17. Aromatic Side Chain Oxidation: Preparation of a Benzoic Acid Derivative

A. Background

Benzoic acid and its derivatives are important building blocks in organic chemistry. The sodium salt of benzoic acid is best known for its use as a food preservative where it provides antimicrobial properties. Currently, the maximum allowed level of sodium benzoate in a food product is 0.1% by weight. Sodium benzoate can be prepared by the reaction of benzoic acid with a base, such as NaOH (figure 1).

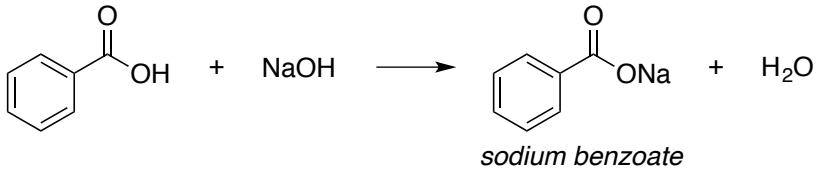


Figure 1. Preparation of Sodium Benzoate

There are a variety of methods that can be employed to prepare benzoic acid and benzoic acid derivatives. One method involves the benzylic oxidation of an alkyl benzene. The two most frequently used reagents for this side chain oxidation are: chromic acid (H_2CrO_4) or a basic potassium permanganate solution followed by acidic workup (figure 2).

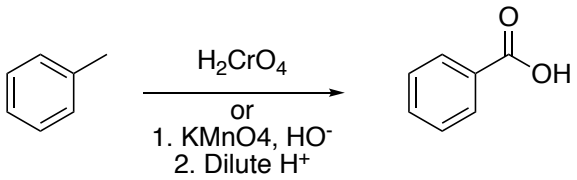


Figure 2. Alkyl Benzene Side Chain Oxidation

Chromic acid is prepared *in situ* by mixing sodium dichromate ($Na_2Cr_2O_7$) and sulfuric acid (H_2SO_4). Mixing sodium dichromate with sulfuric acid initially produces dichromic acid ($H_2Cr_2O_7$). Then, in the presence of water, dichromic acid is broken down into two molecules of chromic acid (H_2CrO_4). The chromium metal in chromic acid is in the +6 oxidation state. (Figure 3)

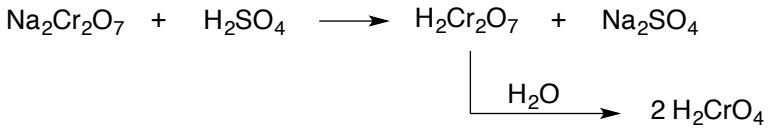


Figure 3. Generation of Chromic Acid

In this laboratory experiment you will use chromic acid to oxidize the side chain of 4-nitrotoluene as shown in figure 4. This reaction is visually quite easy to monitor. Initially, chromium is in the +6 oxidation state [Cr(VI)]. During the reaction, chromium is reduced to the +3 oxidation state

[Cr(III)]. Cr(VI) is bright orange while Cr(III) is green. You will observe this color change during the course of the reaction.

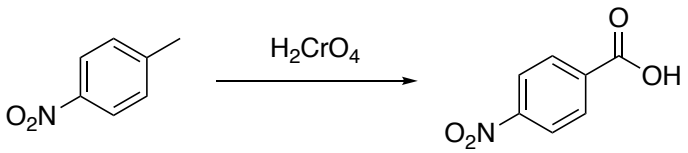


Figure 4. Chromic Acid Oxidation of *p*-Nitrotoluene

We will not go into the mechanism for this oxidation reaction, but it is thought to proceed via a radical intermediate. The reaction requires one or more benzylic hydrogen on the alkyl group that is being oxidized. This requirement is a result of the fact that following the hydrogen atom abstraction at the benzylic position, a resonance stabilized benzylic radical results. This reactive radical intermediate is then rapidly oxidized to the carboxylic acid. (Figure 5)

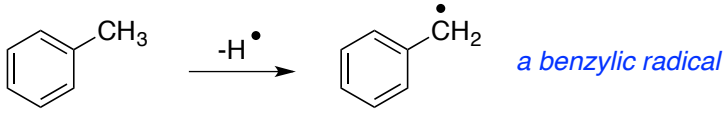


Figure 5. Formation of a Benzylic Radical

B. Experimental Procedure

To a 50 mL Erlenmeyer flask add 150. mg (1.09 mmol) of *p*-nitrotoluene (MW 137) followed by 437 mg (1.47 mmol) of $Na_2Cr_2O_7 \bullet 2H_2O$ (MW 298) and then 2.5 mL of glacial acetic acid. Swirl the flask to help dissolve the solids and heat the solution to 100 °C on the hot plate. Once the solution has reached temperature, turn off the heat and allow the reaction to cool to at least 80 °C before continuing. Carefully, add 0.8 mL of H_2SO_4 dropwise. Be sure to swirl the flask after every few drops to affect mixing. Record any observed changes during the sulfuric acid addition. Once addition is complete, heat the flask back up to 100 °C for 5 min. Remove the flask from the heat and allow it to cool below 80 °C. Add 0.3 mL of ethanol dropwise to the solution (see pre-lab question 2). Next, slowly add water to the solution with continuous swirling until the total volume reaches ~35 mL. Heat the solution at 100 °C for 10 min to aid in dissolving impurities. Allow the solution to cool until the flask can be handled easily (5-10 min). Collect the solid product via Hirsch filtration. Wash the product with 10 mL of cold water or until an off-white solid is obtained.

Recrystallize the solid from a minimum volume of hot ethanol. Collect the crystals via Hirsch filtration.

Determine the yield and record an IR spectrum of your solid product.

Caution: Chromium(VI) is carcinogenic and must be handled with care. Wear gloves, avoid inhaling $Na_2Cr_2O_7$ dust, and be sure to dispose of all chromium waste in the proper waste container.

C. Prelab Questions

1) Look up the MSDS for sodium dichromate online. List the most pertinent health hazards associated with this chemical.

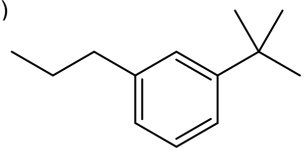
2) At the end of the reaction ethanol is added to reduce excess Cr(VI) remaining in the solution to Cr(III). What is the organic product of this redox reaction?

3) Propose a synthetic pathway to prepare *p*-nitrotoluene from benzene.

4) The benzylic radical is more stable than an alkyl radical because of resonance stability. Show all relevant resonance structures for the benzylic radical.

5) Draw the oxidation product for the chromic acid oxidation of each substrate shown below.

a)



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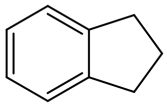

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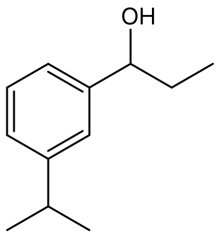

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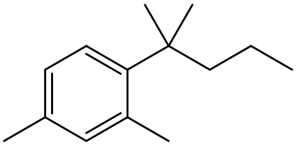

D. Postlab Questions

1) Describe another method that could be used to prepare benzoic acid from benzene besides the chromic acid and dichromate oxidation protocols.

2) Figure 1 shows the conversion of benzoic acid to sodium benzoate. Which one would you expect to be more water-soluble. Explain.

3) How could you convert *p*-nitrobenzoic acid to ethyl *p*-nitrobenzoate?

4) When determining the oxidation state of carbon in an organic molecule, each hydrogen bonded to carbon decreases the oxidation state of carbon by 1 and each oxygen bond to carbon increases the oxidation state of carbon by 1. Using this information, determine the oxidation state of the benzylic carbon in toluene and the carbonyl carbon in benzoic acid. *For example, in H_3C-CH_2-OH the CH_2 carbon has an oxidation state of 0-2+1 = -1.*