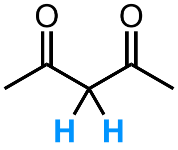
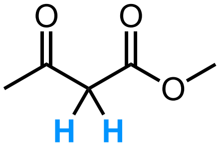
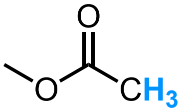
1. **Rank α C—H atoms** in each of the carbonyl compounds below **in order of increasing acidity**. Provide a brief explanation of your order.



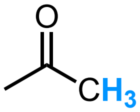
A



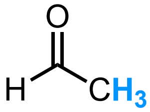
B



C



D



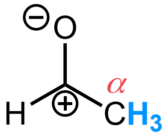
E

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

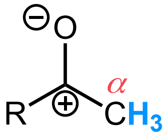
Explanation:

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



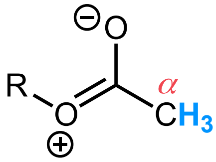
aldehyde
(**E**)



R = alkyl

ketone
(**D**)

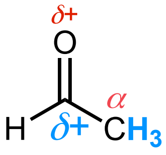
more
acidic than



ester
(**C**)

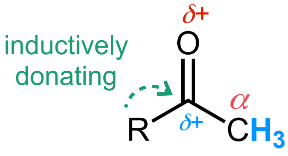
Since there is a full positive charge on the carbonyl carbon in the 2nd best resonance structures of the aldehyde (**E**) and the ketone (**D**), these species will have a more acidic α hydrogens than esters (**C**).

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**)

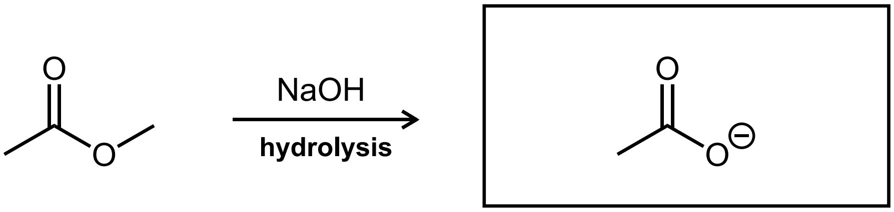
more
acidic than



R = alkyl

ketone
(**D**)

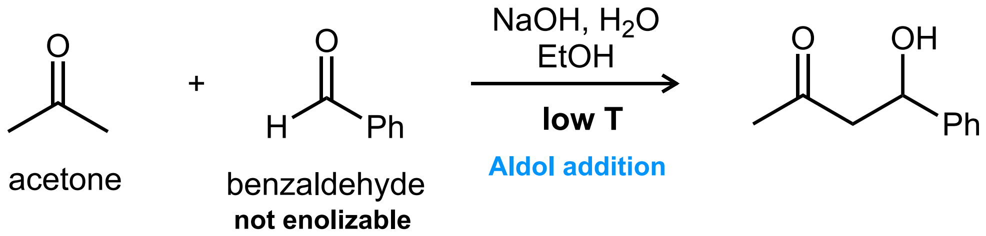
2. **In Claisen condensations**, the alkoxide base $^{1-}$OR is usually selected so that it is identical to the OR group of the ester. **What would be the product of the reaction below**, in which hydroxide is used instead of methoxide



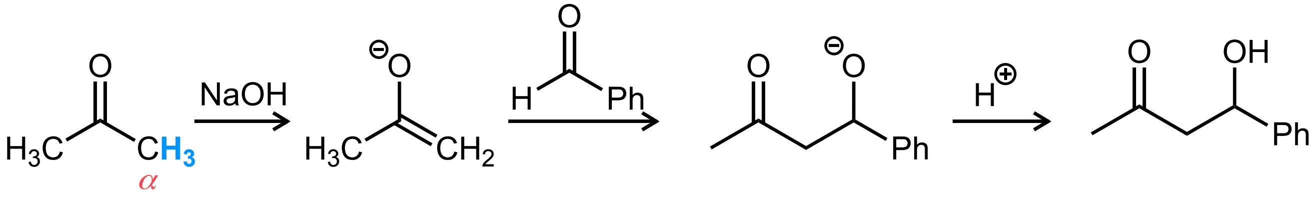
Note: under basic conditions, the carboxylic acid will be deprotonated to form the carboxylate

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.

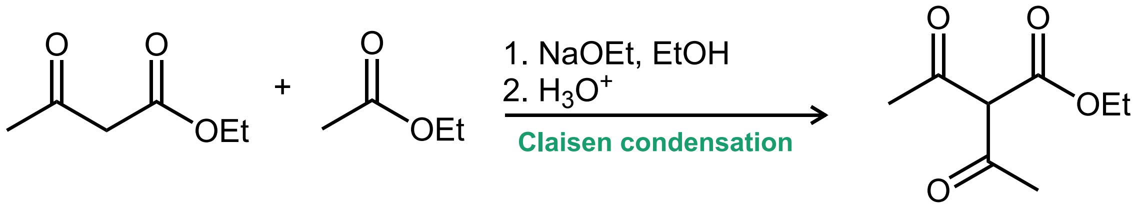
A.



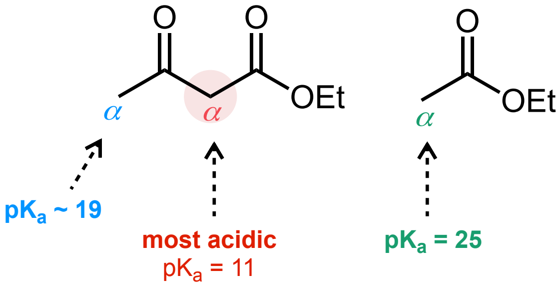
The reaction cannot product another addition product since only acetone is enolizable (has α hydrogens). Benzaldehyde contains no α hydrogens. Therefore, only acetone can form an enolate and be a nucleophile for the addition reaction to benzaldehyde as the electrophile.



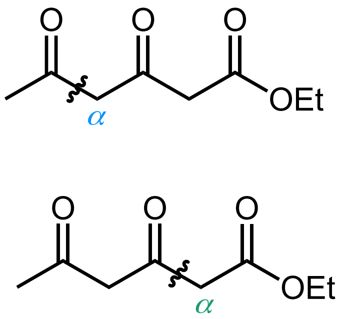
B.



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**

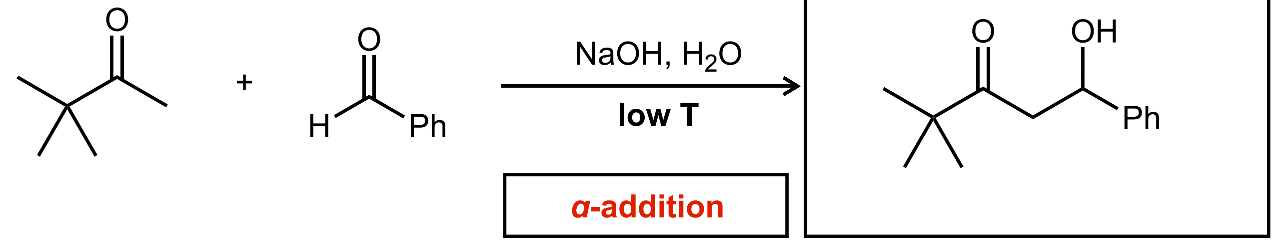


Potential products that are **not observed:**



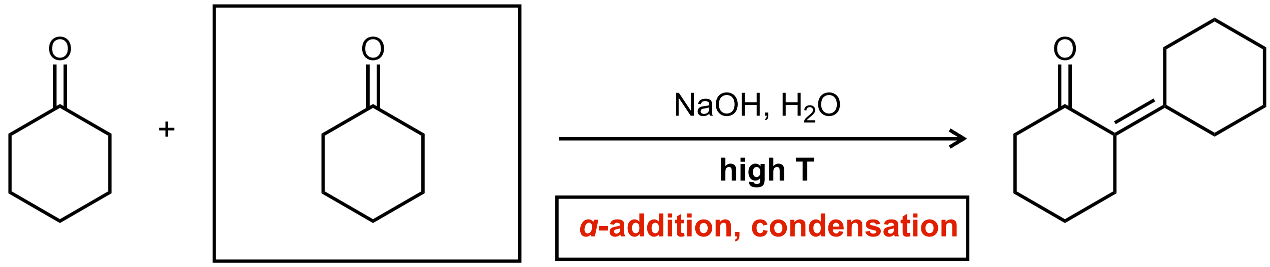
4. Provide the missing **electrophile** or **reaction product** in each scheme below. In each case, **assign the reaction** as an ***α*-alkylation**, ***α*-addition/condensation**, or ***α*-acyl substitution** proccess.

A.



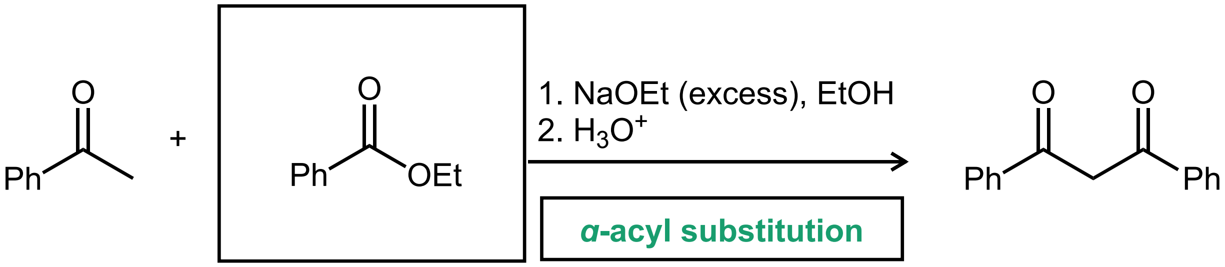
***α*-addition**

B.



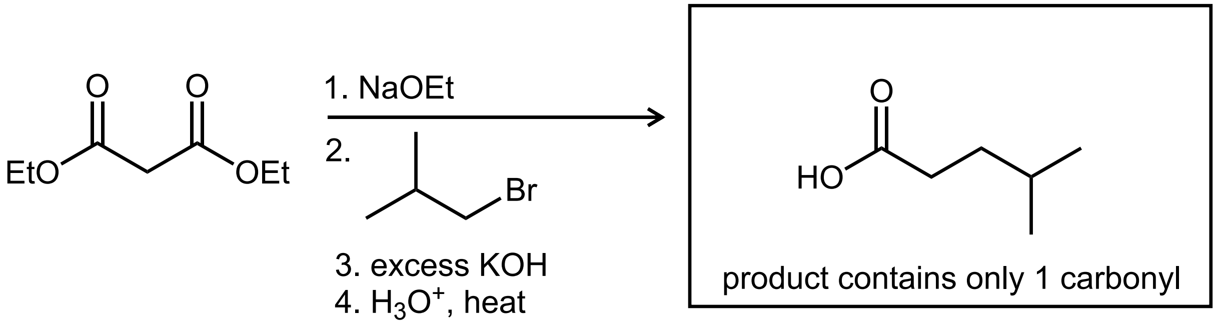
***α*-addition, condensation**

C.



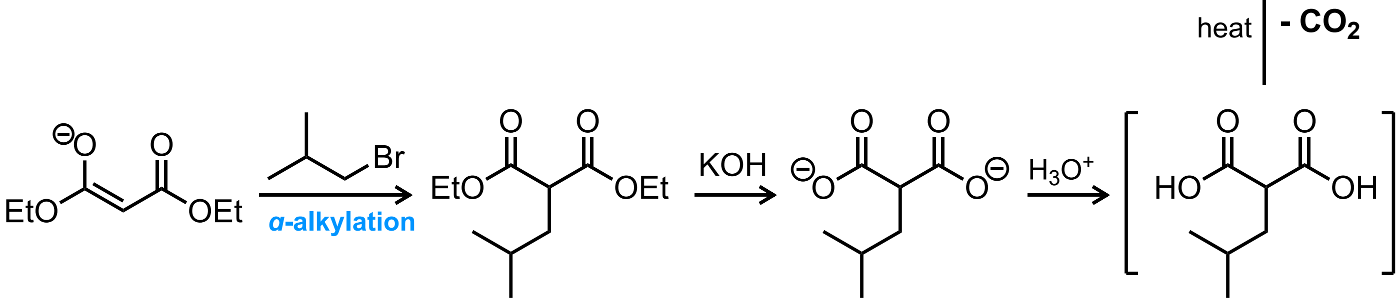
***α*-acyl substitution**

D.

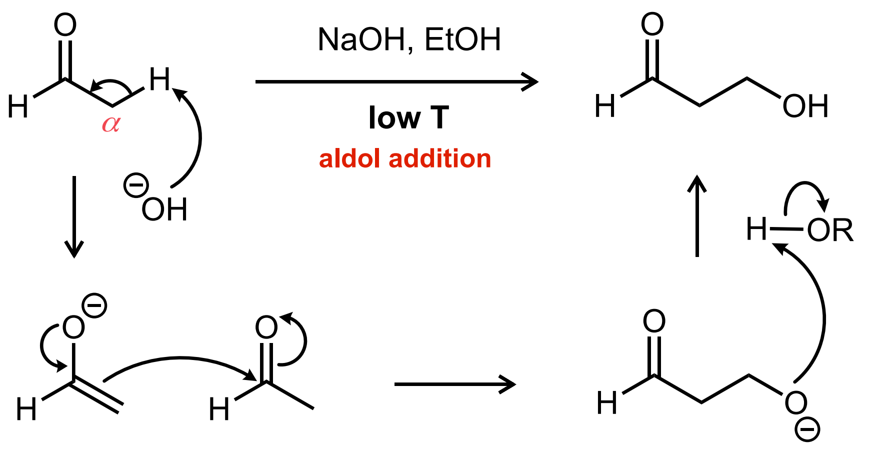


product contains only 1 carbonyl

Step 2 is a: ***α*-alkylation**

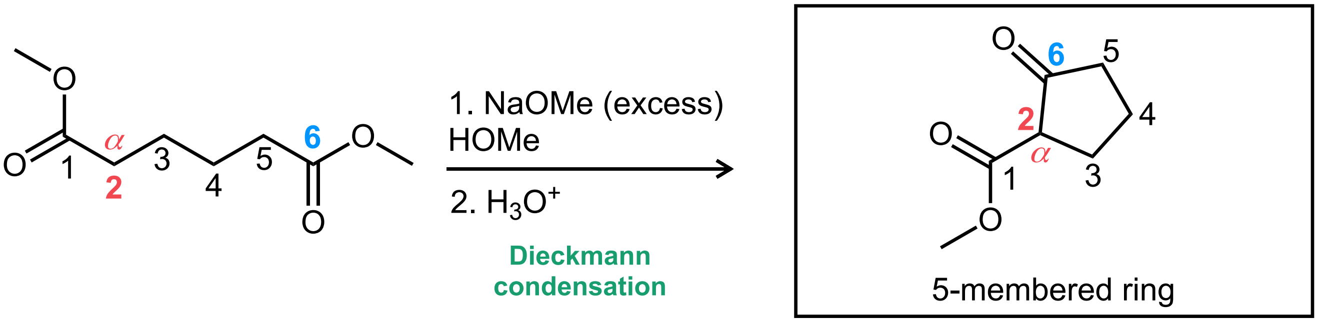


5. **Provide the curved-arrow mechanism** and **product** for the **aldol addition** between two molecules of formaldehyde.

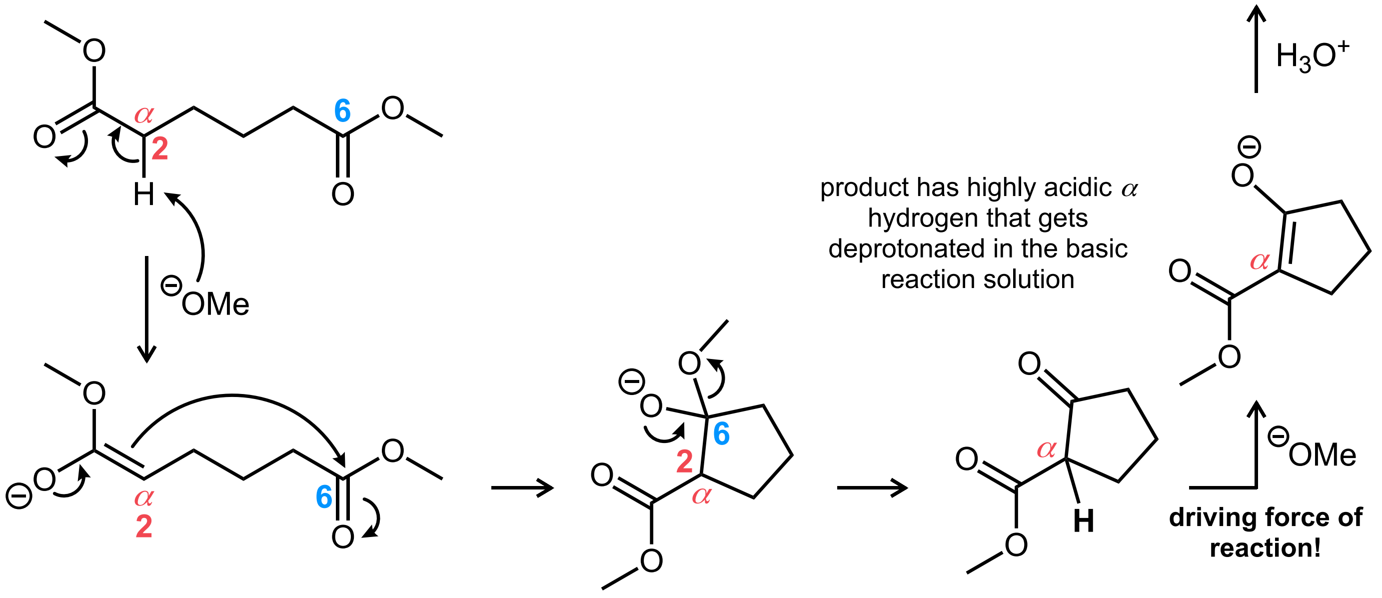


α

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.



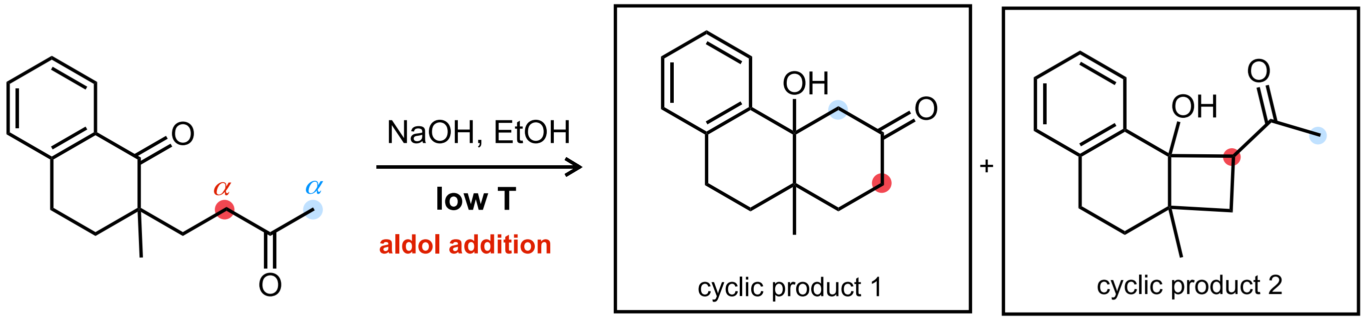
Curved-arrow mechanism



product has highly acidic α hydrogen that gets deprotonated in the basic reaction solution

driving force of reaction!

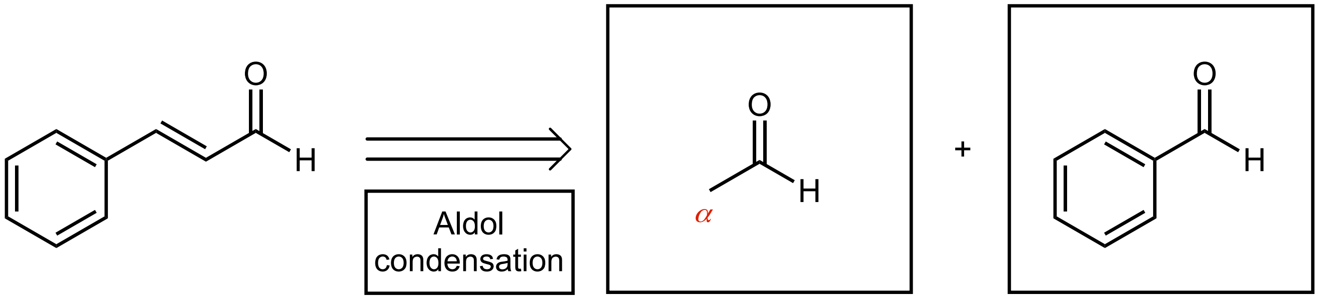
7. In the diketone below, multiple sites are enolizable. Therefore, two potential cyclic products can form from an **aldol addition** reaction. **Draw the potential product of each enolizable site reacting with the ketone in the molecule**. Then, **identif**y which product is the **major product** of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

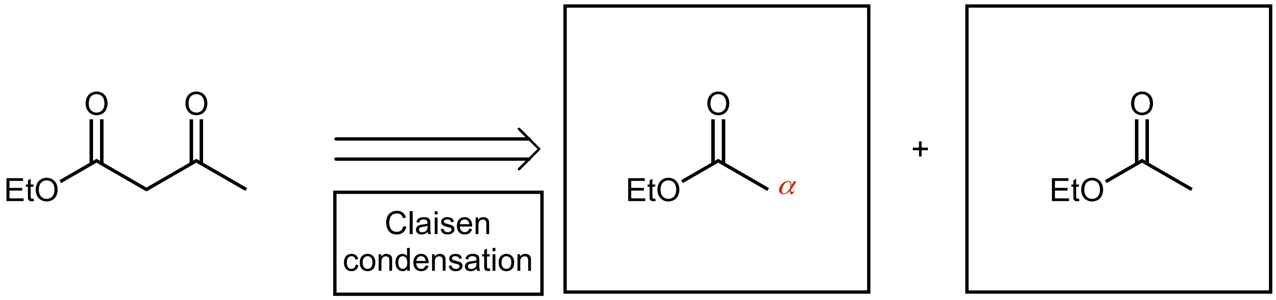
8. Each product below can be formed through one of the reactions described in the associated Core Concept Sheet. **Propose** the structures of the **two starting materials** and **determine which reaction** would form the product shown (alkylation, Aldol addition, Aldol condensation, or Claisen condensation)

A.



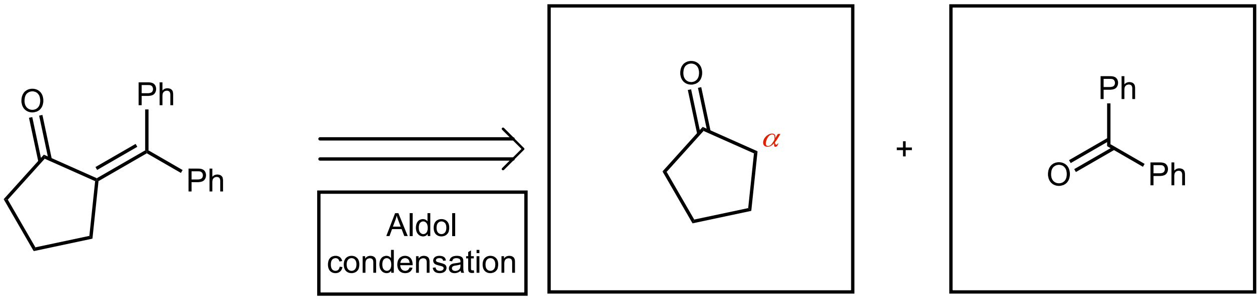
Aldol condensation

B.



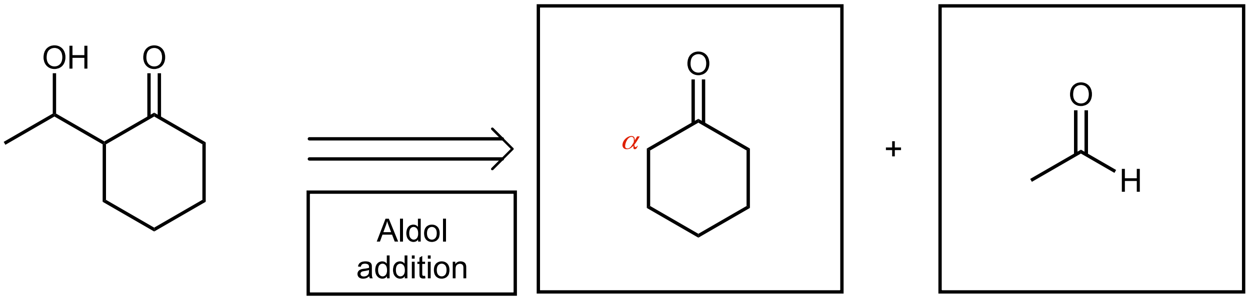
Claisen condensation

C.



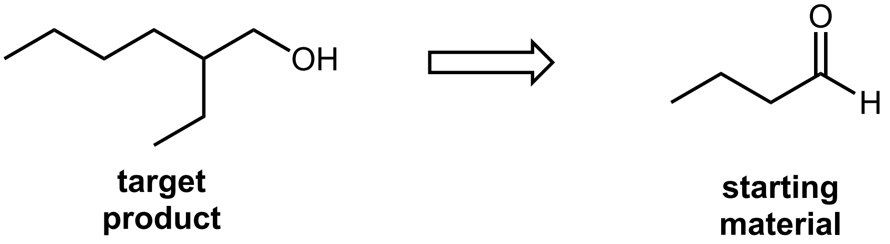
Aldol condensation

D.

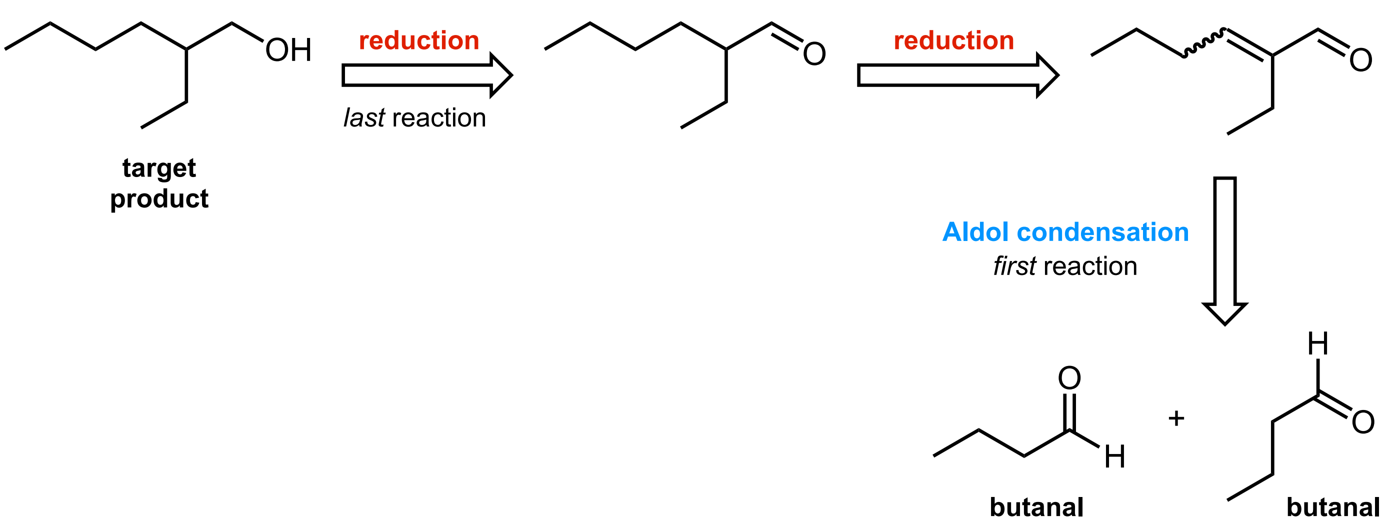


Aldol addition

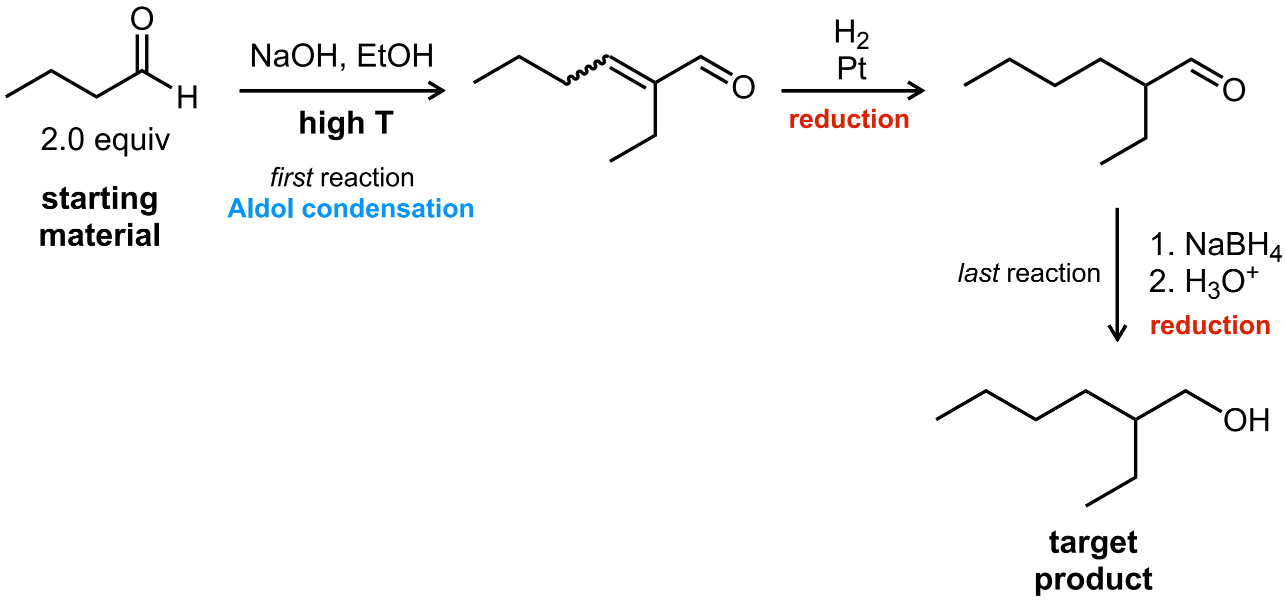
9. **Perform a retrosynthetic analysis** on the target product and **propose a full forward synthesis** of the product from the given starting material.



Retrosynthesis

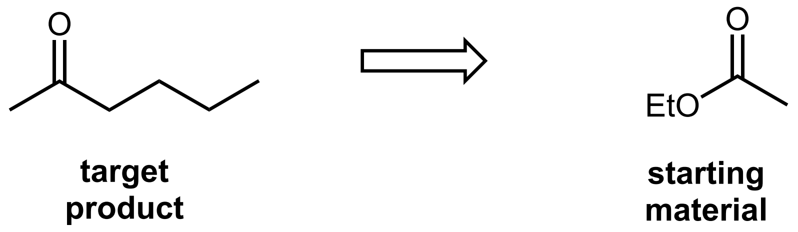


Forward Synthesis

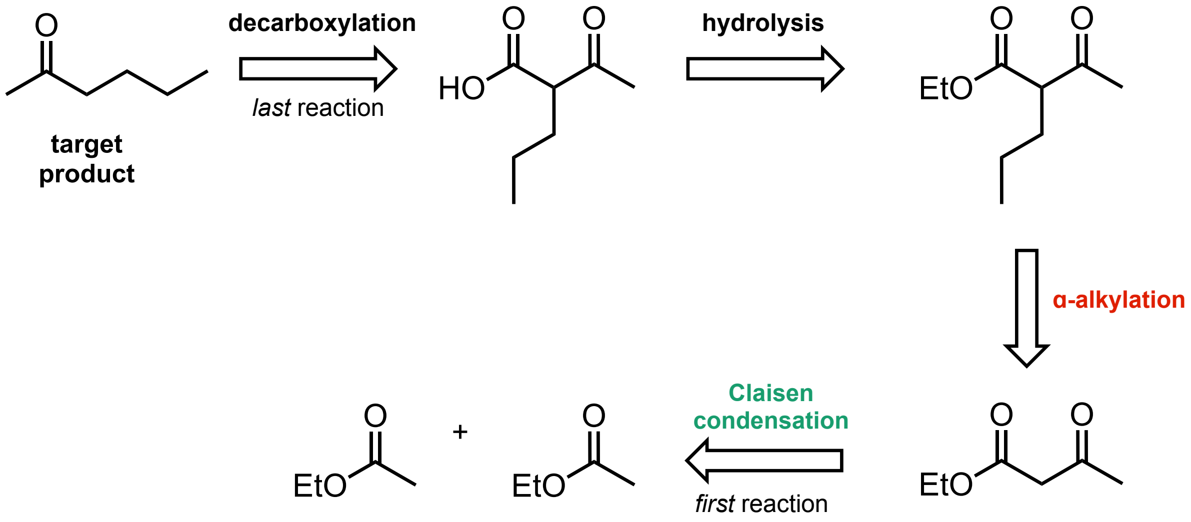


10. **Perform a retrosynthetic analysis** on the target product and **propose a full forward synthesis** of the product from the given starting material.

Hint: the *last* step is a decarboxylation.



Retrosynthesis



Forward Synthesis