Introduction:

The principal plant growth hormone or auxin is indoleacetic acid (1). Many synthetic chemicals have been developed that mimic some of the physiological actions of indoleacetic acid, one notable group being various aryloxyacetic acids. 4-Chlorophenoxyacetic acid (2), 2,4-dichlorophenoxyacetic acid (2,4-D, 3) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T, 4) 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 use as an herbicide as it usually contains minute quantities of one of the most toxic substances known to man: 2,3,7,8-tetracholorodibenzo-p-dioxin (TCDD or dioxin, 5).

4-Chlorophenoxyacetic acid (2) and 2-napthoxyacetic acid (6) 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 (2 & 6) can be used to promote the growth of roots on plant clippings, prevent fruit from falling prematurely, and 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 (7) and the chloroacetate anion (8) followed by treatment with acid to give 2.
Since 4-chlorophenol is caustic, toxic, and fairly difficult to dispense because it has a melting point of 43°C, it is convenient to run the reaction using a stock solution that is 1M sodium 4-chlorophenolate and 2.5M sodium hydroxide. (By "stock solution," this means that this reagent has already been prepared for you, a solution that already contains the correct concentrations of sodium chlorophenolate and sodium hydroxide, available on the Hooded Shelf in the lab.) Addition of chloroacetic acid (Cl-CH₂CO₂H) to this solution gives the chloroacetate anion (8).

**Prelaboratory Exercises:**

1. 4-Chlorophenol is insoluble in water. Explain why it dissolves in 2.5 M aqueous NaOH solution and write the equation for the reaction involved.

2. Write a balanced chemical equation for the reaction that takes place when you add 1 mL of 12 M HCl to the contents of the reaction flask as described below. Why is the solubility lower in acidic solutions?

3. Based on the conjugate bases, compare and explain the relative acidities of 4-chlorophenol and phenol. (Hint: compare resonance structures.)

**Cautions:**

4-Chlorophenolate and sodium hydroxide are both caustic and toxic; **Handle with care!** If you spill either, or a solution of either, on your skin, wash immediately with lots of soap and water.

**Synthesis:**

Into a 10-mL Erlenmeyer flask place 2.5 mL of a 1M sodium 4-chlorophenolate-2.5 M NaOH solution followed by 0.475 gram of chloroacetic acid. After swirling gently to dissolve the chloroacetic acid, heat the mixture on a hot water bath for approximately 30 minutes.

**Isolation and Purification:**

After cooling for a few minutes, add about 1 mL of 12 M HCl (concentrated) dropwise to the flask, with intermittent stirring and stir the resulting white precipitate to insure a complete reaction. If only a small amount of precipitate forms after stirring, add a few more drops, stir, and repeat until no more solid is precipitating. (You may also want to use a droplet on the end of the stir rod to test the pH of the solution. The solubility of carboxylic acids is lowest in acidic aqueous solutions.) Cool the flask in an ice bath for several minutes. Then collect the precipitate by vacuum filtration using a Hirsch funnel and a 25 mL filter flask found in your red kit. Wash the precipitate with cold water and recrystallize from a 1:2 H₂O:EtOH mixture. After recrystallizing, filtering and thoroughly drying the product, weigh and take its m.p.

**Analysis**

You will be instructed to analyze your final product by NMR or MS. Analyze your sample according to your assignment sheet and prepare it as per the instructions on Sample Preparation in the Lab Guide (inside back cover).

**Cleaning Up:**

Filtrates from the reaction can be disposed of by flushing down the drain with water.

**Final Report:**

Give the mechanism for the reaction of 4-chlorophenolate with sodium chloroacetate in the Introduction section of your report. Which substance is a nucleophile? At what point in the experimental procedure does this reaction take place?
PostLab Questions:

1. Since nucleophilic substitution occurs faster with a neutral compound, why not synthesize compound 2 by reacting sodium 4-chlorophenolate and chloroacetic acid? (Hint: compare pKₐ's of 4-chlorophenol and chloroacetic acid.)

2. Starting with 2-naphthol, how could you prepare compound 6? Compound 6 is found on the first page of this handout.