

10. Two-Step Synthesis of Diphenylacetylene from *trans*-Stilbene

A. Introduction

In this week's experiment, you will be doing a two-step synthesis of diphenylacetylene. The first reaction in the synthetic sequence is the bromination of *trans*-stilbene to provide *meso*-stilbene dibromide. Once this product is isolated and purified, you will subject it to dehydrohalogenation conditions to obtain diphenylacetylene (Figure 1).

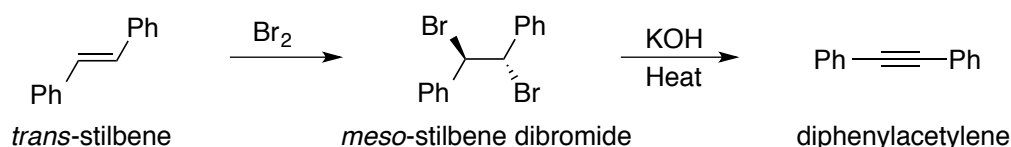


Figure 1. Preparation of Diphenylacetylene from *trans*-Stilbene

1. Introduction to Reactions and Synthesis

The first half of the organic chemistry laboratory covered common techniques that are employed by organic chemists working in the laboratory. From this point forward, you will be performing reactions and synthesis. Synthesis is the preparation of complex molecules from relatively simple and commercially available starting materials. Multistep organic synthesis is incredibly challenging and it can take years to develop a successful synthesis of a complex organic molecule.

When a reaction is carried out, numerous steps are taken to isolate and characterize the final desired product. Many of these steps have been covered in previous labs while new techniques will be explored as you carry out future laboratory experiments. Figure 2 diagrams the series of sequential steps that typically carried out when performing a reaction.

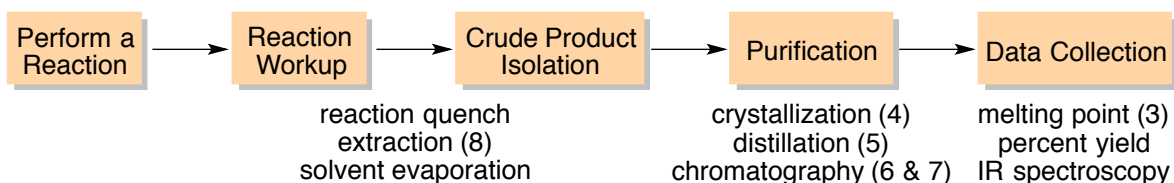


Figure 2. Reaction Protocol

2. Bromination of Alkenes

When a halogen such as Br_2 or Cl_2 is added to an alkene, a halogenation reaction occurs where X_2 is added across the double bond to provide a dihaloalkane. The resulting product will have the two halogens added from opposite sides. This type of addition is called an **anti-addition**. As shown in figure 3, when cyclopentene is brominated, the two bromine atoms end up *trans*, that is they are on opposite sides of the ring. The *trans* relationship of the bromines is due to an *anti*-addition process. In the case of the bromination of cyclopentene, a racemic mixture is formed.

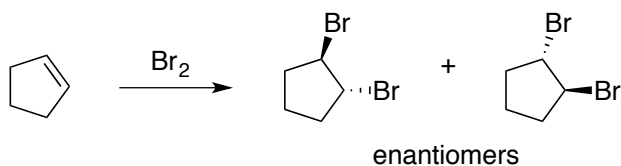


Figure 3. Bromination of Cyclopentene

The reaction is thought to proceed via a bromonium ion intermediate as shown in figure 4. The first step of the mechanism involves addition of a bromine atom across the double bond along with the simultaneous loss of Br^- . This first addition step can and does occur from both sides of the double bond. The bromide ion then reacts with the bromonium ion from the opposite side to give the *trans* product.

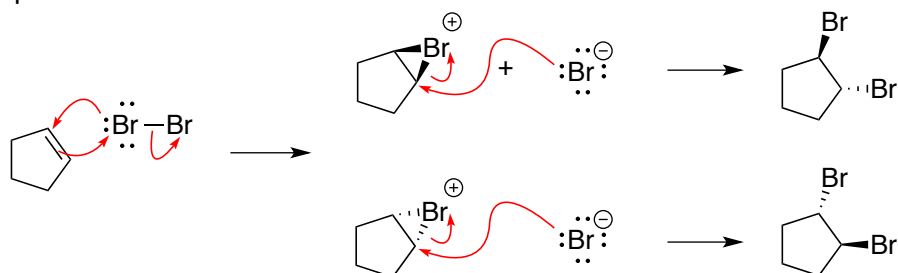


Figure 4. Mechanism for Halogenation

When *trans*-stilbene is used, reaction of the bromide ion by **path a** or **path b** may appear to give different products. Careful examination of these structures reveal that **a** and **b** are identical. In fact, despite this product having two chiral centers, there is a plane of symmetry which makes it achiral (meso). Thus, an enantiomer is not possible. (Figure 5)

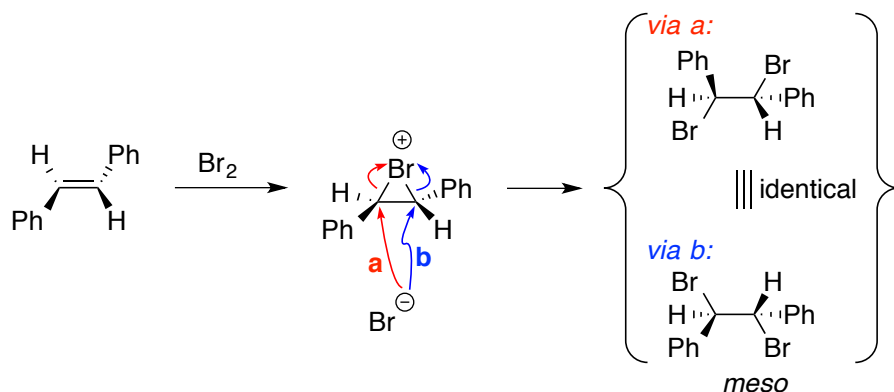


Figure 5. Bromination of *trans*-Stilbene

3. Dehydrohalogenation

Treating a 1,2-dihaloalkane with an excess of strong base, such as KOH, results in two eliminations of HX to produce an alkyne. The first elimination step occurs readily, however, the second elimination requires more forcing conditions (high temperature). The net result is loss of two moles of HBr from the molecule along with the formation of an alkyne product as shown in figure 6.

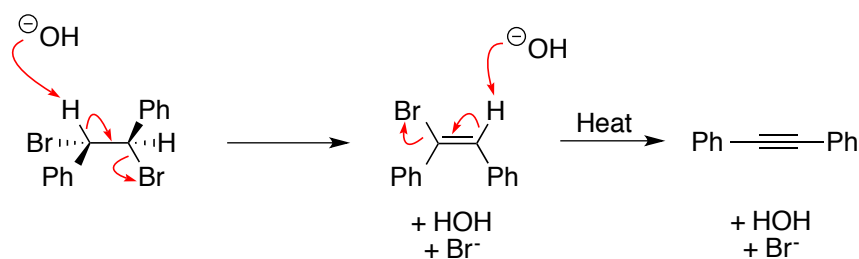


Figure 6. Dehydrobromination

B. Experimental Procedure

1. Bromination of *trans*-Stilbene (Preparation of *meso*-Stilbene Dibromide)

Add approximately 180 mg of *trans*-stilbene (MW = 180 g/mol) and 2.0 mL of dichloromethane (DCM) to a 5 mL conical vial containing a spin vane. Place the vial on the stir-plate in the aluminum block and stir until the stilbene has dissolved.

In a test-tube, obtain approximately 1.2 mL of the 5% Br₂ in DCM solution. This solution is approximately 1.0 M in Br₂. Support this test tube in a small Erlenmeyer flask. **Note: Bromine is toxic and can cause chemical burns. Wear gloves and keep the bromine solution inside the fume hood at all times.**

With stirring, add the bromine solution dropwise to the solution of *trans*-stilbene in the conical vial. Once a light red/brown color persists for several minutes, bromination is complete. The reaction product is a white insoluble solid. Continue stirring to keep the product suspended in solution and add one drop of cyclohexene to destroy the excess Br₂. Stop stirring, cap the reaction vial, and place it in an ice bath for 10-15 min. Collect the solid product using a Hirsch funnel and rinse with 2 mL of cold DCM. Allow the product to dry open to the air for several minutes. Determine the mass of the product, percent yield, and melting point. The product is *meso*-stilbene dibromide (MW = 340 g/mol). You may wish to set a few mg of product aside and determine the melting point at the end of the lab period.

It is critical that you get an accurate mass of product so that you can correctly perform the calculations for the next reaction.

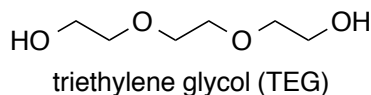
2. Dehydrohalogenation of *meso*-Stilbene Dibromide (Preparation of Diphenylacetylene)

*If you don't have enough *meso*-stilbene dibromide from part 1, you can obtain some from the reagent hood. If you have enough, however, you should use the material that you prepared.

Weigh approximately 150 mg of the *meso*-stilbene dibromide, prepared in part 1, into a 5-mL conical reaction vial. Next add approximately 200 mg of KOH to the vial. Powdered KOH can be obtained by folding up a piece of weighing paper around two KOH pellets and subsequently crushing them with the aluminum block. The KOH should be used immediately as it is hygroscopic – it will rapidly absorb water from the air. **Note: Avoid getting KOH on your skin, as it will cause chemical burns.**

Next, add enough triethylene glycol (TEG) to make the solution 0.6 M in *meso*-stilbene dibromide. The actual volume will depend on the amount of *meso*-stilbene dibromide actually

used. Connect the air condenser to the conical vial and secure it with a nut and o-ring. Heat the reaction mixture to 190 °C in the aluminum block on the hot-plate. Allow the reaction mixture to heat at this temperature for 5 min. Next, allow the vial to cool in the air. Once it has cooled substantially, you can complete cooling in a warm water bath. Add 2 mL of water and then cool the solution in an ice bath. Collect the solid product using a Hirsch funnel.



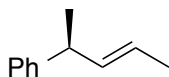
Purification: The crude material can be recrystallized in the Craig Tube using hot 95% ethanol. Be careful not to add too much hot ethanol (0.5 mL should be sufficient). Review the crystallization procedure if necessary. Once the crystals have been collected by centrifugation, determine the yield and melting point of the product.

C. Pre-Lab Questions

1. Write the reaction for the bromination of *cis*-stilbene and draw all stereoisomeric products. What is the relationship between the products?
2. In the bromination of *trans*-stilbene, suppose you started with 300 mg of *trans*-stilbene and used an excess of Br₂. Following the reaction, you isolated 330 mg of *meso*-stilbene dibromide. What is the percent yield of the reaction? *See supplemental handout for help.*
3. How does the addition of cyclohexene destroy excess bromine in the solution?
4. In the second procedure, you are instructed to add enough triethylene glycol (TEG) to make the solution 0.6 M in *meso*-stilbene dibromide. Suppose you 200 mg of *meso*-stilbene dibromide. What volume of TEG would be required?
5. The boiling point of TEG is 285 °C. Explain why it is necessary as the solvent in this experiment. Why can't ethanol be used instead?

D. Post-Lab Questions

1. Suppose the compound shown below were subjected to bromination conditions. Draw all of the possible stereoisomeric products. *Remember: the bromonium ion can form on both sides of the double bond and the bromide can open up the bromonium ion by attack at either carbon.*



2. What was percent yield for each of the reactions that you performed? *Your calculations should be included in the results section of your notebook.*
3. The overall yield for a synthetic sequence can be determined by multiplying together the percent yields for each step of the synthesis. For example, if the yield from the first step is 90% and the yield from the second step is 60%, the overall yield is 54%. Calculate the overall yield for your synthetic sequence.