

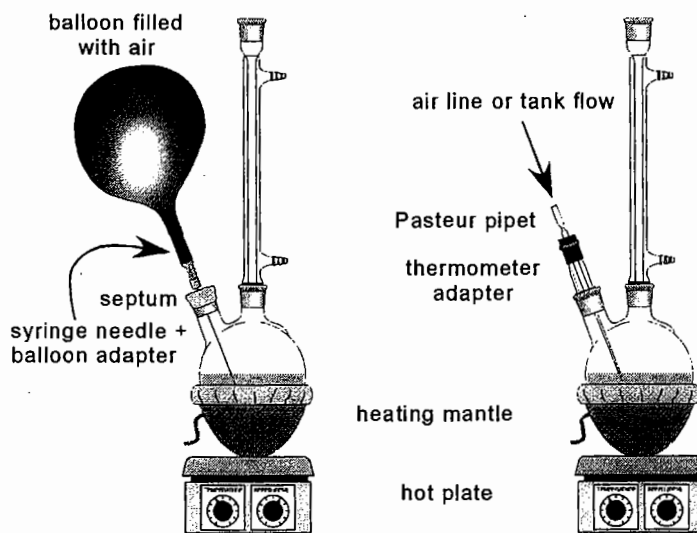
Experiment #6: Oxidative Coupling of Alkynes: The Glaser-Eglinton-Hay Coupling

Experimental Procedure

SAFETY PRECAUTIONS: 2-Propanol and ethyl acetate are flammable; avoid open flames.

Reaction

1. To a 100 mL round-bottom two-neck flask containing a magnetic stir bar, add 30 mL of 2-propanol, 100 mg of cuprous chloride, and 20 drops of tetramethylethylenediamine. Stir with a magnetic stir bar while you assemble the rest of the apparatus – select one of the two setups shown below. (A third alternative, more complex to set up but equally effective, is presented at the end of this experiment.)



Apparatus for Glaser-Eglinton-Hay coupling of 1-ethynylcyclohexanol

Notes

- i. The needle (or pipette) must be positioned so that its tip is below the solution surface.
- ii. Maintain a slow, steady stream of air into the apparatus.
- iii. If a three-neck flask is used, seal the extra neck with a septum – this neck can be used to add the alkyne.
- iv. You may need to refill the balloon from time to time.

2. Add 2 g of 1-ethynylcyclohexanol to the reaction flask, then heat the reaction to a gentle reflux.
3. After about 30 minutes, spot a sample of the reaction mixture on a silica gel TLC plate. Spot the starting material in a separate lane on the same plate for comparison. Elute with a 70:30 mixture of hexanes/ethyl acetate, then use both ultraviolet light and iodine staining to visualize your TLC plate. If your reaction mixture still contains starting material, continue to heat the reaction at reflux until your TLC analysis shows that the reaction is complete. Some guidelines for carrying out a successful TLC analysis that may be useful to you are provided at the end of this experiment.

Workup

4. When the reaction is complete, evaporate the 2-propanol on a rotary evaporator. Ensure that *all* the 2-propanol has been removed – gentle warming will help to drive off the last traces.
5. Add 20 mL of water containing 1 mL of 12 M HCl to the material remaining in the flask. Collect the solid by vacuum filtration and pull air through it until it is dry.

Purification and Characterization

6. If your crude product is still blue or green, repeat step 5 to remove the remaining copper salts. If it is brown or black in color, decolorize it according to procedure 6A. If it is white or off-white, go directly to recrystallization procedure 6B. **Note: The odor of ethyl acetate is not unpleasant in small concentrations, but larger amounts can be troubling. Follow your instructor's recommendation as to whether to carry out these procedures in a fume hood or elsewhere.**
 - 6A. Dissolve the crude product in about 20 mL of ethyl acetate and add approximately 0.25 g of decolorizing carbon [48]. Heat the mixture gently for about 1 minute, then remove the carbon by filtration. Evaporate some of the solvent on a rotary evaporator. It should **not** be necessary to remove all of the solvent in order to cause the white crystalline product to separate.
 - 6B. Recrystallize the crude product by dissolving it in less than 20 mL of hot ethyl acetate, then allowing the solution to cool to room temperature.

48. Do not use more carbon than the amount specified – it will adsorb some of your product and decrease your yield!

7. Collect the product by vacuum filtration and pull air through it until it is dry. (If time allows, cool the solution in an ice bath for 10 minutes or so before isolating the product.)
8. Determine the mass of your product. Analyze the purity of your product by TLC. If time allows, record an infrared spectrum of the product as a KBr pellet. (Helpful tips for the successful preparation of a KBr pellet are provided at the end of this experiment.)

Post-Lab Questions and Exercises

1. Describe the color and melting point range of your product. Report the mass and percent of theoretical yield of the product.
2. In your own words, describe the roles of each of the reagents used during this reaction.
3. Describe your TLC results for both the reaction mixture and the purified product. How many spots did you observe in each case? Was there any difference between the two visualization methods (ultraviolet vs. iodine)? What were the R_f values for the spot(s)?
4. Attach your infrared spectrum (if you obtained one) and identify ("assign") the major peaks in the spectrum. If you did not have time to obtain your own spectrum, assign the major peaks in a spectrum obtained from your instructor.
5. Calculate the atom economy for the reaction.
6. Perform an economic analysis for the preparation of the product.

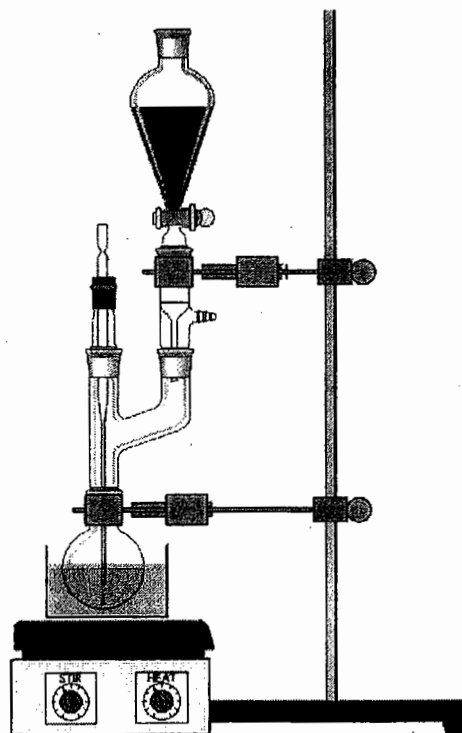
Experiment Development Notes

This experiment was patterned after experiments presented in Wilcox and Wilcox (*Experimental Organic Chemistry*, Prentice Hall, 1995) and Zanger and McKee (*Small Scale Synthesis: A Laboratory Textbook of Organic Chemistry*, W.C. Brown Co., 1995). These reported procedures were substantially modified, most notably by changing the solvent and glassware setup (enhancing the reliability of the experiment in our students' hands) and adding TLC training to the experiment.

Use of Negative Pressure to Supply Air

In the event that the specified apparatus is unavailable, the reaction can be performed using negative rather than positive pressure. In order to do so, the following modifications should be made.

- i. Use a single-neck flask with a water bath for heating (maintain the water bath temperature at roughly 50 – 60°C.
- ii. Attach a Claisen adapter. Insert a Pasteur pipette into a thermometer adapter and place this assembly into the straight neck of the Claisen adapter. The tip of the pipette must be below the surface of the solution.
- iii. Place a straight vacuum adapter into the second neck of the Claisen adapter. Attach the side port to a vacuum source, and attach a separatory funnel containing roughly 30 mL of 2-propanol to the top of the vacuum adapter.
- iv. Draw a *slow* vacuum on the apparatus, causing air to bubble slowly through the solution. If this does not happen, ensure that all of the glass joints are well sealed.
- v. In the course of the reaction, some 2-propanol will be lost by evaporation from your reaction mixture. As needed, add 2-propanol from the separatory funnel to compensate for this loss.



A Short Guide to Successful TLC Analysis

i. *Apply your sample to the TLC plate*

Using a glass capillary, apply a *small* spot of your reaction mixture (or compound dissolved in a suitable solvent) near one end of a TLC plate. The more concentrated your sample, the smaller the spot should be. If your solution is relatively dilute, build up a sufficient amount of compound for analysis by repeatedly spotting the sample at the same place on the TLC plate, waiting for the solvent to

evaporate after applying each portion. If your capillary contains too much sample, it can be difficult to control the size of the spot – simply bleeding some of the solution out of the capillary by very briefly touching it to a piece of tissue before spotting the plate generally helps to control spot size.

Allow the spotting solvent to evaporate completely. If any of this solvent is left behind during elution, it may result in irreproducible changes in R_f values (the distance traveled by the substance divided by the distance traveled by the solvent front).

ii. *Develop the TLC plate*

Place the TLC plate (with the sample spot down) in a developing chamber with a small amount of solvent in the bottom. Make sure the solvent does not cover the sample spot.

If possible, keep the atmosphere in the developing chamber saturated with the vapor of the elution solvent. (This may be easily accomplished by covering the chamber – a watch glass makes an ideal lid.) A strip of filter paper wrapped partially around the inside of the developing chamber is helpful, but not necessary. If used, ensure your TLC plate does not touch the filter paper, as this can cause solvent to bleed in from the edges of the plate, causing spots to drift diagonally across the TLC plate.

Allow the solvent front to approach, but not reach, the top of the TLC plate.

Remove the plate from the developing chamber, mark the solvent front with a soft pencil or a small scratch, and let the plate dry.

iii. *Visualize the spots and calculate the R_f value*

Although some compounds may be visible to the naked eye on a TLC plate, many others are not. Most TLC plates contain ultraviolet light-sensitive phosphors, allowing use of an ultraviolet lamp for visualization. Alternatively, the plate may be placed in a capped bottle containing solid iodine; the

iodine vapors will react with many compounds on TLC plates and cause them to become visible to the naked eye. Many other visualization methods are also available.

Mark the observed spots with a soft pencil and calculate their R_f values.

Tips for the Successful Preparation of KBr Pellets for Infrared Analysis

Thoroughly grind 1 – 2 parts of the compound with approximately 100 parts of dry, infrared-grade KBr with a small mortar and pestle. Do not make the common mistake of using too much compound! Transfer some of the mixture to the pellet press and apply pressure. The resulting pellet should be fairly transparent and uniform in thickness. Some amount of trial and error is usually required to a good pellet.

Common problems in making a KBr pellet

Cracked or partially formed pellet: Too small an amount of mixture in the press. Try again, using a larger amount.

Opaque (and often grainy) pellet: Too large an amount of mixture in the press. Try again, using a smaller amount.

Grainy pellet: Either too much mixture in the press or not enough pressure used to prepare the pellet. You should feel some resistance as the press is closed, but must not treat using the press as a muscle-building exercise! Forcing the press to close can damage it, and it is both surprisingly easy and expensive to damage a press in this way.

White or colored flecks in a transparent pellet: Compound was not sufficiently ground into the KBr. Try again, grinding more thoroughly before attempting to press the pellet.

Common problems in obtaining an IR spectrum

Strongly sloping baseline: Incomplete grinding. Try again, using more care in the initial grinding of the compound with KBr.

Noisy spectrum – high % transmittance values: Not enough compound. Try again, using more compound when preparing the pellet or using a thicker pellet. For instruments using automatic subtraction of a “background” spectrum, ensure that the background spectrum is appropriate.

Noisy spectrum – low % transmittance values: Too much compound or pellet too thick. Try again, using less compound when preparing the pellet or using a thinner pellet. (Simply regrinding the pellet with a little more KBr, then pressing again, can work well.) For instruments using automatic subtraction of a “background” spectrum, ensure that the background spectrum is appropriate.

Upside-down peaks: Ensure that the instrument is set to record % transmission, not absorbance. For instruments using automatic subtraction of a “background” spectrum, ensure that the background spectrum is appropriate.

All peaks broad and featureless: Wet sample. Try again, making sure your compound and the KBr are completely dry.