

Solvent-Free Aldol

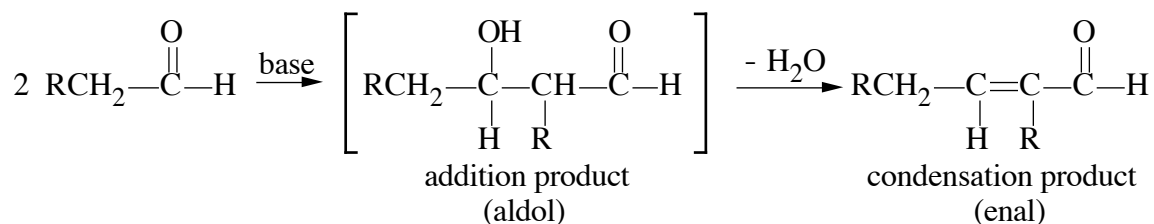
Organic Labs – AEM

References: “Solventless Reactions: the Aldol Reaction.” K M Doxsee, J E Hutchison *Green Organic Chemistry – Strategies, Tools and Lab Experiments*. Thompson Brooks/Cole 2004; 115-119; and “Understanding Solid/Solid Organic Reactions” G. Rothenberg, A P Downie, C L Raston, J L Scott *J. Am. Chem. Soc.* **2001**, 1223, 8701-8708.

Introduction

The aldol condensation is a powerful way of making C-C bonds and introducing useful functionality into the resulting product. Two aldehyde molecules react to form an initial addition product, which is a β -hydroxyaldehyde, but these substances usually eliminate water to form α,β -unsaturated carbonyl compounds. These substances are extremely useful synthetic intermediates.

A General Aldol Condensation



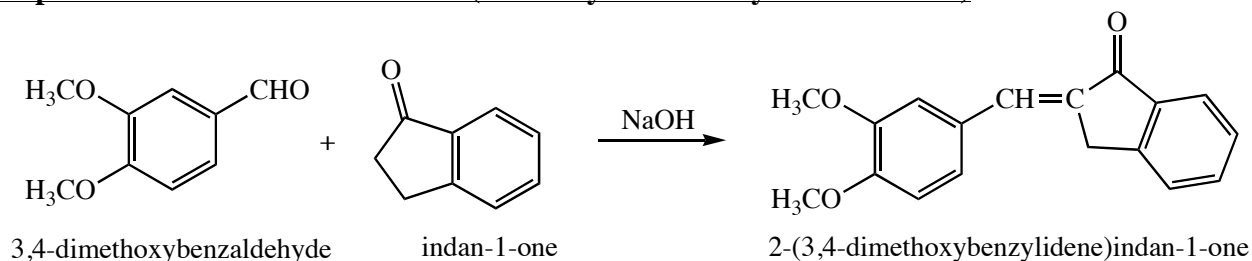
These procedures are most frequently performed under basic conditions, which allows the formation of an enolate from the aldehyde reagent. This enolate then acts as a nucleophile to attack the carbonyl of a different molecule of the starting aldehyde, forming the new carbon-carbon bond. The resulting β -hydroxycarbonyl substance often readily eliminates water to form an α,β -unsaturated carbonyl product. All of the steps of this mechanism are equilibria, with the dehydration step usually being the driving force of the whole process. These equilibria are usually not as favorable for ketones under similar conditions.

Crossed aldol condensations can be problematic, since somehow you must force the two different reagents to perform only one of the mechanistic roles of the aldol process. Two ways that this can be done are discussed here. First, if only one of the carbonyl compounds involved has any α -hydrogens to form the enolate, then it can be forced to take on the enolate function; the compound without any α -hydrogens must be attacked by this enolate in the C-C bond-forming step.

The second way to isolate the mechanistic roles of the carbonyl reagents is to use an aldehyde with no α -hydrogens and a ketone to form the enolate. Recall that the equilibrium of a ketone enolate attacking a ketone carbonyl is less favorable than attacking an aldehyde; this unfavorable equilibrium allows the reaction between that ketone enolate and an aldehyde carbonyl to produce good yields of aldol products. This variation is often called a Claisen-Schmidt reaction.

In this experiment you will perform the crossed aldol condensation given here. In this case, the indan-1-one is a ketone with α -hydrogens, which can form an enolate. This enolate can then readily attack 3,4-dimethoxybenzaldehyde, which has no α -hydrogens.

This Experiment's Aldol Condensation (the one you need in your notebook!)



This particular example has the additional feature of being done without a solvent. The elimination of a solvent means that there is no disposal of reaction solvent required at the end, making this a more environmentally friendly, “green” process. The absence of solvent works here because of melting point depression of impure materials. When the two solid reagents mix, they act as impurities on each other, depress each other’s melting points, and liquefy. The resulting liquid can then be combined with the finely ground base, initiating the aldol process and forming the product, which is a new solid.

Safety Issue: Solid sodium hydroxide is extremely caustic. Be very careful not to get any of this material on your skin or mucous membranes! It is also quite hygroscopic (absorbing moisture from the air), so keep the bottle closed at all times unless in use.

Procedure

Carrying out the Reaction. Place about 0.25 g of 3,4-dimethoxybenzaldehyde and about 0.2 g of 1-indanone in a small beaker; record the exact masses of the reagents that you use. Using a sturdy glass rod, scrape and crush the two solids together until they become a brown oil. Be careful not to break the beaker or the glass rod! Notice the melting point depression of these two solids as they mix together. Add about 0.05 g of finely ground solid NaOH; use a mortar and pestle to grind this if it is not done for you. Continue to scrape and mix until the mixture completely solidifies. Allow the mixture to stand for 15 minutes after it has solidified.

Reaction Work-up. Add about 2 mL of 10% HCl (aq). Break up the chunks of the solid product as best you can and scrape the mixture with the acid to allow neutralization of the base from the reaction. Check the pH of the solution to be sure that it is now acidic; if it is not, add a bit more acid and mix it in well. Isolate the solid product from the mixture using suction filtration, wash with water and let it air dry on your suction apparatus for about 10 minutes.

Purification and Characterization. Recrystallize your product, the 2-(3,4-dimethoxybenzylidene)-indan-1-one, using ethanol. (You will need about 20 mL of ethanol for this recrystallization and most do not need to decolorize or gravity filter....) When it is completely dry, determine the mass of your product and compute the theoretical and percent yield. Characterize it by mp, IR, and/or NMR, as directed by your professor. [Note: the physical property data is somewhat hard to find for this product; the only data that you must have is its MW (280.32 g/mol) and its mp (183-185°C).]

Clean up. Neutralize the reaction work-up solution and flush it down the drain with lots of water. The recrystallization solvent can also be flushed down the drain with lots of water. After they are graded, the product solid should be put in the solid hazardous waste container.