12BL Experiment 8: Green Chem: Solvent-Free Aldol Condensation-Dehydration

Safety: Proper lab goggles/glasses must be worn (even over prescription glasses). As always, ask where organic waste containers are located in the lab.

Background: The word "green" has become synonymous with sustainability. The chemical manufacturing industry uses the term "green chemistry" to mean the design of processes that reduce or eliminate negative environmental impacts, such as the production of hazardous waste. Federal statutes, such as the Resource Conservation and Recovery Act (RCRA), require specific disposal procedures for wastes that are defined as hazardous based on factors that include ignitability, corrosiveness, reactivity, or toxicity. As a result, proper management of hazardous wastes can be quite costly for chemical manufacturing companies. For more information on the 12 Principles of Green Chemistry, you can visit:
http://www.epa.gov/sciencematters/june2011/principles.htm

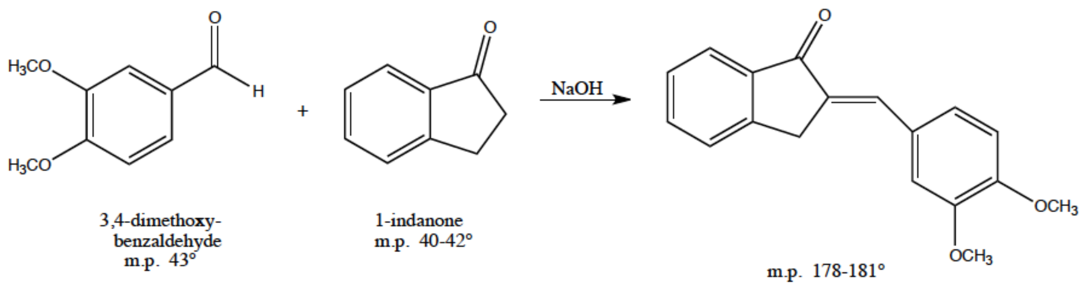
The pharmaceutical industry is engaged primarily in the synthesis of organic compounds and produces a significant amount of chemical waste with the majority arising from the use of organic solvents. Therefore, one way to make a manufacturing process more "green" is to reduce the ratio of solvent waste per kilogram of product. Another thing to consider is the kind of solvent being used. You have worked with several different organic solvents this year in the laboratory course. One characteristic that makes a solvent hazardous is toxicity. Solvents can be placed into different classes based on potential toxicity to humans or the environment.

Class I: Significant Environmental Impact
Class II: Moderate Environmental Impact
Class III: Low Environmental Impact

You will research and categorize six commonly used organic solvents into these classes using Material Safety Data Sheets (MSDS's) as part of your prelab. **The solvents are: acetone, dichloromethane, ethanol, hexane, methanol and toluene.**

In some instances, it is possible to eliminate the solvent from a reaction altogether, resulting in a solvent-free process. In today's experiment, you will carry out an Aldol Condensation reaction without the use of a solvent. In an Aldol-Condensation, two carbonyl compounds join together in a condensation and then undergo a spontaneous dehydration (recall, E2 = strong based induced dehydration). The two reactants, 3,4-dimethoxybenzaldehyde and 1-indanone, each have very low melting points. When they are mixed together, their melting points are lowered, in the same way that impurities will lower the melting point of any organic compound. These two compounds will actually become liquids at room temperature when mixed together, which allows the molecules to interact with each other. Solid sodium hydroxide is added to the liquid mixture to facilitate the reaction. An aldol condensation-dehydration product results – an alpha-beta unsaturated ketone.

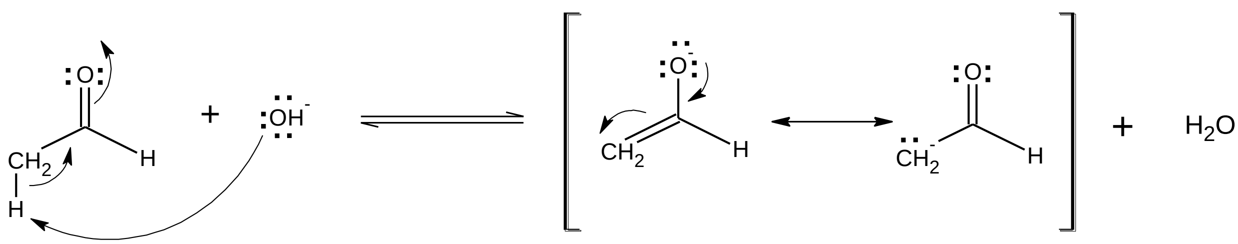
Aldol Condensation Equation:



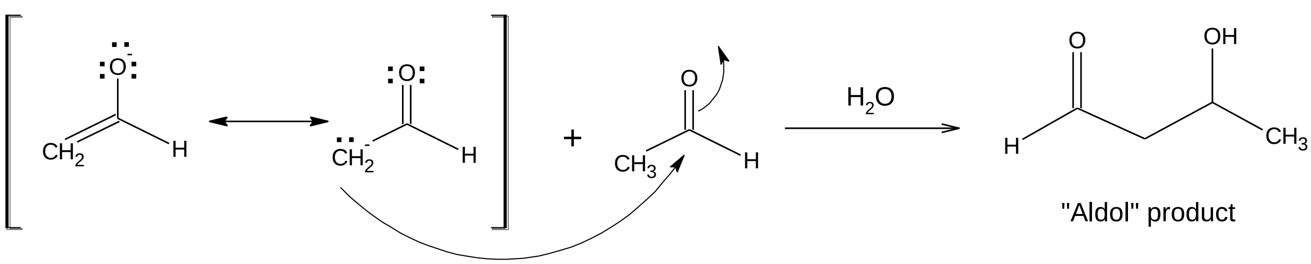
http://www.bc.edu/schools/cas/chemistry/undergrad/org/spring/GreenChem.pdf

Aldol-Condensation Mechanism:

The aldol reaction represents one of the most powerful methods of carbon-carbon bond formation used in organic synthesis. The base-catalyzed aldol reaction relies on the fact that a nucleophilic enolate ion (formed by alpha-deprotonation of a carbonyl compound) will attack the electrophilic carbon of a carbonyl group leading to a new C-C bond:



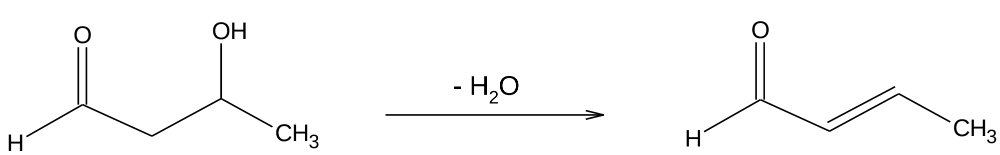
"Enolate ion"



"Aldol" product

"Enolate ion"

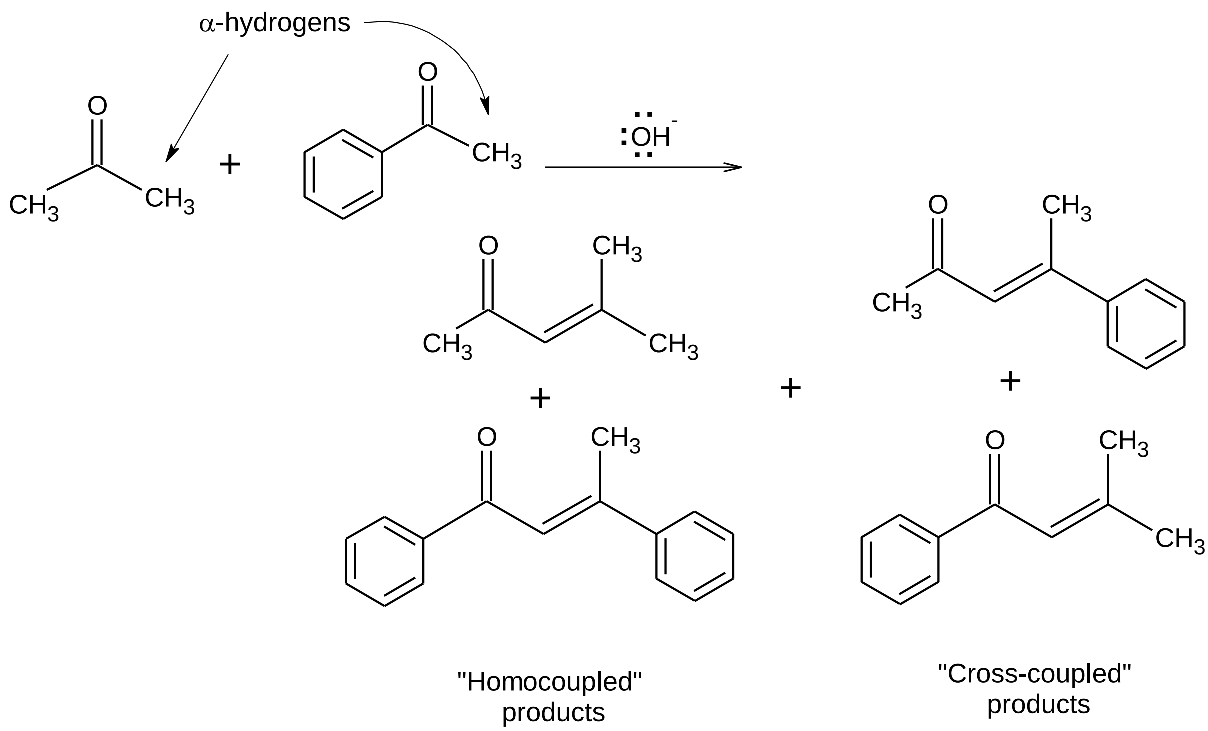
Dehydration (E2) of the intermediate aldol product often occurs spontaneously to give the conjugated alpha-beta unsaturated carbonyl product:



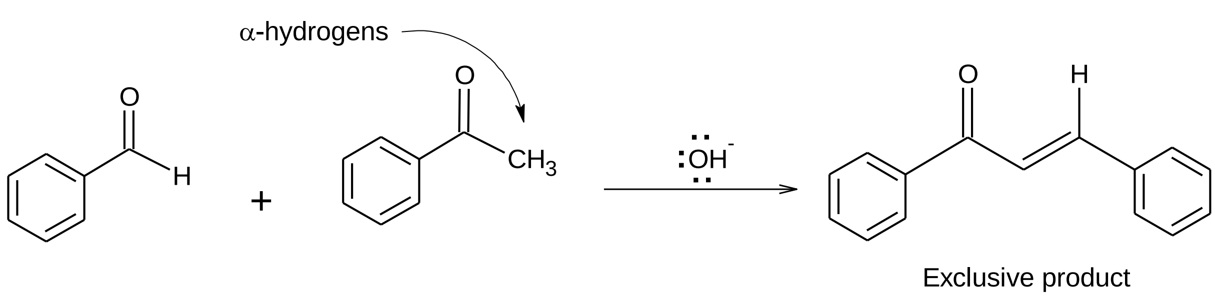
"Aldol" product

α,β-Unsaturated aldehyde

Aldol reactions between two different carbonyl compounds (called "crossed" aldol reactions) where each compound contains alpha-hydrogens can lead to complex mixtures of products. Each compound can potentially form an enolate and attack either itself or the other compound leading to mixtures of both "homocoupled" and "cross-coupled" products:



If, however, only one of the reactants contains alpha-hydrogens, the reaction can produce good yields of a single product:



"Green" **Aldol** Condensation - Chemistry at Winthrop University

Objective: To successfully synthesize 2-(3,4-dimethoxybenzylidene)-indan-1-one. To understand and learn the mechanisms of aldol condensation and dehydration.

Procedure:

1. Add 0.25 g of your aldehyde (3,4-dimethoxybenzaldehyde) and 0.20 g of your ketone (1-indanone) in a 50 mL beaker.

2. Crush solids with a glass rod or spatula until they become a colored oil. Pressing harder won't make it happen faster. Take your time.

3. Add 0.05g of ground NaOH.

4. Mix and scrape until a pale yellow-green solid forms.

5. Let this mixture stand for 15 minutes at room temperature.

6. Add 2 mL of 10% HCl. Mix thoroughly. NOTE: It is important to break up any chunks of the solid product as best you can to allow neutralization of the NaOH from the reaction.

7. Check the pH. If it is not acidic continue to add small portions of acid while mixing until it becomes acidic.

8. Isolate the solid product from the mixture using suction filtration; wash with small portions of ice cold water.

9. Recrystallize using a 90:10 ethanol/water mixture (90%) (use no more than 25 mL). *Remember – you should know how to perform a recrystallization; review if necessary.

10. Set product on a pre-weighed watch glass. Put in oven for 10 minutes to dry.

11. When it is completely dry, determine the mass of your product.

12. Compute the theoretical and percent yield. (postlab)

13. Run a melting point and IR on final product.

14. Completely analyze your IR.

Procedure adapted by Shasta Ott
http://chemlab.truman.edu/OrganicLabs/solventless-aldol.pdf
http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=4&cad=rja&sqi=2&ved=0CDsQFjAD&url=http%3A%2F%2Funcw.edu%2Fchem%2Fdocuments%2Faldol.ppt&ei=4TY6UuGIGbTUyQGw_IDYBQ&usg=AFQjCNEuT7wOUYoovxxx6MhjRDDsCePEcw

12BL Prelab Expt 8: Solvent-Free Aldol Condensation-Dehydration

1. In the tables in #2, research and clearly define what the following mean:

    a. OSHA

    b. PEL

    c. LD50

    d. LC50

2. **Classifying the Solvents:** Research the MSDS (Material Safety Data Sheet) reports for each of the 6 solvents listed in the background and complete a table for <u>each solvent</u>. Work should be typed or very neatly written & thorough.

Solvent_______________

Health Hazards	
Skin	
Ingestion	
Inhalation	
Eyes	
Carcinogen	
Exposure limits	
OSHA (PEL)	
Solubility in water	
Toxicity	
Routes of entry	
LD50 and LC50 data for animals	
Chronic effects on humans	
Products of biodegradation	

Solvent________________

Health Hazards	
Skin	
Ingestion	
Inhalation	
Eyes	
Carcinogen	
Exposure limits	
OSHA (PEL)	
Solubility in water	
Toxicity	
Routes of entry	
LD50 and LC50 data for animals	
Chronic effects on humans	
Products of biodegradation	

Solvent________________________

Health Hazards	
Skin	
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Solvent__________________

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Solvent_________________

Health Hazards	
Skin	
Ingestion	
Inhalation	
Eyes	
Carcinogen	
Exposure limits	
OSHA (PEL)	
Solubility in water	
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Routes of entry	
LD50 and LC50 data for animals	
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Solvent_________________

Health Hazards	
Skin	
Ingestion	
Inhalation	
Eyes	
Carcinogen	
Exposure limits	
OSHA (PEL)	
Solubility in water	
Toxicity	
Routes of entry	
LD50 and LC50 data for animals	
Chronic effects on humans	
Products of biodegradation	

3. Using the information compiled in the tables, categorize the eight solvents by class, <u>according to their potential toxicity to humans or the environment</u>.

Class I: Significant Environmental Impact

Class II: Moderate Environmental Impact

Class III: Low Environmental Impact

4. Draw structures for acetone and acetaldehyde. Circle the alpha hydrogens. Clearly explain which molecule has the more strongly acidic alpha hydrogens. Please review what an acidic atom is!

5. For the more acidic molecule in #4, draw the enolate ion & its resonant form that forms during an aldol condensation reaction.

12BL Postlab Expt 8: Solvent-Free Aldol Condensation-Dehydration

Data

1. Mass of 3,4-dimethoxybenzaldehyde used: ________________

2. Moles of 3,4-dimethoxybenzaldehyde used: _______________
(show calculation thru dimensional analysis)

3. Theoretical yield in grams of product: _________________
(show calculation thru dimensional analysis)

4. Isolated mass of pure product: _____________

5. Percentage yield of product: ______________________________
   (show calculation)

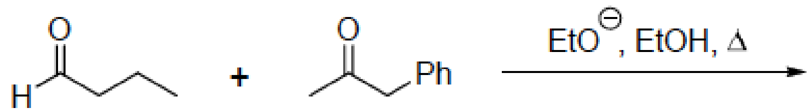
6. Melting point of your product: __________________

7. Literature melting point of product: ____________________

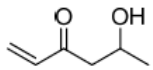
8. Explain why the two solid reactants in this experiment became a liquid when they were intimately mixed together.

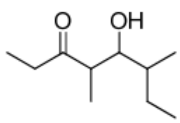
9. Show the detailed mechanism for the crossed aldol condensation-dehydration reaction of 1-indanone with acetaldehyde. *Make sure you identify which reactant has the more strongly acidic alpha H and will become the carbanion! (Be neat and clear showing all arrows, charges, structures, lone pairs, and bonds appropriately).

10. The Aldol condensation-dehydration reaction between the two reactants below can lead to four different conjugated alpha-beta unsaturated products. (*notice that both reactants have an acidic alpha H and could potentially form a carbanion, C:. Thus upon coupling with another carbonyl, you have the following combinations: A: + A, A: + K, K: + K, K: +K). Show the structures of the products and show ONE mechanism for the formation of one of the products.

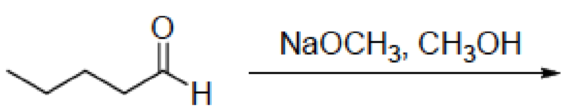


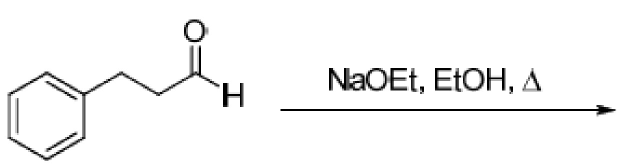
11. Give the reactants that are required to form each of the following Condensation products. Check your work!





12. Give the structure of the major organic product for each of the following. Check your work.





13. Attach completely analyzed IR to postlab – all bonds and their wavenumbers must be labeled in their appropriate positions on the IR. Include structure of the product on the IR as well.