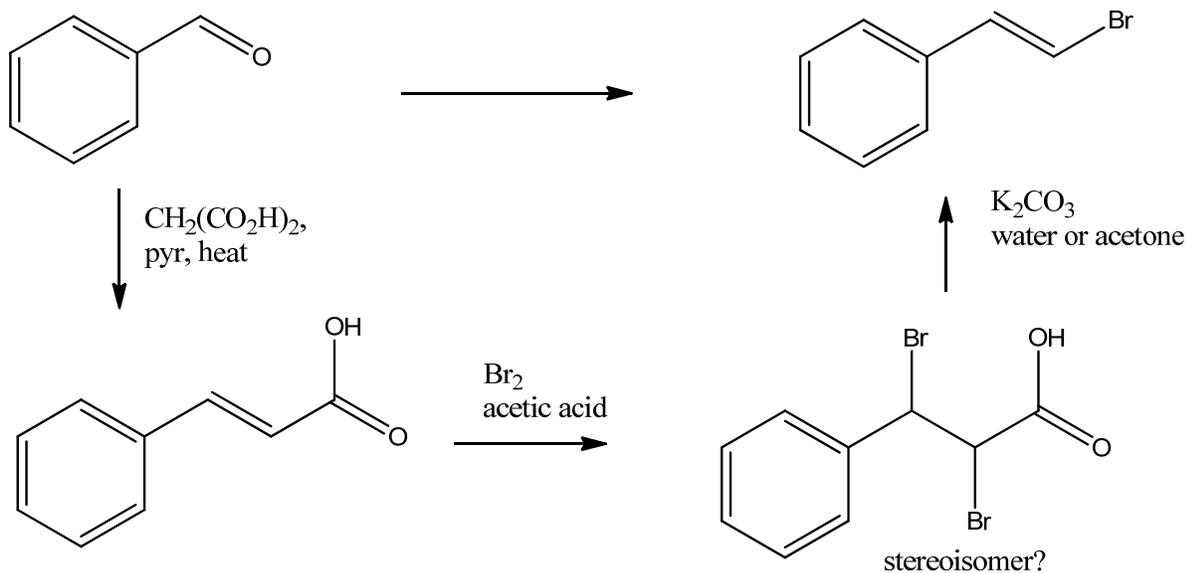


Multistep synthesis of *trans*-2'-Bromostyrene

Purpose: To stereoselectively synthesize *trans*-2'-Bromostyrene in good yield and high purity.

Main reactions:



Procedures:

Step 1: Formation of *trans*-cinnamic acid

In a 10-25 mL roundbottom flask, place a magnetic stirbar, 1.5 g of malonic acid and 120 mg of α -alanine. Add 3 mL of pyridine in the hood (caution: stench!) Add 0.580 mL of benzaldehyde and then add a water-jacketed reflux condenser to the flask. Heat the mixture in a sandbath at 130 °C for 1.5 hours. Allow the reaction mixture to cool to room temperature. Use a Pasteur pipet to transfer the reaction mixture to a 50 mL Erlenmeyer flask containing about 12 mL of cold water. Wash the roundbottom with 3 mL of cold water and transfer to the Erlenmeyer flask. Add 6 M HCl in small portions until a white precipitate forms and the solution is weakly acidic. (It should take about 8 mL of 6 M HCl.) Collect the solid product by vacuum filtration. Wash the collected solid with three 2 ml portions of cold water, then pull air through the filter for about 15 minutes to dry the product as well as possible. Leave the solid in an open beaker to dry until the next lab period. Obtain a yield and characterization data (NMR, IR, melting point). Before conducting the next procedure, be sure that you have 0.500 g of product with a melting point within about 5° of the accepted value.

If you do not have this amount or high enough purity, see your AI to receive some authentic *trans*-cinnamic acid. (You will receive a minor point deduction if you take authentic sample, but it is better to do so than to not get the rest of the lab done.)

Step 2: Formation of 2,3-dibromo-3-phenylpropanoic acid

Place 0.500 grams of *trans*-cinnamic acid in a 25 mL roundbottom flask with a stirbar. Add 1.2 g of pyridinium bromide perbromide (caution! Lachromator) in the hood. Add 12 mL of glacial acetic acid to the flask and then attach a water-jacketed condenser. Heat the mixture with stirring in a sandbath at 120-125 °C for 45 minutes. Cool the solution to room temperature. Using a Pasteur pipet, transfer the reaction mixture, in small portions, to a 50 mL Erlenmeyer flask. Rinse the reaction flask with small portions of acetic acid and transfer the rinse to the Erlenmeyer flask. Cool the flask in an icebath for 5 minutes, then slowly add three 5 mL portions of cold water to the reaction mix with swirling. Collect the pale yellow precipitate by vacuum filtration. Wash the isolated solid with three 2-mL portions of cold water. The solid should become white after these washings. Dry the solid as thoroughly as possible by pulling air through it for 15 minutes. Transfer the product to a beaker to store until the next lab period. After it is dry, obtain a mass and melting point of the product. Look up the accepted melting points of the compounds below to determine the stereochemistry of your product. Is it racemic *erythro* 2,3-dibromo-3-phenylpropanoic acid or is it racemic *threo* 2,3-dibromo-3-phenylpropanoic acid?

If you do not have enough of this product to go on to the next step, see your AI to receive some authentic *trans*-cinnamic acid to redo the lab.

Step 3: Formation of *trans*-2'-bromostyrene

For this reaction, you have a choice of two sets of conditions based on the stereochemistry you observed with your dibromide. You will choose one or the other. If you want to do an E1 mechanism, use water as solvent. If you want to do an E2 mechanism, choose acetone.

Choice A. E1 reaction conditions:

Place 300 mg of your dibromide and 300 mg of potassium carbonate in a 25 mL roundbottom flask. Add 5 mL of distilled water and a reflux condenser. Heat the reaction in a 120 °C sand bath until the solids dissolve, and then heat for an additional 10 minutes. You should observe a yellow oil form. Cool the reaction to room temperature and use a Pasteur pipet to transfer the reaction mixture to a centrifuge tube. (You will use this as a miniscale separatory funnel.) Add 2 mL of methylene chloride to the roundbottom to rinse it, and add the methylene chloride to the centrifuge tube. Shake and separate the organic layer into a small Erlenmeyer flask. Extract the aqueous phase with two more 2 mL portions of methylene chloride and combine all the methylene chloride extracts. Dry the organic layer with magnesium sulfate, then transfer the liquid to a small roundbottom flask. Remove the solvent with a rotovap. (Do not heat the rotovap too high or you will boil off your intended product.) Obtain a mass of product, then obtain a ¹H NMR spectrum in CDCl₃.

Choice B. E2 reaction conditions:

Place 300 mg of your dibromide and 300 mg of potassium carbonate in a 25 mL roundbottom flask with a stirbar. Add 5 mL of dry acetone and a reflux condenser. Heat the reaction in an 80 °C sand bath for 60 minutes. Cool the reaction to room temperature and evaporate the acetone to give a solid/oily crude product. Add 5 mL of distilled water to dissolve all solids. A

yellow oil should form. Use a Pasteur pipet to transfer the reaction mixture to a centrifuge tube. (You will use this as a miniscale separatory funnel.) Add 2 mL of methylene chloride to the roundbottom to rinse it, and add the methylene chloride to the centrifuge tube. Shake and separate the organic layer into a small Erlenmeyer flask. Extract the aqueous phase with two more 2 mL portions of methylene chloride and combine all the methylene chloride extracts. Dry the organic layer with magnesium sulfate, then transfer the liquid to a small roundbottom flask. Remove the solvent with a rotovap. (Do not heat the rotovap too high or you will boil off your intended product.) Obtain a mass of product, then obtain a ^1H NMR spectrum in CDCl_3 .

Lab 9 assignment: Turn in a hardcopy of your lab notebook (carbon copy or photocopy) and spectra attached to a full formal report

- Due at the beginning of lab during the week of April 13
- 100 pts based on in-lab performance, completion of all sections, correctness of content, formal style, and effective writing
- The main theme of the introduction should be synthesis of fragrances and the necessity of correct stereochemistry in odors. Find TWO papers using SciFinder Scholar. Use them as references in your introduction section.
- Submit an electronic copy through Turnitin.com prior to your lab section, or it will be considered LATE

Discussion: You should include these general topics.

- Discussion of the synthesis, including percent yields and characterization of each product. Use data to support your claim for the identity and purity of each synthetic intermediate and the final product. If it didn't work, what could be improved?
- Discuss the stereoselectivity of each step. What data do you have that suggests the cinnamic acid is *trans*? Which dibromide stereoisomer was formed? What mechanism is consistent with the formation of this product? Why did you choose the solvent you chose in the last step? Did it work to produce your intended *trans* product or not?
- Use your proton NMR to discuss the product distribution in the final product. Did you form pure product, or was it a mixture of stereoisomers? If it was a mixture, what was the product distribution?