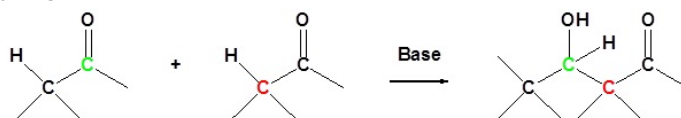


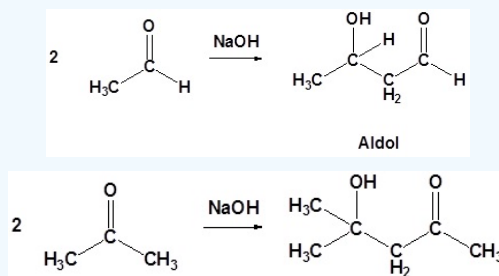
## 23.8: THE ALDOL REACTION AND CONDENSATION OF KETONES AND ALDEHYDES

A useful carbon-carbon bond-forming reaction known as the **Aldol Reaction** is yet another example of electrophilic substitution at the alpha carbon in enolate anions. The fundamental transformation in this reaction is a dimerization of an aldehyde (or ketone) to a beta-hydroxy aldehyde (or ketone) by alpha C-H addition of one reactant molecule to the carbonyl group of a second reactant molecule. Due to the carbanion like nature of enolates they can add to carbonyls in a similar manner as Grignard reagents. For this reaction to occur at least one of the reactants must have alpha hydrogens.



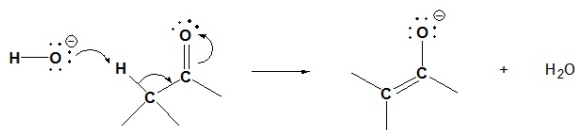
The aldol reactions for acetaldehyde and acetone are shown as examples.

### Example: Aldol Reactions

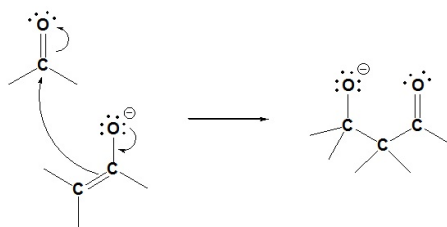


### ALDOL REACTION MECHANISM

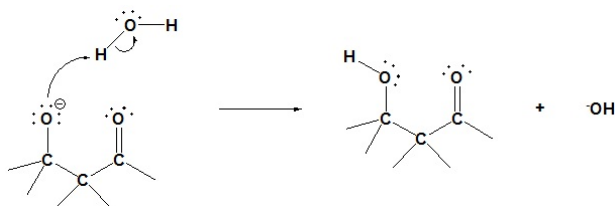
Step 1: Enolate formation



Step 2: Nucleophilic reaction by the enolate



Step 3: Protonation



### ALDOL CONDENSATION: THE DEHYDRATION OF ALDOL PRODUCTS TO SYNTHESIZE A, B UNSATURATED CARBONYLS (ENONES)

The products of aldol reactions often undergo a subsequent elimination of water, made up of an alpha-hydrogen and the beta-hydroxyl group. The product of this  **$\beta$ -elimination** reaction is an  $\alpha,\beta$ -unsaturated aldehyde or ketone. Base-catalyzed elimination occurs with heating. The additional stability provided by the conjugated carbonyl system of the product makes some aldol reactions thermodynamically driven

and mixtures of stereoisomers (*E* & *Z*) are obtained from some reactions. Reactions in which a larger molecule is formed from smaller components, with the elimination of a very small by-product such as water, are termed **Condensations**. Hence, the following examples are properly referred to as **aldol condensations**. Overall the general reaction involves a dehydration of an aldol product to form an alkene:

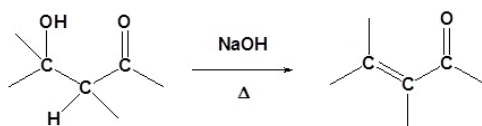


Figure: General reaction for an aldol condensation

Going from reactants to products simply

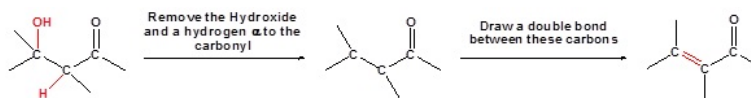
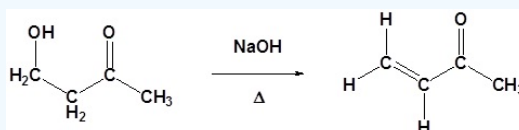


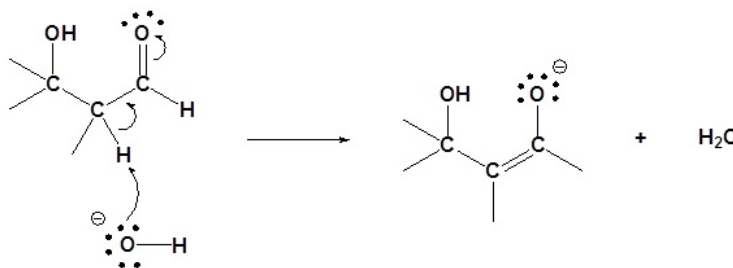
Figure: The aldol condensation example

### Example: Aldol Condensation from an Aldol Reaction Product

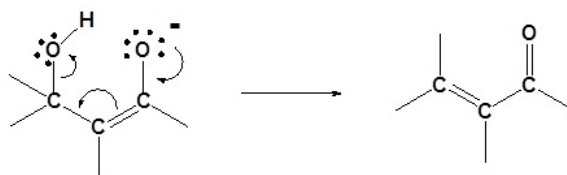


## ALDOL CONDENSATION BASE CATALYZED MECHANISM

1) Form enolate

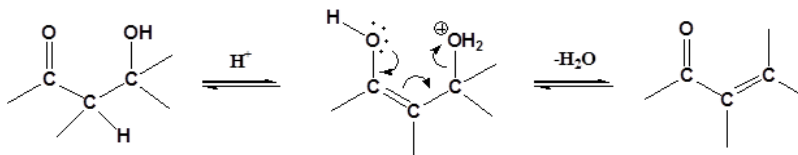


2) Form enone



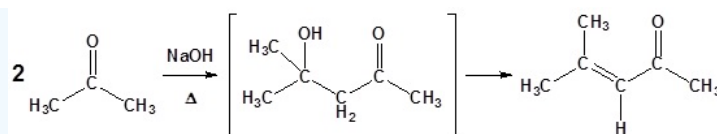
## ALDOL CONDENSATION ACID CATALYZED MECHANISM

Under acidic conditions an enol is formed and the hydroxy group is protonated. Water is expelled by either an E1 or E2 reaction.



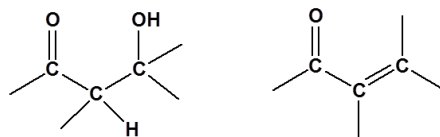
When performing both reactions together always consider the aldol product first then convert to the enone. Note! The double bond always forms in conjugation with the carbonyl.

### Example: Aldol Condensation Directly from the Ketones or Aldehydes



## ALDOL REACTIONS IN MULTIPLE STEP SYNTHESIS

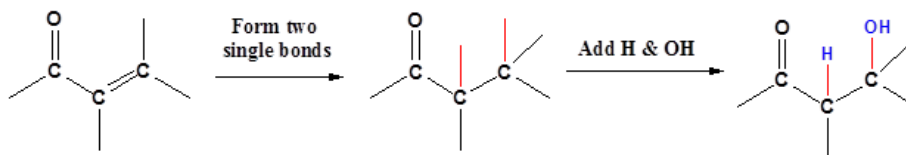
Aldol reactions are excellent methods for the synthesis of many enones or beta hydroxy carbonyls. Because of this, being able to predict when an aldol reaction might be used in a synthesis is an important skill. This is accomplished by mentally breaking apart the target molecule and then considering what the starting materials might be.



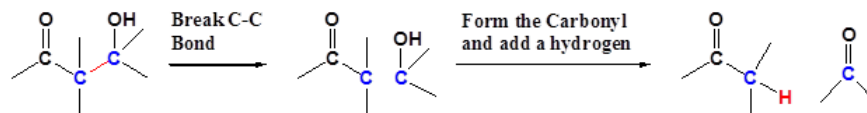
Fragments which are easily made by an aldol reaction

Steps to 'reverse' the aldol reaction (from the final aldol product towards identifying the starting compounds).

1) From an enone break the double bond and form two single bonds. Place an OH on the bond furthest from the carbonyl and an H on the bond closest to the carbonyl.

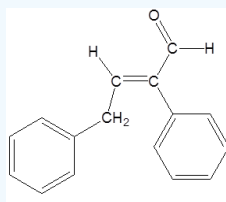


2) From the aldol product break the C-C bond between the alpha carbon and the carbon attached to the OH. Then turn the OH into a carbonyl and add an hydrogen to the other carbon.

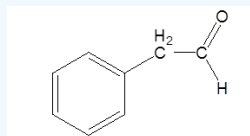


### Example: Determining the Reactant when given the Aldol Condensation Product

What reactant must be used to make the following molecule using an aldol condensation?



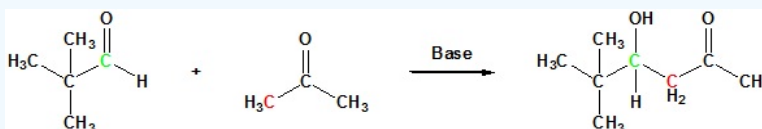
**Solution**



## MIXED ALDOL REACTIONS AND CONDENSATIONS

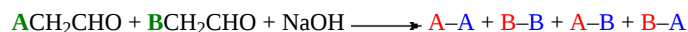
The previous examples of aldol reactions and condensations used a common reactant as both the enolic donor and the electrophilic acceptor. The product in such cases is always a dimer of the reactant carbonyl compound. Aldol condensations between different carbonyl reactants are called **crossed** or **mixed** reactions, and under certain conditions such crossed aldol condensations can be effective.

### Example: Mixed Aldol Reaction (One Product)

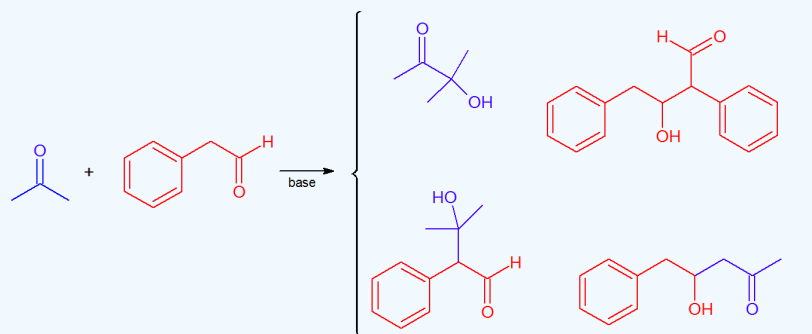


The success of these mixed aldol reactions is due to two factors. First, aldehydes are more reactive acceptor electrophiles than ketones, and formaldehyde is more reactive than other aldehydes. Second, aldehydes lacking alpha-hydrogens can only function as acceptor reactants, and this reduces the number of possible products by half. Mixed aldols in which both reactants can serve as donors and acceptors generally give complex mixtures of both dimeric (homo) aldols and crossed aldols. Because of this most mixed aldol reactions are usually not performed unless one reactant has no alpha hydrogens.

The following abbreviated formulas illustrate the possible products in such a case, red letters representing the acceptor component and blue the donor. If all the reactions occurred at the same rate, equal quantities of the four products would be obtained. Separation and purification of the components of such a mixture would be difficult.

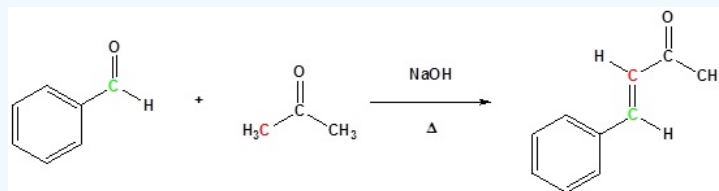


### Example: Products of a Mixed Aldol Reaction



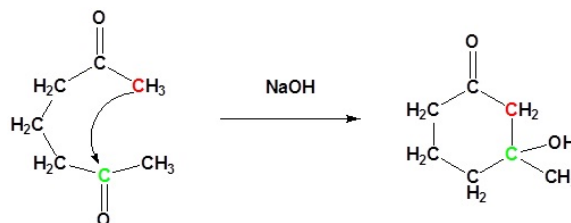
The aldol condensation of ketones with aryl aldehydes to form  $\alpha,\beta$ -unsaturated derivatives is called the **Claisen-Schmidt** reaction.

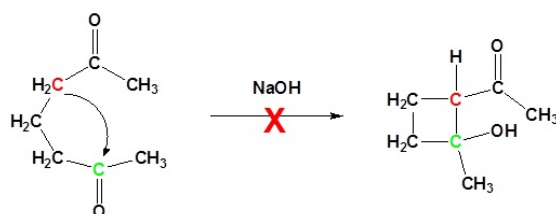
### Example: Claisen-Schmidt Reaction



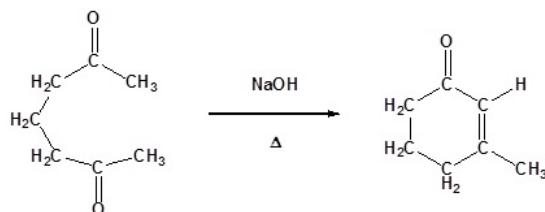
## INTRAMOLECULAR ALDOL REACTION

Molecules which contain two carbonyl functionalities have the possibility of forming a ring through an intramolecular aldol reaction. In most cases two sets of  $\alpha$  hydrogens need to be considered. As with most ring forming reaction five and six membered rings are preferred (less ring strain).



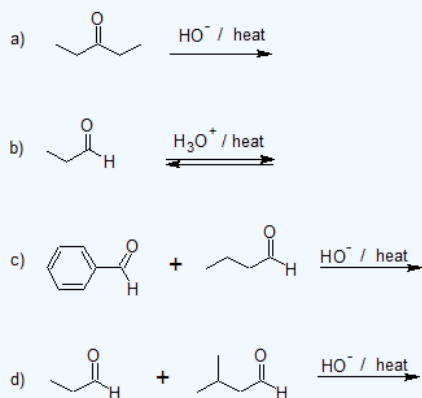


As with other aldol reaction the addition of heat causes an aldol condensation to occur.



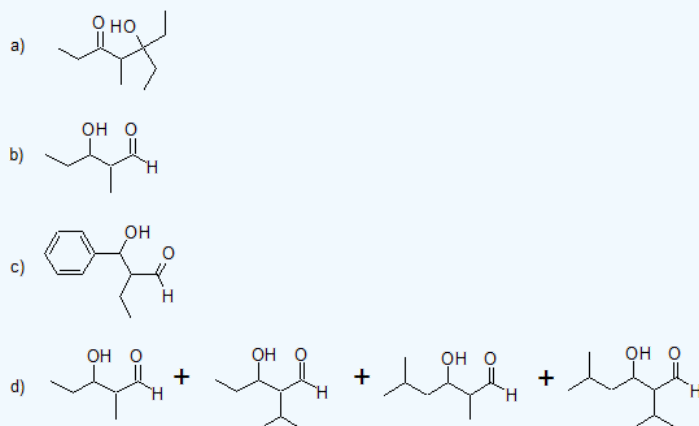
### Exercise

12. Draw the bond-line structures for the products of the reactions below. Note: One of the reactions is a poorly designed aldol condensation producing four different products.



Answer

12.



### CONTRIBUTORS AND ATTRIBUTIONS

- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, [Athabasca University](#))
- Prof. Steven Farmer ([Sonoma State University](#))
- William Reusch, Professor Emeritus ([Michigan State U.](#)), [Virtual Textbook of Organic Chemistry](#)

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