Experiment 8

Aldol Condensation: Synthesis of Indigo. Vat Dyeing.

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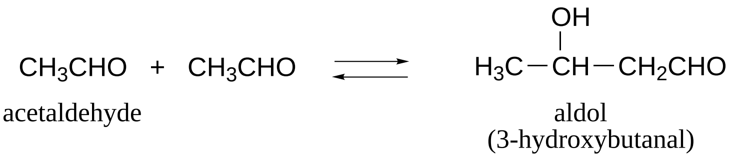
Reading: *Organic Chemistry* by Francis Carey, 4th edition, pp. 708-711 (18.6); pp. 715-720 (18-9-18.10).

An extremely important class of carbon-carbon bond forming reactions are those which involve reaction of a compound which has relatively acidic hydrogens (i.e., alpha hydrogens on an aldehyde, ketone, ester, nitrile, or nitro compound) with a compound having a carbonyl group. When the reactants involved are either aldehydes or ketones, the reaction is called an “aldol condensation.” For example, two molecules of acetaldehyde condense to form the four-carbon compound known as aldol:

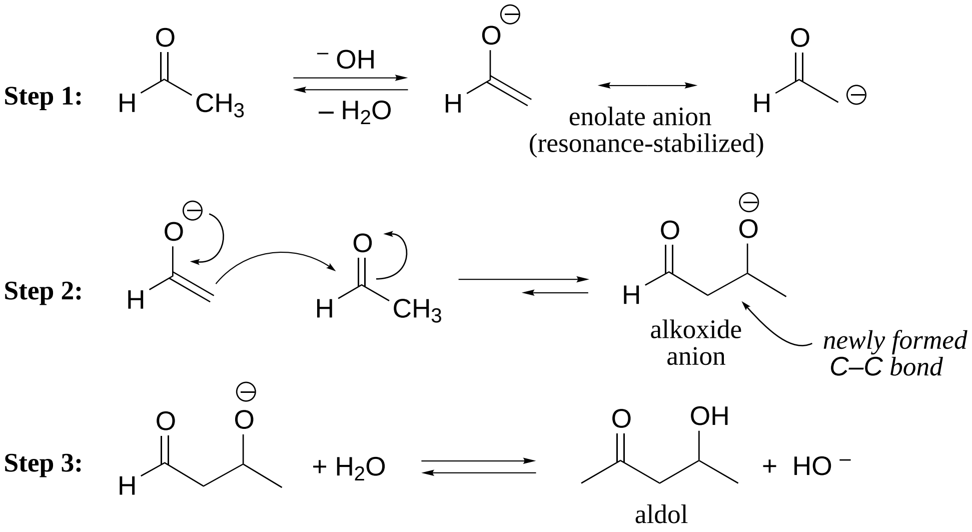


$$CH_3CHO + CH_3CHO \rightleftharpoons H_3C-\overset{\displaystyle OH}{\overset{|}{C}H}-CH_2CHO$$

acetaldehyde

aldol (3-hydroxybutanal)

The above reaction may be either acid or base catalyzed; however, base catalysts are generally preferred. The mechanism of the base catalyzed condensation reaction of acetaldehyde to form aldol is given below. The first step is removal of an alpha proton to give a resonance-stabilized enolate anion. In the second step, the enolate anion attacks the carbonyl carbon of a second molecule of acetaldehyde to form a carbon-carbon bond and an alkoxide anion. In the third step, the alkoxide anion abstracts a proton from water to regenerate the hydroxide catalyst. Since all of these steps are reversible, a successful synthesis is contingent on the product being more stable than the reactants, or on some technique for driving the equilibrium towards products.



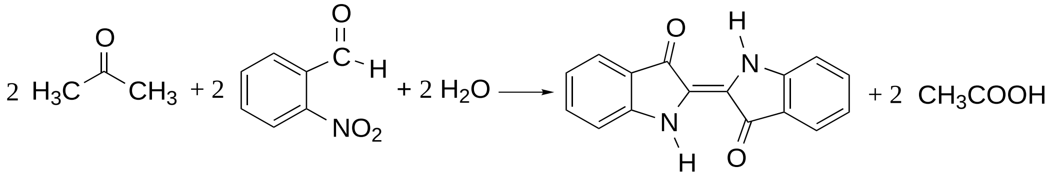
An aldol condensation between two different aldehydes or ketones is called a *crossed-aldol condensation*. Such condensations generally result in an undesirable mixture of products, although in some cases a single product may be obtained in good yield. An example of this is the crossed aldol condensation between acetone and benzaldehyde to give dibenzalacetone, which was carried out in past semesters of this course.

$$2\ \underset{\text{benzaldehyde}}{C_6H_5CHO} + \underset{\text{acetone}}{CH_3COCH_3} \longrightarrow \underset{\text{dibenzalacetone}}{C_6H_5CH{=}CHCOCH{=}CHC_6H_5} + 2\ H_2O$$

Crossed condensation is successful in this case because benzaldehyde has no α-protons, so it cannot undergo condensation with itself and because the carbonyl group of benzaldehyde is far more reactive than that of acetone. As is generally true of aldol condensations involving aromatic aldehydes, the aldol product readily undergoes dehydration to give an α, β-unsaturated carbonyl compound in which the double bond formed is conjugated with both the carbonyl group and the aromatic ring. This step is irreversible under the reaction conditions and serves to drive the equilibrium toward the formation of the product. The extensive conjugation of dibenzalacetone causes it to absorb light in the visible region which gives it its yellow color.

An interesting example of an aldol condensation is the synthesis of indigo. Indigo, as explained in the *Essay* preceding this experiment, is the dye used in blue jeans. In ancient times, indigo was isolated from plant sources, such as Indigofer. In India, it was used to dye cloth and in Egypt, mummies were sometimes wrapped with indigo-dyed ribbons. It became known in Europe after the discovery of the sea route to India. It was used for dyeing wool by the Gauls, and “their wives and daughters painted their bodies with it, when they appeared naked at the sacred festivals. Caesar relates the same of the Britons, who however did it in order to appear more terrible in battle”.[*] In the sixth century in France and in Germany, indigo was isolated from a plant known as “woad”. The first chemical synthesis of indigo was reported by Adolf von Baeyer in 1880. This introduction of synthetic indigo met with violent opposition from growers of woad, and the use of synthetic indigo was prohibited in England, Germany, and France. The French king, Henry IV, “even went so far as to issue an edict, condemning to death any one who used that pernicious drug called ‘devils food’.”[†]

The method which you will use to synthesize indigo was developed by Baeyer in the 1880s and, while it is not the procedure used commercially to synthesize indigo today, it does work well to produce small quantities of indigo to use to dye samples of cloth. The balanced reaction for the synthesis of indigo is:



acetone o-nitrobenzaldehyde indigo

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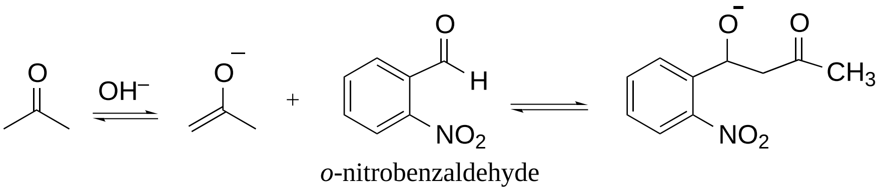
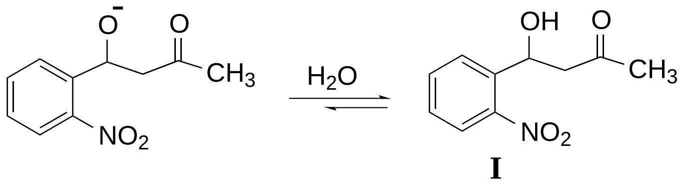
[*] from *The Rise and Development of Organic Chemistry, Carl Schorlemmer,* p. 253, 1894.

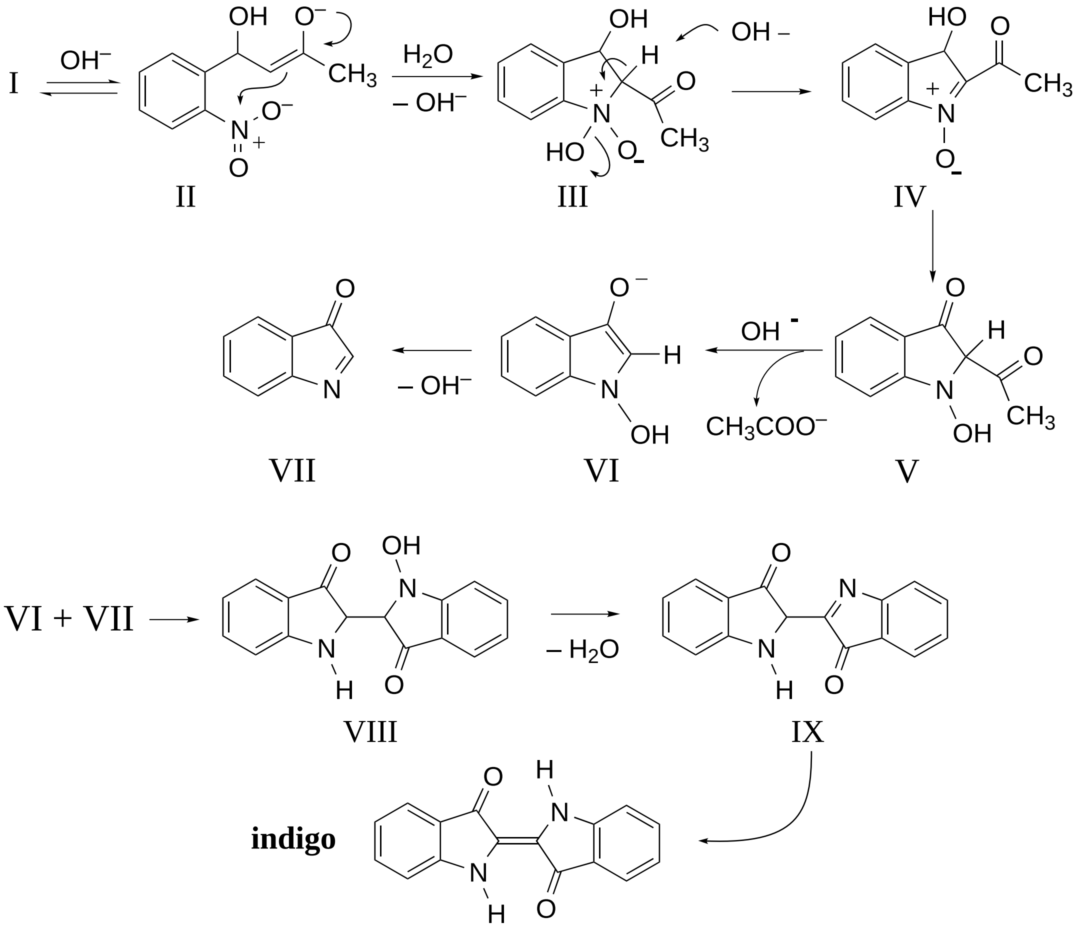
[†] ibid.

The first step in the synthesis is an aldol condensation. Acetone, base, and *o*-nitrobenzaldehyde are mixed to give the hydroxy ketone **I**:

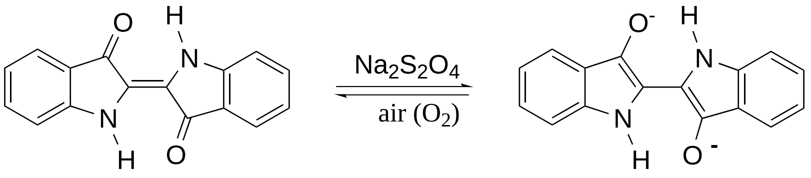




The hydroxy ketone (**I**) has been isolated and identified. In this experiment, however, it continues to react in a series of condensations, tautomerizations, a retro-Claisen condensation, and eliminations to produce indigo within a matter of seconds. The exact nature of these steps is unknown, and the scheme outlined below is pure speculation, although chemically plausible.

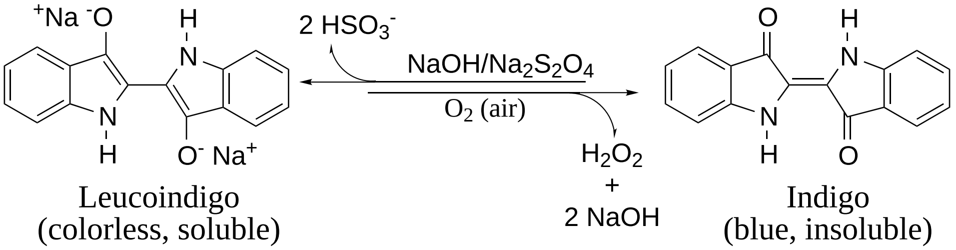


The blue, water-insoluble indigo is isolated and then treated with sodium dithionite, a reducing agent, to produce the pale yellow, water-soluble leucoindigo:



indigo

leucoindigo



Leucoindigo
(colorless, soluble)

Indigo
(blue, insoluble)

A solution of the leucoindigo is used to dye a piece of cloth. The cloth is then air-dried, which oxidizes the leucoindigo back to the indigo form. The cloth which you use is a small square of a special fabric called Multifiber Fabric 10, which has the following fibers woven into it: spun acetate rayon, cotton, a spun polyamide (Nylon 6,6), Dacron, Orlon, and wool.

You will probably find that the indigo will dye each fiber to a different extent.

Safety Precautions

o-Nitrobenzaldehyde, indigo, and 1 N NaOH can cause skin irritation. Wear your gloves throughout the experiment. Indigo will stain your skin and clothes—beware! Acetone, ethanol, diethyl ether, and sodium dithionite are flammable.

Procedure Section

Note: Sometime during this lab period, you need to set up your esterification reaction for next week. Your TA will assign you an ester and give you the directions for starting the reaction.

Dissolve 0.5 g of *o*-nitrobenzaldehyde in 5 mL of acetone in a small beaker. Add a stir bar, place the mixture on a stir motor, and commence stirring. Add 5 mL of water, then 2.5 mL of 1 N NaOH dropwise. Continue stirring for about 10 min, then chill the blue mixture in an ice bath.

Collect the indigo by vacuum filtration, noting the statement in the box below:

> *IMPORTANT! The blue indigo solution must be poured onto the center of the (pre-wetted with water) filter paper while your vacuum aspirator is running. Do not let the blue solution come into contact with your Buchner funnel, or it will irreversibly color the funnel.*

Rinse successively with a little water, ethanol, and diethyl ether. Transfer the indigo to a watch glass and determine your yield, but do not determine the melting point (the melting point of indigo is beyond the range of our melting point apparatuses).

A. Dyeing with Indigo

Weigh out 0.1 g of indigo and mix it with 0.15 g of sodium dithionite in a small beaker. Use a glass rod to grind the solids together. Add 10 mL of 1 N NaOH and a boiling chip; heat the mixture on a steam bath. As soon as the solution becomes colorless, dip a piece of test fabric in it. Remove the fabric as soon as it is saturated, rinse it with cold water, and blot it dry with a paper towel. Allow it to air dry and record your observations.

Wastes

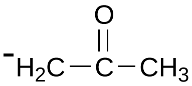
Aqueous Waste: The dye mixture left over from dyeing the test fabric.

Organic Waste: The filtrates.

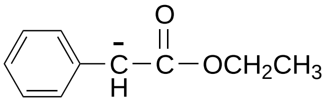
Recovery Jar: Unused product, indigo.

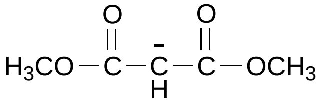
Study Questions

1) Draw the resonance structures for the following enolate ions:

a) 

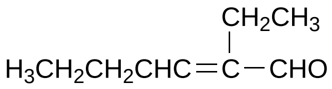
$${}^{-}H_2C-\overset{\overset{\displaystyle O}{||}}{C}-CH_3$$

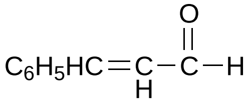
b) 

c) 

$$H_3CO-\overset{\overset{\displaystyle O}{||}}{C}-\underset{H}{\overset{-}{C}}-\overset{\overset{\displaystyle O}{||}}{C}-OCH_3$$

2) Using aldol or crossed aldol condensation reactions, suggest a synthesis of the following compounds:

a) 
$H_3CH_2CH_2CHC{=}C(CH_2CH_3){-}CHO$

b) 
$C_6H_5HC{=}C(H){-}C({=}O){-}H$

3) What would happen if you spilled a solution of sodium dithionite on your blue jeans?

Extra Study Question

Propose mechanisms for the following conversions in the proposed scheme for the synthesis of indigo given in the introduction to this experiment:

a) Structure IV to structure V. Hint: the mechanism includes a series of tautomerizations. Examples of tautomerization are illustrated below.

Tautomerization of carbonyl:

Tautomerization of an iminium ion:

b) Structure V to structure VI. Hint: think about the reversibility of the aldol condensation.