Introduction: In this experiment, you will carry out a two-part synthesis. In Part I, you will perform the diastereoselective addition of bromine to trans-cinnamic acid. This results in the formation of only one pair of enantiomers of 2,3-dibromo-3-phenylpropanoic acid. Using melting points, you will determine if the major product is either the (2R, 3S), (2S, 3R) pair or the (2R, 3R), (2S, 3S) pair. In Part II, you will react your 2,3-dibromo-3-phenylpropanoic acid with a strong base, giving an unknown compound. Infrared spectroscopy will be used to confirm the identity of this product.

Objectives

- Synthesize 2,3-dibromo-3-phenylpropanoic acid from trans-cinnamic acid.
- By melting point, determine which stereoisomers of 2,3-dibromo-3-phenylpropanoic acid are obtained.
- React 2,3-dibromo-3-phenylpropanoic acid with a strong base and determine the product by infrared spectroscopy.

Pre-Lab Questions

1. Draw wedge and slash diagrams for all four possible isomers of 2,3-dibromo-3-phenylpropanoic acid. Be sure to label each stereogenic center as either R or S.

2. Is the bromination of an alkene an example of anti- or syn-addition? Explain. Draw the mechanism for the addition of bromine to cyclohexene to help illustrate your answer.

Reading

Addition under reflux: Mohrig, Figure 7.2

Electrophilic Addition to Alkenes. Smith, 2nd Ed., Sections 10.8-10.14
Week 1: Synthesis Part 1

CAUTION: Bromine solution and its vapors are highly corrosive and toxic. Dispensing the reagent and the experiment must be performed in a fume hood.

- Prepare a ~50 °C water bath on a stirring hotplate.
- In a 50 mL round-bottom flask equipped with a stirring bar, combine trans-cinnamic acid (10 mmol) and glacial acetic acid (6 mL). Assemble an apparatus for addition under reflux as shown in Mohrig, Figure 7.2.
- Add 10 mL of a 1M solution of bromine in acetic acid to the separatory funnel. Place the reaction flask in the 50 °C water bath and begin stirring.
- Dropwise, add 1-2 mL of the bromine solution to the reaction flask, allow the color of the solution to fade to light orange and repeat the addition. Continue this until all the bromine solution has been added.
- Once addition is complete, continue stirring for an additional 15 minutes. If the solution goes completely colorless, add additional bromine solution until a light orange color persists and stir for 10 minutes.
- Once stirring is complete, add cyclohexene dropwise until the reaction mixture turns light yellow.
- Cool the reaction flask first to room temperature, then in an ice-water bath. Within, 15 minutes crystallization should occur, scratch the inside of the flask if necessary.
- Vacuum filter the precipitate and wash with ice-cold water until the acetic acid odor is no longer noticeable.
- Recrystallize the product from 50% aqueous ethanol.
- Obtain a weight and melting point of the dried product.

Week 2: Synthesis Part 2

- In a 50 mL beaker, add 2,3-dibromo-3-phenylpropionic acid from Part 1 (no more than 2 g) and 10 mL of a 25% solution of potassium hydroxide in methanol.
- Bring the solution to boil on a sand bath and stir with a stirring rod until most of the methanol has evaporated. To the pasty residue, add an additional 10 mL of methanol and repeat the process.

CAUTION MATERIAL MAY SPLATTER!

- Cool the residue and vacuum filter the crude product to remove the residual methanol. Wash the crude product with a small amount of ice-cold methanol.
- Transfer the solid to a beaker and dissolve in 50 mL water and cool in ice-water bath. Add concentrated HCl dropwise until slightly acidic.
- Crystallization should occur. If the product comes out as oil, it may be necessary to scratch the flask or add a seed crystal.
- Vacuum filter the crude product and recrystallize from acetonitrile.
- Obtain a weight, melting point and IR of the dried product.

Clean-Up

- Please clean IR plates return them to the holding tin after use!
- Filtrate from week 1 may be diluted with copious water and flushed down the sink.
- Filtrate from week 2 may be flushed down the sink.

Post-Lab Questions

1. Explain why only one pair of enantiomers are formed in Part 1 of this experiment. Draw a mechanism to help explain your answer. Represent the proper stereochemistry in your structures!
2. What starting material would you need to form the other pair of enantiomers in Part 1?
3. What type of reaction is demonstrated in Part 2? Show a mechanism to illustrate formation of the product you proposed.