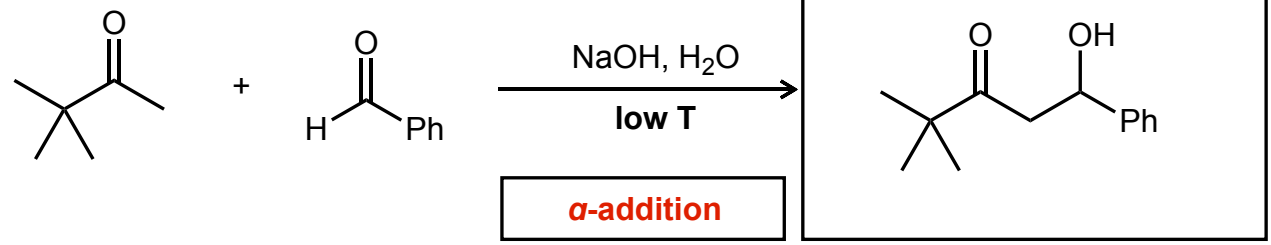


Potential products that are **not observed:**

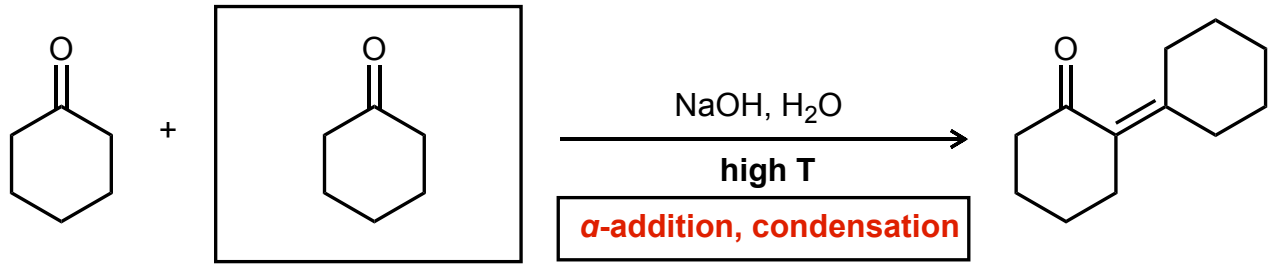


4. Provide the missing **electrophile** or **reaction product** in each scheme below. In each case, **assign the reaction** as an ***α*-alkylation**, ***α*-addition/condensation**, or ***α*-acyl substitution** proccess.

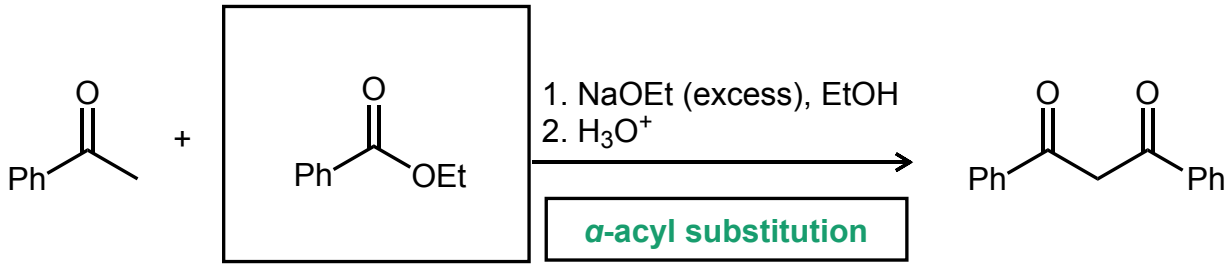
A.



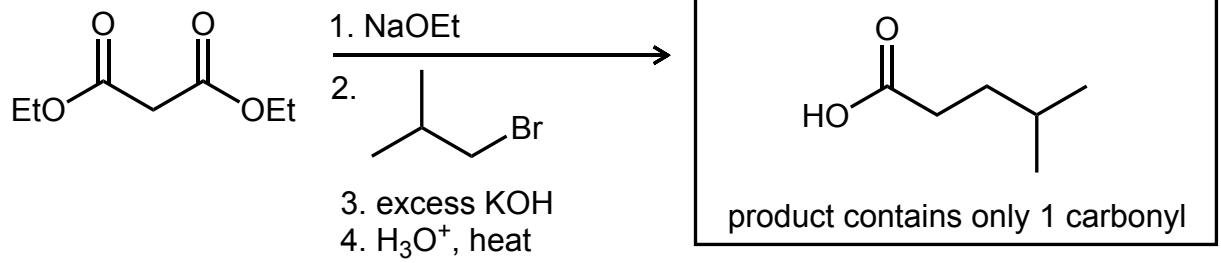
B.



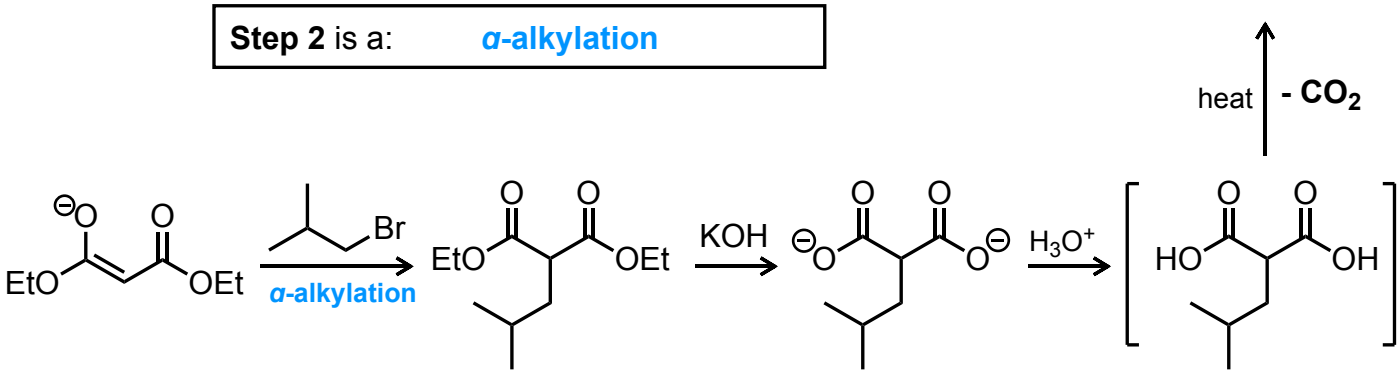
C.



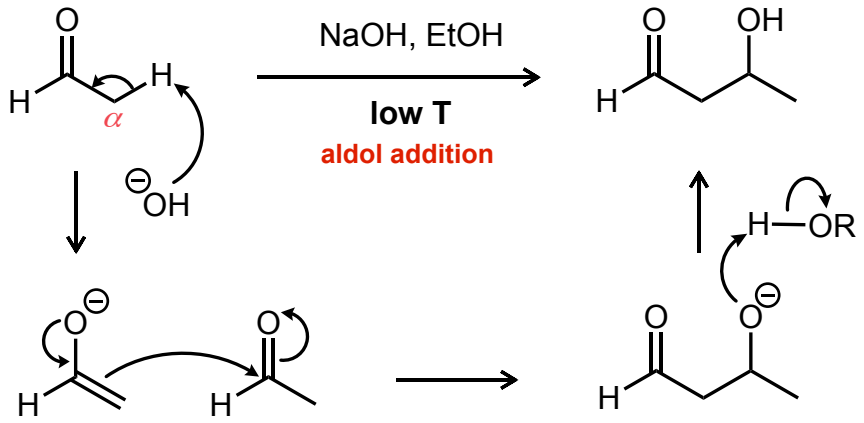
D.



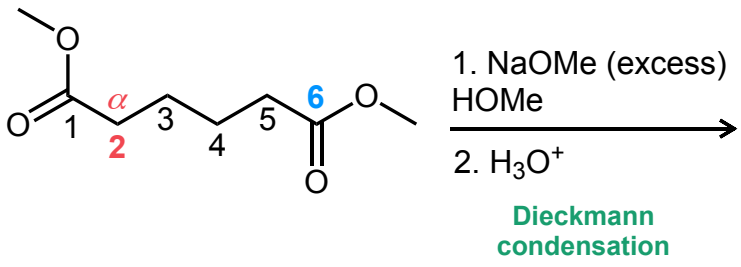
Step 2 is a: ***α*-alkylation**

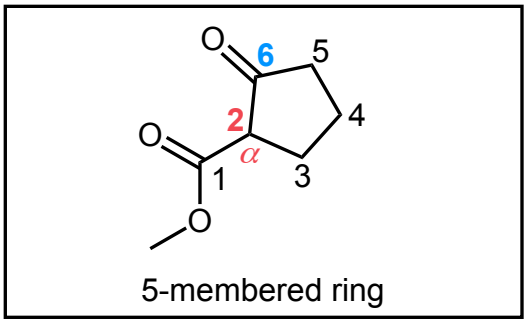


5. **Provide the curved-arrow mechanism** and **product** for the **aldol addition** between two molecules of acetaldehyde.

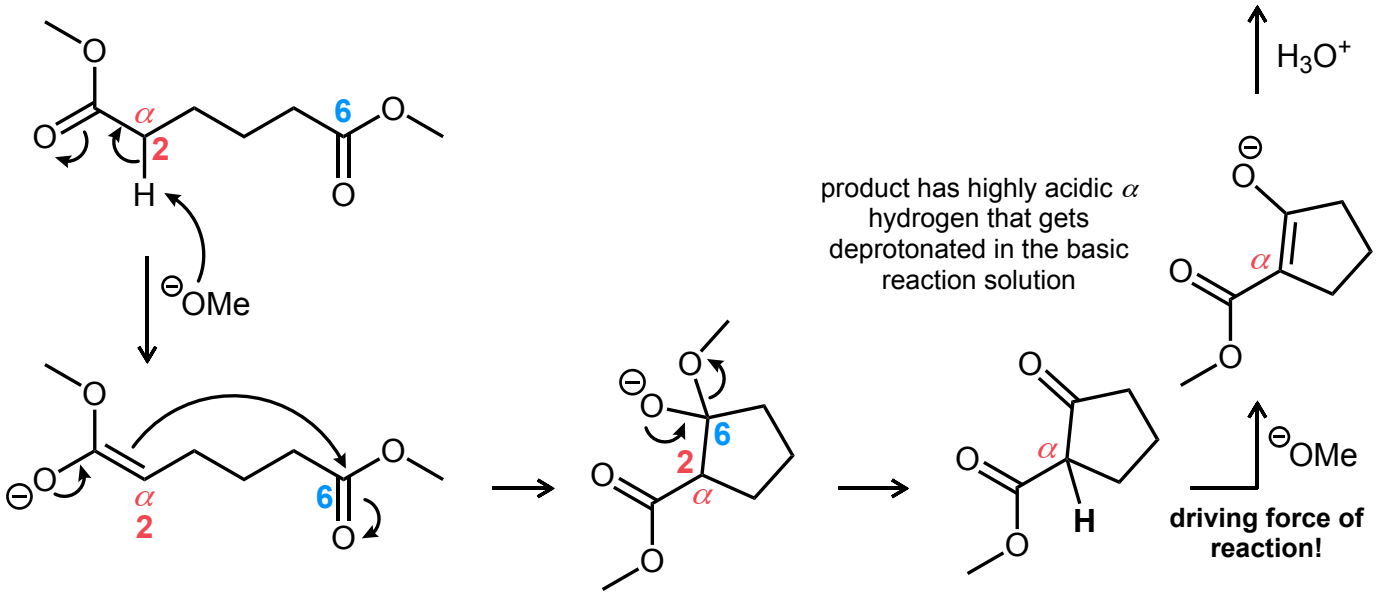


6. **Provide the major product** of the intramolecular Claisen condensation reaction below, also known as the Dieckmann condensation. Then, **draw the curved-arrow mechanism** for its formation.

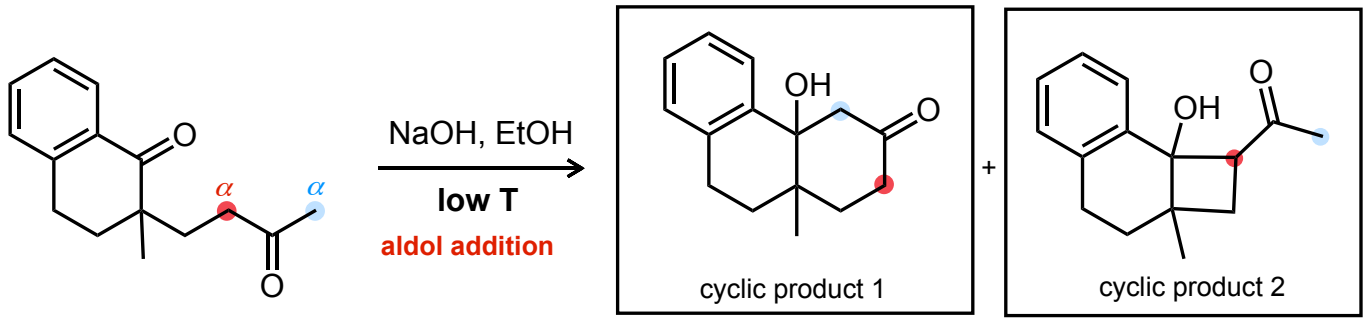




Curved-arrow mechanism



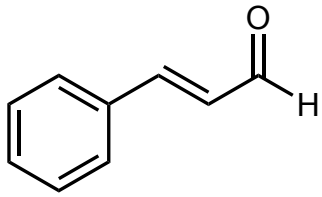
7. In the diketone below, multiple sites are enolizable. Therefore, two potential cyclic products can form from an **aldol addition** reaction. **Draw the potential product of each enolizable site reacting with the ketone in the molecule**. Then, **identify** which product is the **major product** of the reaction.



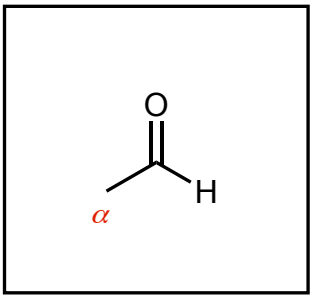
The major product in the reaction is the 6-membered ring. Commonly, intramolecular reactions that form rings work best for the formation of unstrained rings, such 5- and 6-membered rings.

8. Each product below can be formed through one of the reactions described in the associated Core Concept Sheet. **Propose** the structures of the **two starting materials** and **determine which reaction** would form the product shown (alkylation, Aldol addition, Aldol condensation, or Claisen condensation)

A.



Aldol condensation



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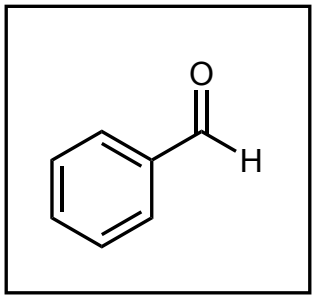
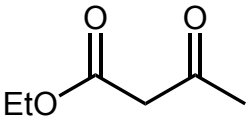
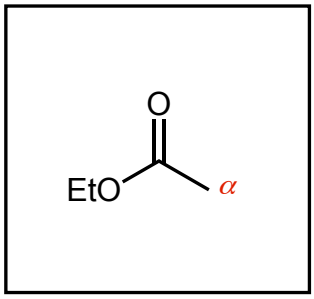


B.



Claisen condensation



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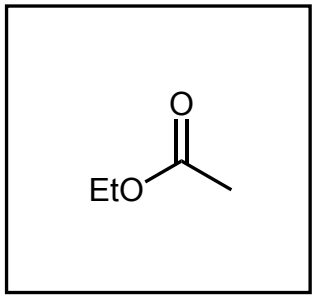

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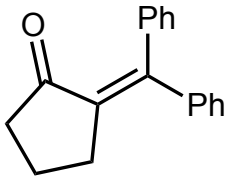
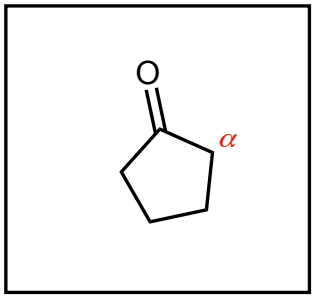


Aldol condensation



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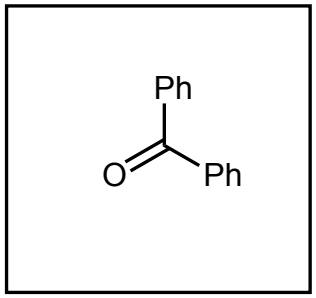
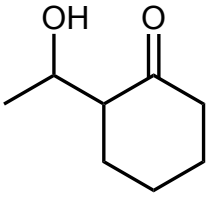
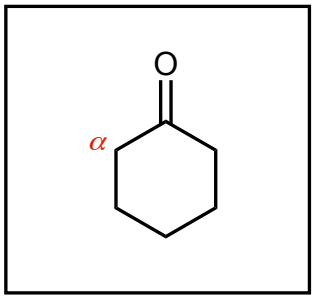


D.



Aldol addition



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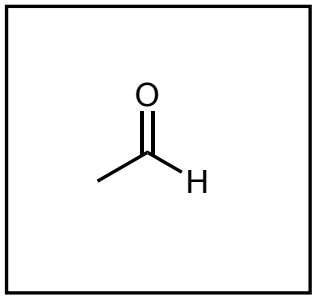
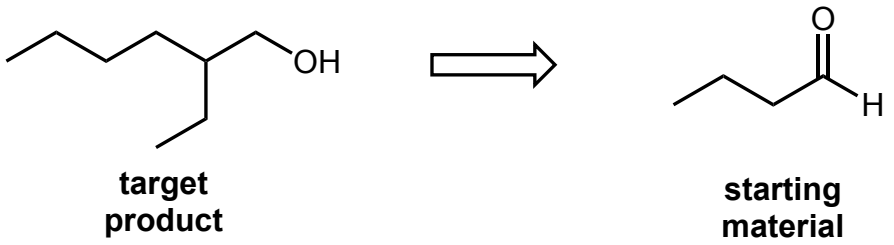
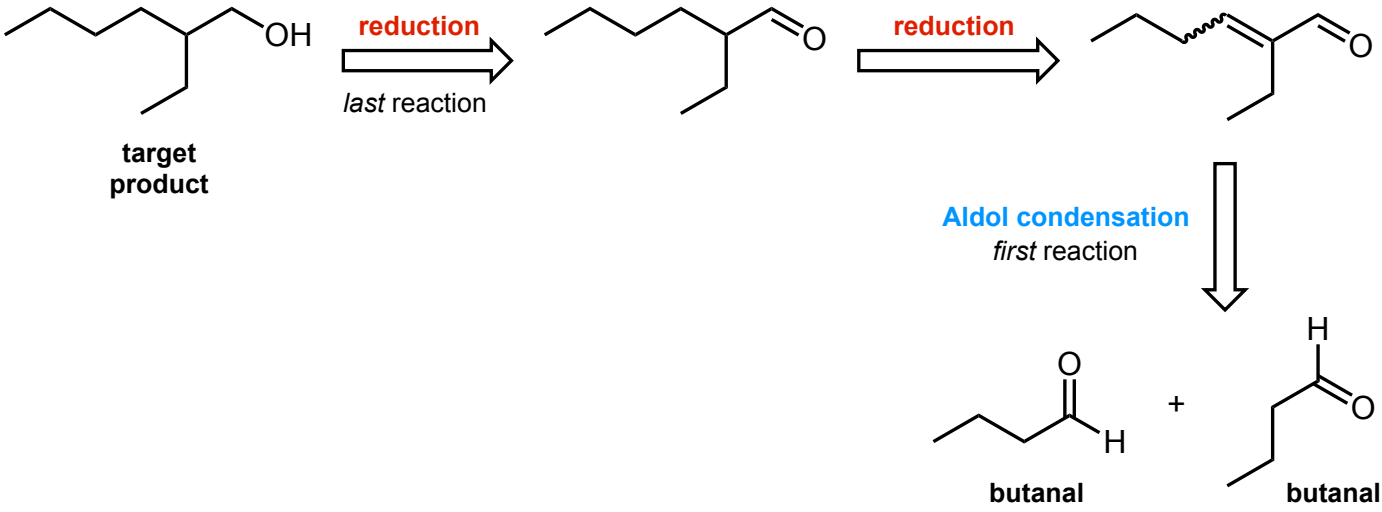


9. **Perform a retrosynthetic analysis** on the target product and **propose a full forward synthesis** of the product from the given starting material.



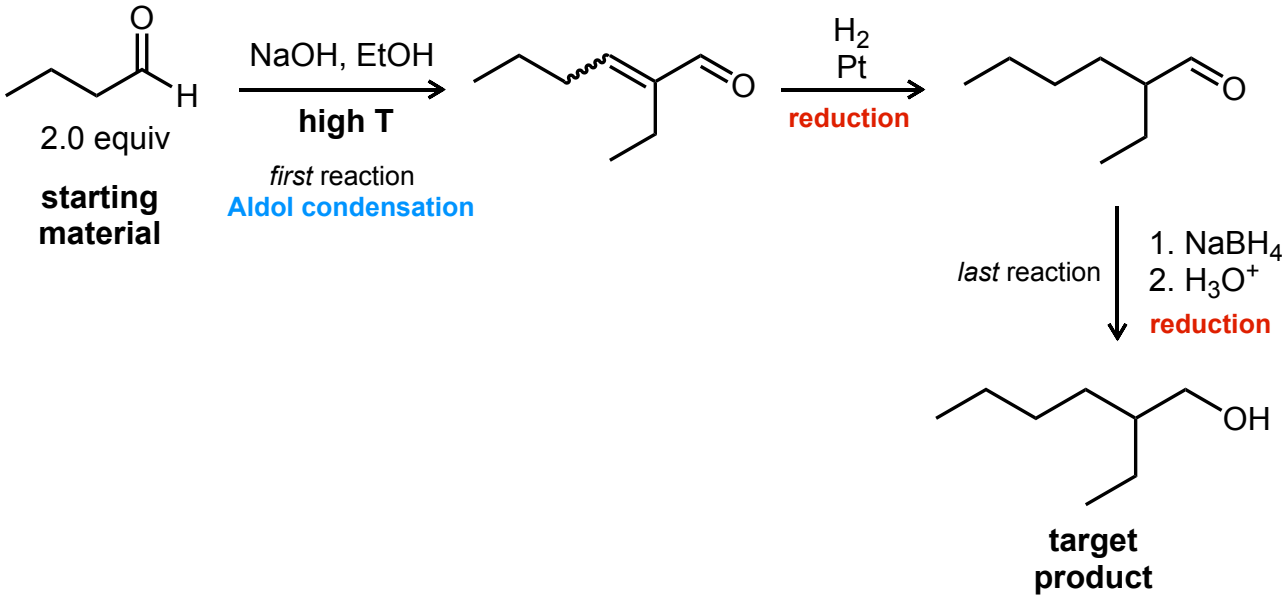
target product **starting material**

Retrosynthesis



target product **butanal** **butanal**

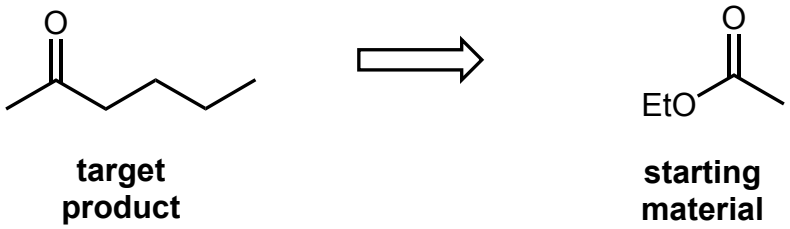
Forward Synthesis



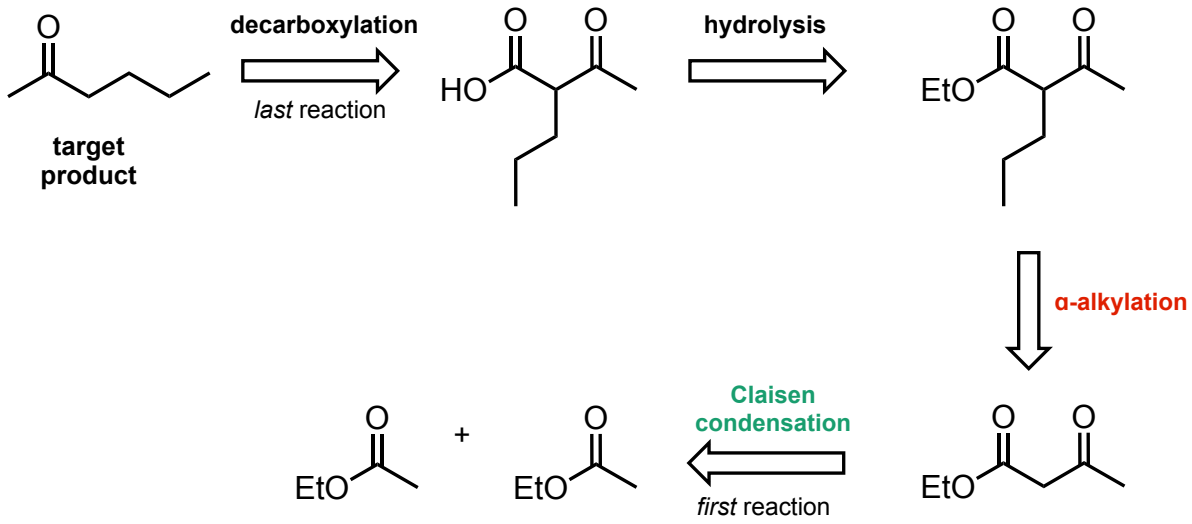
starting material **target product**

10. **Perform a retrosynthetic analysis** on the target product and **propose a full forward synthesis** of the product from the given starting material.

Hint: the *last* step is a decarboxylation.



Retrosynthesis



Forward Synthesis