CHEM 51LB: EXPERIMENT 1
PREPARATION OF A SYNTHETIC PLANT HORMONE [1]
WINTER 2012: MONDAY, JANUARY 9 – FRIDAY, JANUARY 13

REACTIONS: Acid-Base, Nucleophilic Substitution
TECHNIQUES: Recrystallization, Infrared Spectroscopy

In this experiment, we will practice adapting an existing procedure from chemical literature to the appropriate scale for our class. Attached, you will find an article from the Journal of Chemical Education containing a procedure for the synthesis of a plant hormone. It will be your job to **propose a microscale procedure** *(scaled-down)* to **synthesize approximately 100 mg of the plant hormone**, *p*-chlorophenoxyacetic acid (4-chlorophenoxy-acetic acid). This will require an understanding of stoichiometry and basic arithmetic.

READING ASSIGNMENT:

***J.Chem.Edu.* 1981, *58*, 76. (attached)**
Technique 9: Designing a Chemical Reaction in Techniques in Organic Chemistry 3rd Ed. pgs 85–90.
Supplementary information in Janice Gorzynski Smith (2nd ed), Chapter 9.

CAUTION

1.0 *M* Sodium 4-chlorophenolate/2.5 M sodium hydroxide (NaOH) is caustic and toxic. Wear gloves, work in the hood, and wash immediately if it comes into contact with bare skin.
6 M HCl is corrosive and causes burns. Notify the instructor if any acid is spilled.
Chloroacetic Acid is irritating to skin and mucous membranes. Do not breathe vapors. Wear gloves and do all work in the hood.

Physical Properties of Some of the Reagent and Products

	mp (°C)	bp(°C)	density	solubility
Chloroacetic acid	62-64	189	-	soluble
4-Chlorophenol	43-44	220	1.2238	sparingly soluble
4-chlorophenoxy-acetic acid	156-157	-	-	sparingly soluble

[1] Adapted from "*p*-Chlorophenoxyacetic Acid – Preparation of a Synthetic Plant Hormone", William F. Wood, *Journal of Chemical Education*, **1981, *58***, 76.

EXPERIMENTAL NOTES:

Based on the article, **propose a microscale procedure** *(scaled-down)* to **synthesize approximately 100 mg of the plant hormone**, *p*-chlorophenoxyacetic acid (4-chlorophenoxy-acetic acid). Your microscale procedure should reflect not only a rescaling of amount of chemicals, but also reflect the size and selection of glassware (see Figs 44.6—4.9 Microscale glassware and other microscale apparatus as shown in pp 35—36 in ***Techniques*****).** Before writing the microscale experimental procedure, you should analyze the procedure and calculate the molecular proportions of the reagents. ***Construct a table that includes physical properties of all reagents, products, and possible by-products, moles before scaling down, and moles after scaling down. Show your work on how you scaled-down for ONE compound. This table is in addition to your normal table of chemicals!***

The following stock chemicals and reagents will be provided:

1.0 *M* Sodium 4-chlorophenolate-2.5 M sodium hydroxide (NaOH)
6 *M* HCl
Chloroacetic Acid
1:1 mixture of H_2O/EtOH

Synthesize the plant hormone following your own microscale procedure. After the crude product is recrystallized from ethanol/water, record the mass of the dried product and obtain a melting range for the recrystallized plant. Your product must be turned in to your TA in a properly labeled vial.

NOTES FOR WRITING YOUR DISCUSSION:

Your Theory section should include:

- A brief overview of S_N2 chemistry and factors that affect the reaction.
- A brief discussion of how the particular conditions used affect the reaction.
- A balanced chemical equation for the reaction of chloroacetic acid with aqueous NaOH solution.
- A mechanism for the reaction of sodium chloroacetate with 4-chlorophenolate.

Your Results section should include:

- Appearance and melting point of the product.
- Yield of the product and calculation of % yield.

Your discussion section should include:

- Discuss the identity of the compound you isolated at the end.
- Discuss the % yield and purity of the product.

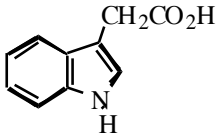
Your Sources of Error/Future Experiments section should include:

- Explain (on the molecular level) what might have decreased the yield of the reaction.
- Propose different experiments that may give you better yield and/or more solid proof of identity and purity.

Journal of Chemical Education, **1981**, ***58***, 76 (copy)

p-Chlorophenoxyacetic Acid-Preparation of a Synthetic Plant Hormone

The principal plant growth hormone, or auxin, is indoleacetic acid (I). Many synthetic chemicals have developed to mimic some of the physiological actions of indolacetic acid, one notable group being various aryloxyacetic acids. 4-Chloro-phenoxyacetic acid (II), 2,4-dichlorophenoxyacetic acid (2,4-D, III) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T, IV) are compounds of high auxin activity. The latter two compounds, 2,4-D and 2,4,5-T, are so powerful that they can literally cause plants to grow themselves to death. Man has exploited this phenomenon by using these chemicals as herbicides for broad leaf plants. Recently, 2,4,5-T has been partially banned from the use as an herbicide as it usually contains minute quantities of one of the most toxic substances known to man--2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD or dioxin, V).



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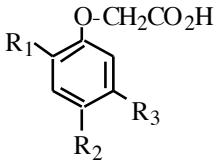
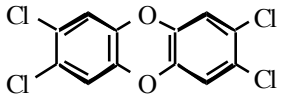
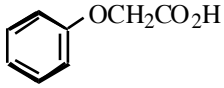


II: R_1=H, R_2=Cl, R_3=H
III: R_1=Cl, R_2=Cl, R_3=H
IV: R_1=Cl, R_2=Cl, R_3=Cl



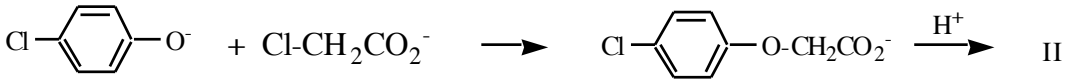
V



VI

4-Chlorophenoxyacetic acid and 2-naphthoxyacetic acid (VI) are much less potent than 2,4-D or 2,4,5-T and thus can be used for purposes other than herbicides. In low concentrations, these compounds (II & VI) can be used to promote the growth of roots of plant clippings, prevent fruit from falling prematurely and cause unfertilized fruits to develop (parthenocarpy). Both of these compounds are used commercially in products that cause tomatoes to set fruit when conditions are not right for natural pollination.

The synthesis of *p*-chlorophenoxyacetic acid is readily accomplished by a nucleophilic displacement reaction between the 4-chlorophenolate anion (VII) and the chloroacetate anion (VIII) followed by treatment with acetic acid to give II.



VII VIII

Since 4-chlorophenol is caustic, toxic, and fairly difficult to dispose because it has a melting point of 43°C, it is convenient to run the reaction using a stock solution that is 1.0 *M* sodium 4-chlorophenolate and 2.5 *M* sodium hydroxide. Addition of chloroacetic acid (Cl-CH_2CO_2H) to this solution gives the chloroacetate anion (VIII).

In regards to the toxicity and caustic nature of the starting materials and product, the author cautions that this experiment should be performed only under close supervision of the students, in lower level or beginning chemistry classes.

Experimental

Sodium 4-Chlorophenolate (VII) - Sodium Hydroxide Solution

A stock solution of 1**M** sodium 4-chlorophenolate (and 2.5 *M* NaOH) was prepared by dissolving 140 g (3.5 moles) NaOH in 800 mL of water (Caution--exothermic) and then adding 128.6 g (1 mole) of 4-chlorophenol. Water was then added to bring the volume to 1 L. **Caution**, **this solution is caustic and toxic**; wash immediately if it comes in contact with bare skin.

4-Chlorophenoxyacetic Acid (II)

Into a 125-mL Erlenmeyer flask was placed 50 mL of a 1 *M* sodium 4-chlorophenolate-2.5 *M* NaOH solution (**Caution--caustic and toxic**) followed by 9.5 g (0.1 mole) of chloroacetic acid. After gentle swirling to dissolve the chloroacetic acid, the mixture was heated on a steam bath[1] for at least 30 min. After cooling for a few minutes, 40 mL of 6 M HCl was added to the flask and the resulting white precipitate stirred to ensure a complete reaction. The flask was cooled in an ice bath for several minutes. The precipitate was then collected by suction filtration and was washed with cold water. Recrystallization from 20 mL of a 1:2 H_2O:EtOH mixture gave 5.0 g (53% yield) of large white needles: mp 155-157 (lit 156-7); IR (KBr), 3200-2300, 1710, 1600, 1480, 1430, 1230, 1070, and 810 cm^{-1}: NMR (acetone-d_6) δ 4.68 ppm (s, 2H), 6.92 (d=9.5 Hz, 2H), 7.3 (d, J=9.5 Hz, 2H) and 7.77 (s, 1H).

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[1] If steam baths are unavailable use a boiling water bath.

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