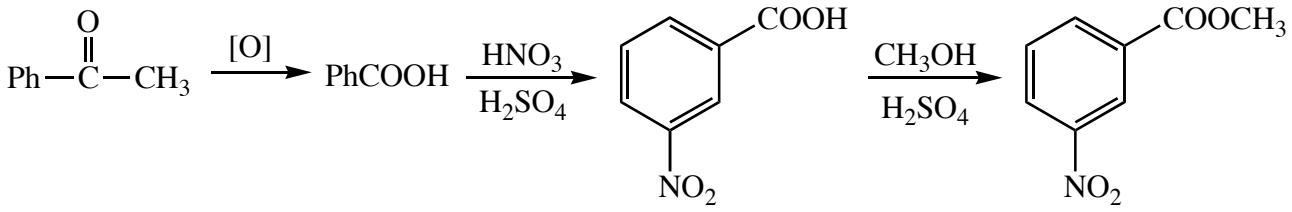
Multi-Step Synthesis of Methyl *m*-Nitrobenzoate

AEM – last update August 2012

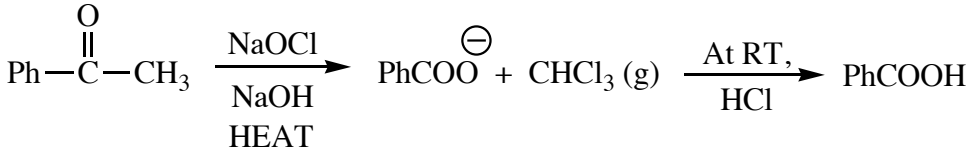
This multi-step synthesis is drawn from a Journal of Chemical Education Article called "**And the Winner is… A Multi-Step Synthesis for the Introductory Organic Course"**. Its reference is S. S. Stradling; C. L. Gage *J. Chem. Ed.* **1985**, *62(12),* 1116-1117. We have chosen one of three possible synthetic routes for preparing a single substance, methyl *m*-nitrobenzoate. We will only use the one route, so that all of you will start with the same reaction step: the oxidation of acetophenone to benzoic acid. The benzoic acid that you prepare must then be characterized (by mp, IR, and/or NMR) before you go on to the next reaction step, so several lab periods will pass before we move on to step 2. You will then nitrate this benzoic acid to m-nitrobenzoic acid via electrophilic aromatic substitution. Again, characterization of this product must occur before you move on to the final step, which is a Fischer Esterification to produce methyl *m*-nitrobenzoate. Abbreviated versions of the three reaction steps are given here, with more complete versions of each of the overall reactions given with each lab prompt separately.

All Three Steps of the Multi-Step Reaction Sequence:



Step 1: the Oxidation of Acetophenone to Produce Benzoic Acid

Overall Reaction:



CAUTION! You are using strong base, strong acid, and bleach in this reaction. Some of these caustic materials will be heated, which compounds their danger. Use great care when working with these solutions! Also, the chloroform by-product is an anesthetic and a potential carcinogen; make sure your

hoods are working continuously and close the hood sash as much as you can while carrying out the bleach oxidation step.

This reaction will be heated on the lowest setting on your hotplate in the hood; turn on your hotplate to its lowest setting as soon as you get to lab. You do not want to overheat the reaction; gentle heat is important!

In a large beaker (at least 400 mL) combine about 2.5 to 3 mL of acetophenone (know its mass) with 40 mL of bleach (5% aqueous NaOCl) per gram of acetophenone and 2.5 mL of 10% NaOH (aq) per gram of acetophenone. Warm this mixture on the *steaming* water bath for about 30-60 min, stirring with your glass rod about every 5 minutes. During this heating time, the chloroform that is produced should boil out of the mixture. At the beginning of this process, you can observe an oily layer of acetophenone floating on top of the aqueous mixture; at the end of the reaction, the oily phase should no longer be visible since it has reacted to form product. If you still have a significant oily layer after heating for 30 minutes, consult your professor.

Once the oxidation is complete, slowly add 1 mL of acetone to destroy any excess bleach and then cool in an ice bath to RT. Slowly add conc. HCl with a pipet until a significant amount of precipitate has formed. When you cannot detect more precipitate forming, check that the pH is 2-3 or less; if not, continue to add HCl until that is so. Cool the mixture in an ice bath to complete crystallization of the benzoic acid product and isolate this product by suction filtration. Wash the product well with water and then let it air dry on the aspirator for a while. It can then further dry in your lab drawer until the next lab period.

When the product is completely dry, obtain its mass and calculate the theoretical and percent yield for your reaction. Check its purity by mp, IR, and/or NMR, as directed by your professor. The product is usually of sufficient purity to use for the next step, but if that is not the case, you can recrystallize it from water.

Clean-up. Check the pH of all the solutions, neutralize as needed and flush down the drain with lots of water.