

Factors that could help increase the S_N2 are determining a good electrophile and nucleophile. The rate is carbon dependent, of which oxygen bond is connected. Which will tell us the strength of the nucleophile; hence the nucleophile will always be an alkoxide. Also, the reactions will produce more rapidly in the kinds of solvents used in the reaction synthesis. The reaction will produce more rapidly when it's polar. Aprotic solvents are used because the solvent and hydrogen bond will solvate the nucleophile. So, the commonly used solvents such as dimethyl sulfide (DMSO), and dimethyl formamide (DMF), and acetonitrile(CAN) are common solvents used in the Williamson ether synthesis reactions.

Experimental Procedure

Obtain and crush 4 tablets of 325mg strength Tylenol using a mortar and pestle, this should add up to 1.3g acetaminophen. Make sure to weight it on the balance. Add the resulting powder to a 50 mL round-bottom flask. Add 2.5 g of potassium carbonate, 15ml of 2-butanone, and one boiling stone to the acetaminophen. In the fume hood, add 1 mL of iodoethane to the reaction mixture, and then set up your apparatus as seen in (figure 3, shown below). Reflux the reaction mixture for 1 hour. Cool the reaction mixture to below its boiling point and vacuum filter the solids. Wash the bottle 2x with 5 mL of ethyl acetate.



Figure 3

Then take a TLC of the reaction mixture before workup. The TLC plate should contain three lanes: 1) pure acetaminophen; 2) co-spot (reaction mixture + pure acetaminophen); 3) reaction mixture. Examine the TLC plate under UV light and circle the spots you observe.

Now, transfer the filtrate to a separatory funnel and extract the solution (organic layer, will be on top), separate with 20ml of 5% NaOH_{aq} and 20ml of water. Transfer the cloudy organic layer to a clean Erlenmeyer flask and dry using sodium sulfate (add Na₂SO₄ until the solid no longer clumps). Swirl the flask as you add the Na₂SO₄- the phenacetin solution should become clear. Decant the dried phenacetin to a 50 mL round bottom flask, and remove the solvent using the rotary evaporator. The "rotovaps" will increase the surface area and create a solid. Recrystallize the resulting solid using hot ethanol. Remember that for recrystallization you want to use the minimum amount of hot ethanol possible to just dissolve the solid, and that you should keep both ethanol and the beaker with your solid + ethanol hot at all times during the dissolution process. Once all the phenacetin is dissolved, remove the solution from heat and let it cool first to room temperature and then in an ice bath. Scratch to induce recrystallization if none occurs in the ice bath. Filter the final product and dry attached to vacuum. Weight your final product and calculate percent yield. Make sure you do this before performing any tests or characterization. Characterize the product by TLC, melting point analysis, and IR spectroscopy. For the TLC, prepare a tiny amount of solution of your product in ethyl acetate and use the same solvent system as you did the reaction mixture. Calculate the R_f values of all spots on all TLC plates.

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Table of Contents Pkg Acp Chemistry Lab Experiments

1. Understanding the eBook Pkg Acp Chemistry Lab Experiments
 - The Rise of Digital Reading Pkg Acp Chemistry Lab Experiments
 - Advantages of eBooks Over Traditional Books
2. Identifying Pkg Acp Chemistry Lab Experiments
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Pkg Acp Chemistry Lab Experiments
 - User-Friendly Interface
4. Exploring eBook Recommendations from Pkg Acp Chemistry Lab Experiments
 - Personalized Recommendations

- Pkg Acp Chemistry Lab Experiments User Reviews and Ratings
- Pkg Acp Chemistry Lab Experiments and Bestseller Lists
- 5. Accessing Pkg Acp Chemistry Lab Experiments Free and Paid eBooks
 - Pkg Acp Chemistry Lab Experiments Public Domain eBooks
 - Pkg Acp Chemistry Lab Experiments eBook Subscription Services
 - Pkg Acp Chemistry Lab Experiments Budget-Friendly Options
- 6. Navigating Pkg Acp Chemistry Lab Experiments eBook Formats
 - ePub, PDF, MOBI, and More
 - Pkg Acp Chemistry Lab Experiments Compatibility with Devices
 - Pkg Acp Chemistry Lab Experiments Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Pkg Acp Chemistry Lab Experiments
 - Highlighting and Note-Taking Pkg Acp Chemistry Lab Experiments
 - Interactive Elements Pkg Acp Chemistry Lab Experiments
- 8. Staying Engaged with Pkg Acp Chemistry Lab Experiments
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Pkg Acp Chemistry Lab Experiments
- 9. Balancing eBooks and Physical Books Pkg Acp Chemistry Lab Experiments
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Pkg Acp Chemistry Lab Experiments
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Pkg Acp Chemistry Lab Experiments
 - Setting Reading Goals Pkg Acp Chemistry Lab Experiments
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Pkg Acp Chemistry Lab Experiments
 - Fact-Checking eBook Content of Pkg Acp Chemistry Lab Experiments

- Distinguishing Credible Sources
13. Promoting Lifelong Learning
- Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
- Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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