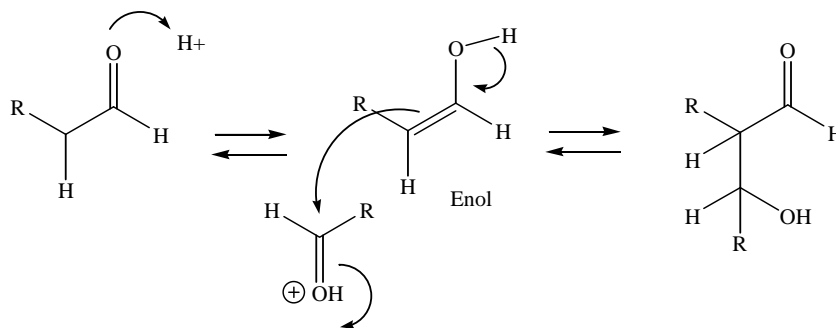


## Background Information

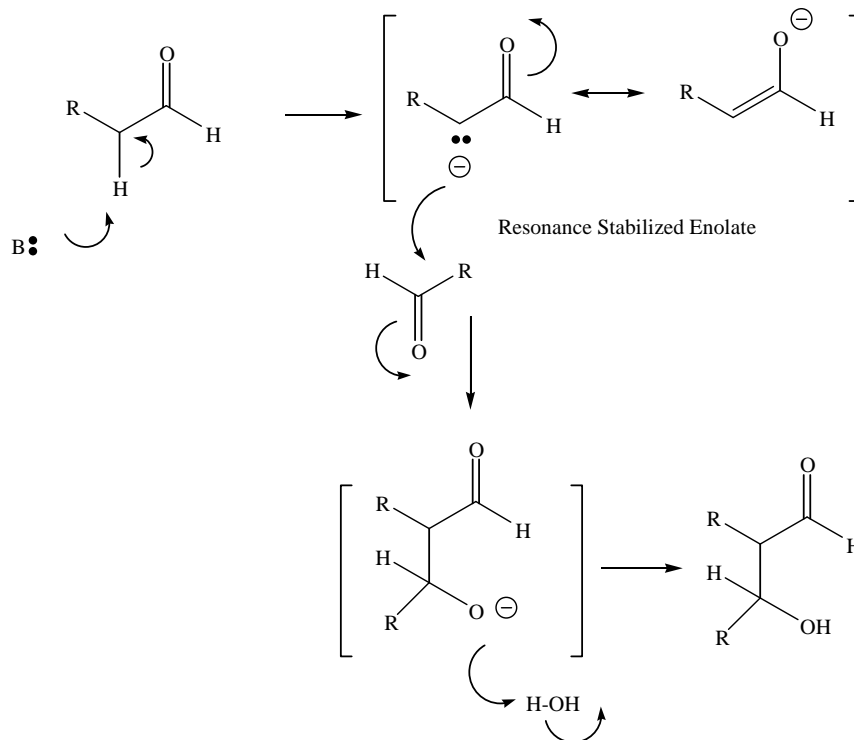
### Introduction to Condensation Reactions

Condensation reactions occur between the  $\alpha$ -carbon of one carbonyl-containing functional group and the carbonyl carbon of a second carbonyl-containing functional group. Aldehydes, ketones and esters are the three types of carbonyl-containing functional groups that most commonly undergo condensation reactions. The most common condensation reactions occur between two aldehydes (referred to as the aldol condensation), between an aldehyde and a ketone (referred to as a mixed aldol condensation) or between two esters (referred to as a Claisen condensation).

Condensation reactions are typically catalyzed either by acid or base. Under acidic conditions, the first carbonyl-containing functional group is converted to an enol. The  $\alpha$ -carbon of the enol then reacts with the carbonyl carbon of the second carbonyl-containing functional group to generate the condensation product, referred to as a  $\beta$ -hydroxycarbonyl.



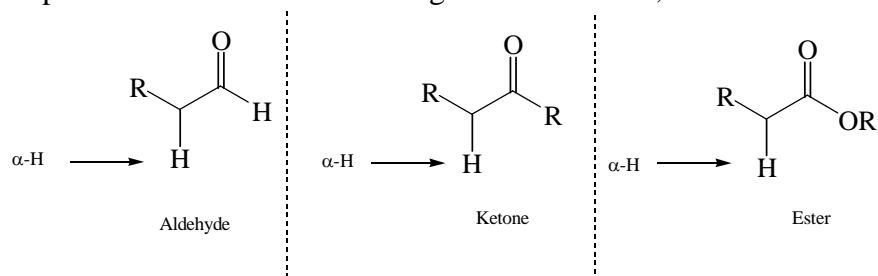
Under basic conditions, the first carbonyl group is converted to an enolate, which then reacts with the carbonyl carbon of the second carbonyl-containing functional group. The condensation product in the base-catalyzed reaction is also referred to as a  $\beta$ -hydroxycarbonyl.



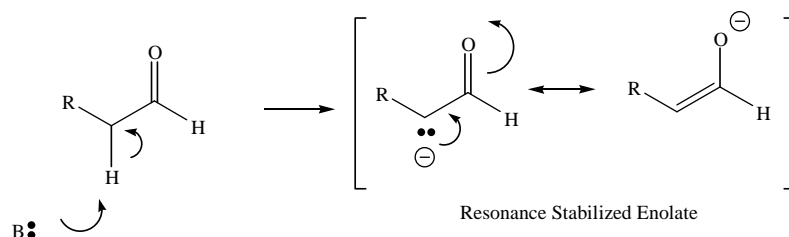
## Synthesis of Dibenzalacetone by the Aldol Condensation

### Enolates

Carbonyl containing functional groups, particularly aldehydes, ketones and esters, that contain at least one  $\alpha$ -hydrogen atom are susceptible to reaction with base to generate an anion, referred to as an enolate.



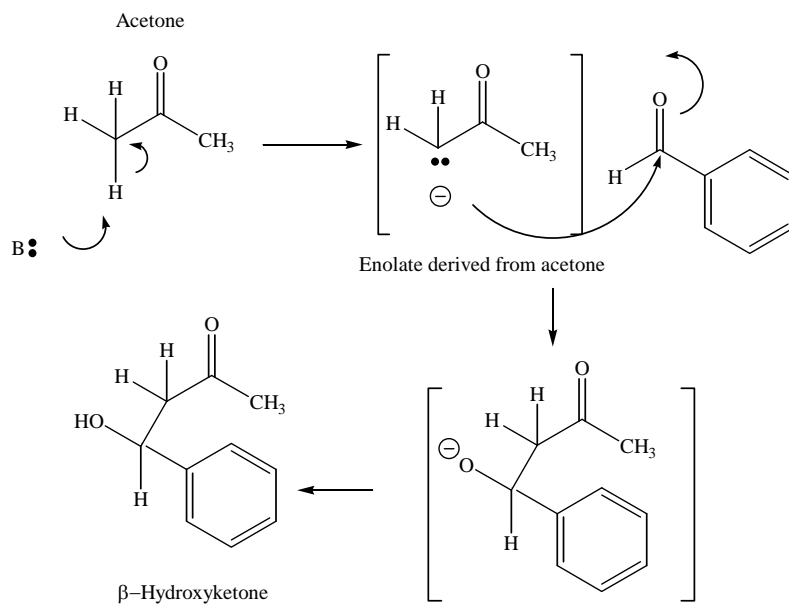
Enolates are nucleophilic reaction intermediates that are stabilized via resonance with the carbonyl pi bond.



Enolates react readily with a wide variety of electrophiles. While both the  $\alpha$ -carbon and the oxygen atom of the enolate have negative character, enolates generally react with electrophiles exclusively through the negatively charged carbon. When enolates react with the carbonyl-carbon of other carbonyl compounds, the reaction is referred to as a condensation.

### Mixed Aldol Condensations

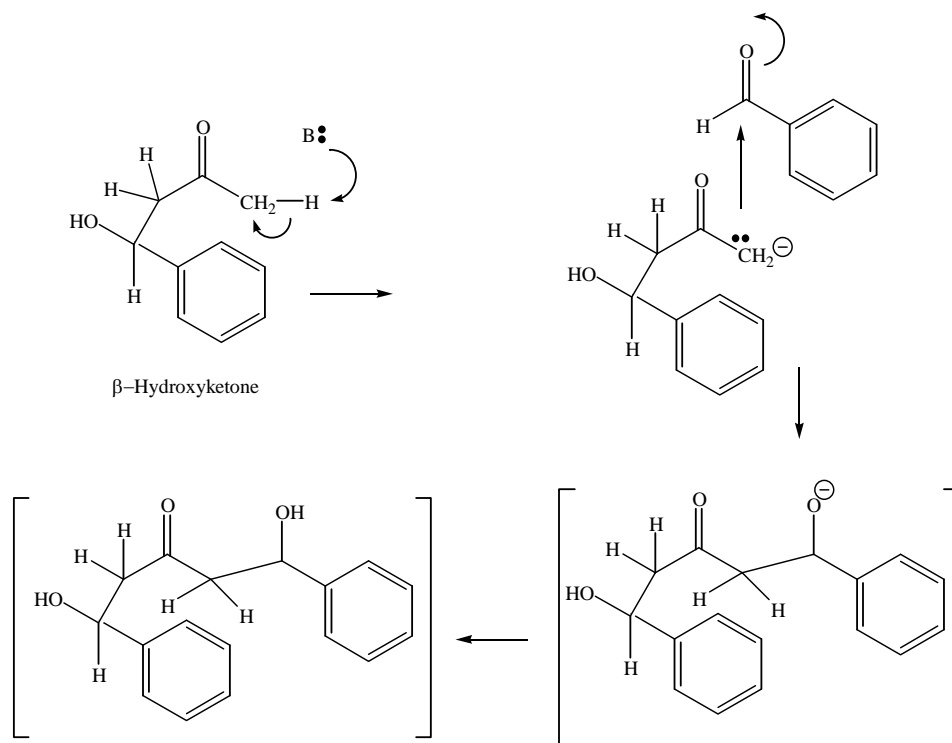
When the reactive enolate in a base-catalyzed condensation reaction is derived from a ketone and the reactive carbonyl-carbon ( $E^+$ ) is part of an aldehyde functional group, the condensation is referred to as a *mixed aldol condensation*. The condensation reaction in the dibenzalacetone experiment occurs between an enolate derived from acetone and the electrophilic carbonyl carbon of benzaldehyde. Benzaldehyde is best suited to serve as electrophile in this reaction since it has no  $\alpha$ -hydrogens (so it cannot serve as enolate), and its carbonyl-carbon is more electrophilic than the carbonyl carbon of acetone (since the aldehyde has less steric crowding around its carbonyl group).



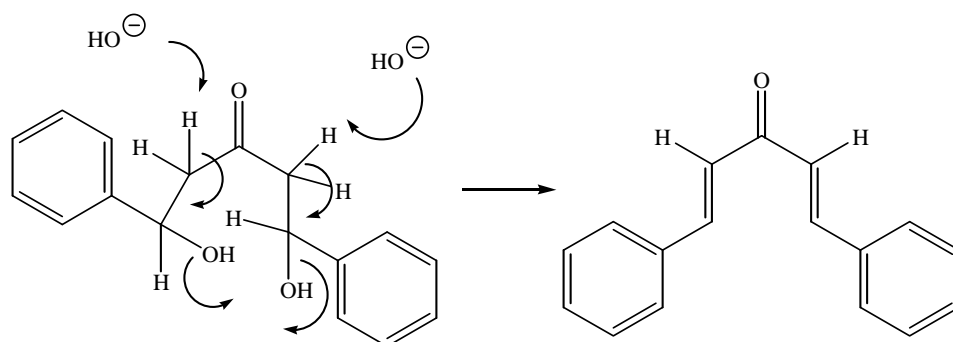
## Synthesis of Dibenzalacetone by the Aldol Condensation

In some cases, the  $\beta$ -hydroxyketone condensation product is the final product of the mixed aldol condensation. However, the  $\beta$ -hydroxyketone that forms upon reaction of the acetone enolate and benzaldehyde continues to react under the reaction conditions used in this experiment. Two additional reactions occur with this  $\beta$ -hydroxyketone due to the presence of excess base and excess benzaldehyde in the reaction mixture.

Since there still are  $\alpha$ -hydrogens associated with the ketone functional group of the  $\beta$ -hydroxyketone, and there is excess base available, the condensation reaction continues. A second enolate is generated which reacts in the same manner as shown above, with the benzaldehyde (also present in excess).



$\beta$ -Hydroxyketones and other  $\beta$ -hydroxycarbonyl compounds often are not stable in highly alkaline (basic) media, and are susceptible to  $E_2$  elimination reactions. The remaining  $\alpha$ -hydrogen atoms react with base, while the  $\beta$ -hydroxyl group serves as leaving group. In the dibenzalacetone reaction, both  $\beta$ -hydroxy groups are eliminated.



When condensation products ( $\beta$ -hydroxycarbonyl compounds) undergo  $E_2$  elimination, the resulting product is referred to as an  $\alpha,\beta$ -unsaturated carbonyl. In the case of the dibenzalacetone reaction, the product is referred to as an  $\alpha,\beta$ -unsaturated ketone. These products are very stable (due to resonance stabilization) and are the major

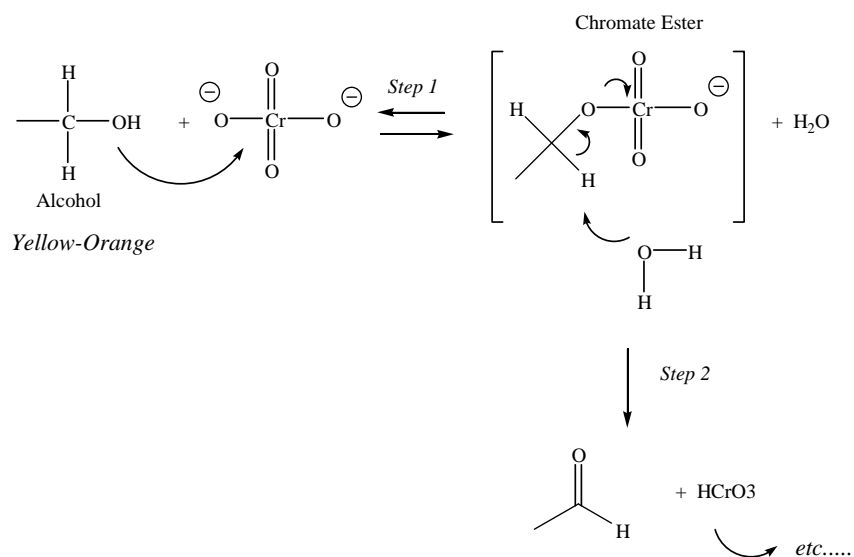
## Synthesis of Dibenzalacetone by the Aldol Condensation

products formed under thermodynamic conditions. The alkene that is generated is in conjugation with the carbonyl compound. The alkenes present in dibenzalacetone have stereochemistry associated with them, however the product in which both alkenes have trans stereochemistry is the major product since it is more stable than the trans, cis or cis, cis products.

### Chemical Tests

#### Jones Test

The orange-yellow Jones reagent will immediately turn green in the presence of 1° and 2° alcohols and aldehydes. The color change is typically observed only for these functional groups and this color change constitutes a “positive” result. Tertiary alcohols do not react with Jones reagent. Sometimes amines, ethers, ketones, alkenes and alkynes will give a positive test after 2-5 seconds due to contamination with alcohols. Phenols are not alcohols but will react with the Jones reagent to give a very dark solution. The Jones reagent is chromium trioxide (CrO<sub>3</sub>) in sulfuric acid (H<sub>2</sub>SO<sub>4</sub>). It is a potent oxidizing agent which rapidly oxidizes primary alcohols and aldehydes to carboxylic acids, and secondary alcohols to ketones. Alcohols react with the yellow-orange Jones reagent containing a Cr (VI) atom. Over the course of the organic oxidation, the Cr is reduced to Cr (III). The first two steps of the reaction mechanism help to explain why tertiary alcohols do not undergo oxidation with the Jones reagent. In step 2, water reacts with a proton of the chromate ester that is bonded to the carbon atom of the former alcohol functional group. Tertiary alcohols do not have a hydrogen atom bonded to this carbon, therefore the reaction could not proceed beyond this point

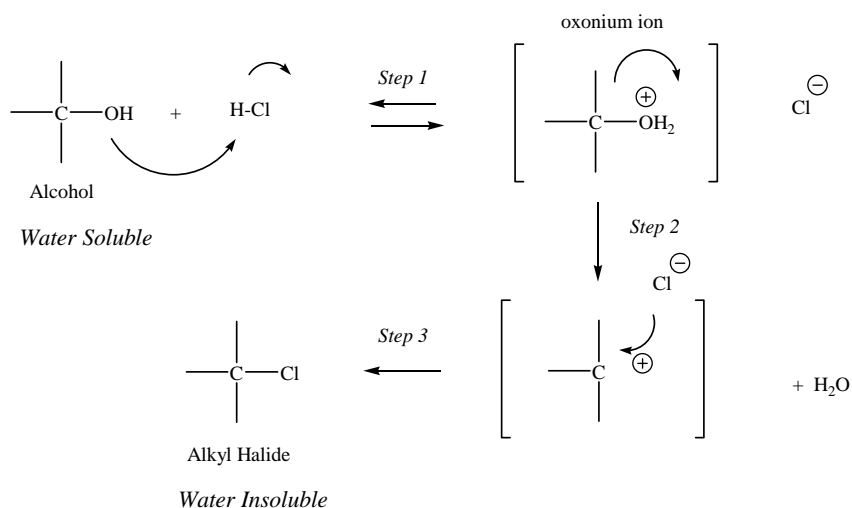


#### Lucas Test

The Lucas reagent is an aqueous solution of strong acid (HCl) and zinc chloride. An insoluble layer, cloudiness, color change (red or orange) or an emulsion will form with 1°, 2°, 3° allylic, 3° alkyl and *some* 2° alcohols and constitutes a “positive” result. Students should compare his/her results of the unknowns with the results for known compounds when trying to decide whether a result is positive or negative. Alkenes may give a “false” positive result due to HCl reacting with the alkene through an electrophilic addition. Phenols and enols will not give a positive result. The alcohol starting material must be sufficiently soluble in aqueous environments (i.e., the Lucas reagent) for the reaction to take place. Therefore, only water-soluble, 1°, 2°, 3° allylic, 3° alkyl and some 2° alkyl alcohols of low molecular weight will provide positive results in this test.

The reaction that occurs in the Lucas test is an S<sub>N</sub>1 nucleophilic substitution. Only alcohols that can generate stable carbocation intermediates will undergo the reaction. The acid catalyst activates the OH group of the alcohol by protonating the oxygen atom. The C-OH<sub>2</sub><sup>+</sup> bond breaks to generate the carbocation, which in turn reacts with the chloride ion (nucleophile) to generate an alkyl halide product. A general mechanism for this S<sub>N</sub>1 reaction is provided below.

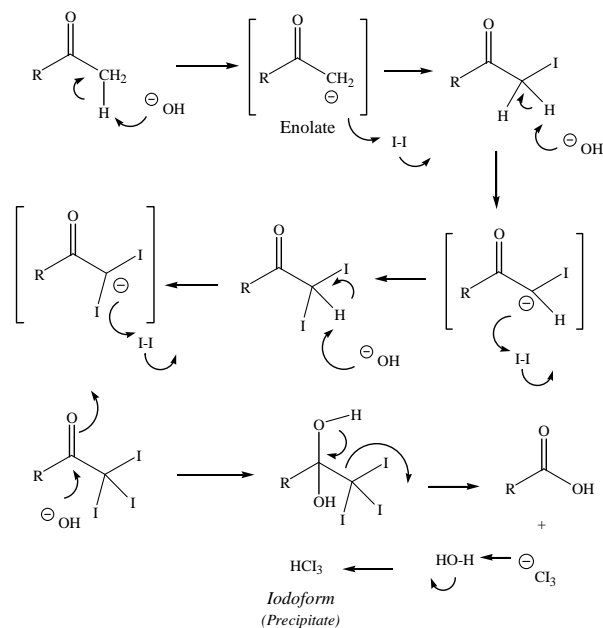
## Synthesis of Dibenzalacetone by the Aldol Condensation



### Iodoform Test

The iodoform reagent is a mixture of iodine ( $\text{I}_2$ ) and potassium iodide (KI) and this reagent reacts *only* with *methyl* ketones (not other kinds of ketones). The formation of a yellow, foul-smelling precipitate indicates the presence of a methyl ketone, acetaldehyde or compounds (some alcohols) that can be oxidized to a methyl ketone. Reaction of a methyl ketone with strong base promotes the formation of an enolate which reacts with the electrophilic  $\text{I}_2$  to generate an  $\alpha$ -iodomethyl ketone. Addition of two more equivalents of base and  $\text{I}_2$  lead to formation of the  $\alpha$ -triiodoketone. Hydroxide ion then reacts with the carbonyl carbon of the ketone in a nucleophilic acyl substitution, liberating iodoform ( $\text{CHI}_3$ ) from the reaction mixture. Iodoform is not soluble in the reaction conditions and precipitates from the reaction mixture, indicating the reaction has occurred.

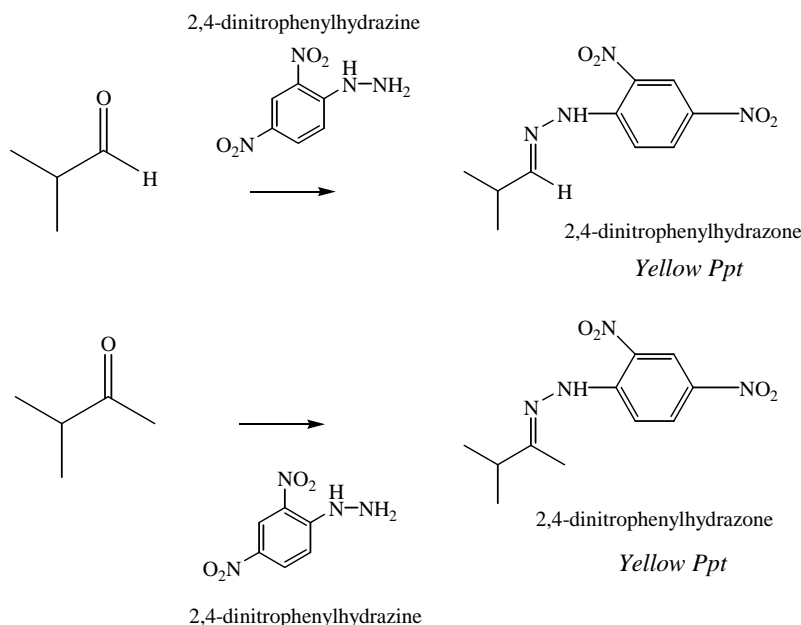
Only methyl ketones (not other types of ketones) can undergo the iodoform reaction because only methyl ketones have three H atoms on the  $\alpha$  carbon which are necessary to form the iodoform product. Acetaldehyde has an  $\alpha$ -methyl group which behaves the same as methyl ketones. Alcohols that upon oxidation form methyl ketones will also undergo this reaction.



## Synthesis of Dibenzalacetone by the Aldol Condensation

### Brady's Test

The Brady's reagent is an acidic solution of 2,4-dinitrophenylhydrazine in ethanol or other alcoholic solvent. The phenylhydrazine reacts with ketone or aldehyde functional groups through a nucleophilic acyl addition reaction to give rise to a 2,4-dinitrophenylhydrazone product. The hydrazine reagent and the aldehyde or ketone are soluble in the reaction mixture. However, the yellow hydrazone product is not soluble in alcoholic solvents and will precipitate from the reaction mixture. Observation of the hydrazone precipitate indicates the reaction has occurred. The formation of a yellow-orange precipitate is an indication that the tested compound contains an aldehyde or ketone functional group. Some allylic alcohols (cinammyl alcohol, vitamin A) may also give positive results.



### Bromination Test

Reaction of bromine with alkenes or alkynes occurs through an electrophilic addition mechanism. The pi bonds of the benzene ring do not react. The brown colored bromine reagent becomes incorporated into the organic hydrocarbon, producing a colorless product. If the bromine reagent is used in excess, or if no reaction occurs, the solution will remain brownish in color. The dissipation of the brown color of the bromine reagent indicates that the tested compound contains an unsaturated hydrocarbon, that is not aromatic. Benzylic carbon or nitrogen atoms that are either primary or secondary will also react with bromine and cause a dissipation of the brown color.

