Exp’t 811
The Claisen-Schmidt Condensation: A Two for One Deal!
Adapted by B. Aldinger (Penn. State Univ.) from a microscale procedure used by the Hofstra University, NH, in its undergraduate labs. The procedure is based on an experiment by Nanette Wachter-Jurcsak and Kendra Reddin, *J. Chem. Ed.* 78, 9 (2001)

Introduction:
The ability to form carbon-carbon bonds is a very important tool in organic synthesis. This mixed Aldol reaction between an aldehyde and a ketone is known as the Claisen-Schmidt Condensation and is covered in many introductory organic chemistry courses. Usually in a mixed Aldol condensation, the enol of a ketone adds to the carbonyl of an aldehyde and the reaction stops there. Such mixed Aldol reactions with aromatic aldehydes are especially susceptible to elimination of water from the initial Aldol to form a highly conjugated $\alpha,\beta$-unsaturated ketone. Due to loss of water, in this experiment, the product is a 1,4 unsaturated ketone whose double bond can be added to by the enolate of the starting ketone. The result is an achiral symmetric molecule.

Through $^1$H-NMR analysis you will learn that the methylene hydrogens (marked $H_a$ and $H_b$) in 3 are diastereotopic. This has also been analyzed through the use of geometric isomers. This experiment differs from these in that it utilizes a symmetric molecule that has no chiral centers to explore the meaning of diastereotopism. With the advent of high-field NMR equipment, you will be able to explore the unique splitting patterns characteristic of this molecule.

Cautions:
Sodium hydroxide is corrosive and can cause severe burns. Wear goggles and gloves when handling the concentrated solution. Acetophenone and 2-pyridinecarboxaldehyde irritate the eyes and should be measured out in a hood. Ethanol, acetophenone, and 2-pyridinecarboxaldehyde are combustible and should be kept away from flames.

Synthesis:
First, you must purify the 2-pyridinecarboxaldehyde (2). DO NOT GET ANY LIQUID ON YOUR HAND UNLESS YOU WANT TO BE STAINED BROWN FOR A WEEK. Place 3 mL of the thick impure liquid into a test tube and heat in a sand bath on medium temperature. Suck up the vapors above the liquid into a Pasteur pipette and expel the condensate into another test tube. Stop when 0.5 mL of the pure yellow liquid has been collected.
To a 10 mL Erlenmeyer flask containing 1 mL of 95% ethanol with a magnetic stir bar add 0.26 mL of acetophenone (1) and 0.10 mL of purified 2-pyridinecarboxaldehyde (2). Stir the solution while adding 1.0 mL of 2.5 M aqueous NaOH at room temperature. The solution will turn a deep golden yellow. Allow the solution to stir for 2-4 h; longer is better. Collect the powdery white precipitate by vacuum filtration with a small fritted Buchner funnel.

**Isolation & Purification:**

Rinse the filter cake small amounts of cold ethanol. Allow to dry, collect, and weigh the product. OPTIONAL: If more than 25 mg product is obtained, perform a recrystallization from 95% ethanol to give small quartz-like crystals.

**Cleaning Up:**

Place excess 2-pyridinecarboxaldehyde and the reaction filtrate into the NHO waste container in your hood.

**Analysis:**

Take a mp of the product (lit. 119-121 °C) Take a proton NMR in CDCl₃ using the 400 MHz NMR. Ask your TA for instructions before using this instrument. Also acquire an IR spectrum. Annotate relevant peaks on all spectra taken.

**Final Report:**

How does this reaction combine the Aldol condensation and Michael Addition? Also, include an analysis of the splitting that occurs in the NMR spectrum of the product. Define the word “diastereotopic.”

**References:**