

Experiment 14 —

*Alkylation of *p*-dimethoxybenzene*

Pre-lab preparation. (1) Write the balanced equation for the reaction that you will be carrying out, including structures of reactants and product. (2) look up relevant physical properties of reactants and product. (3) Read the procedure for advice on how to determine quantities, then, (4) directly below each reactant and product (but not solvents or catalysts), list (a) the molecular weight, (b) the mass (and volume, if relevant), (c) the number of moles, (d) the mol ratio relative to your limiting reagent, and (e) any relevant physical data (e.g., if you plan to measure out a liquid by volume, you would have looked up the density, right? This is a good place to record that, as well as any other data that will help you figure out how to handle the compounds.) (5) Write the mechanism of the first *t*-butylation. Then write something like “yadda yadda yadda” for the second, since it’s exactly the same sequence of steps. (6) This reaction is expected to make just one of three possible isomeric di-*tert*-butyl products. Why do we not expect to get the other two isomers?

In this experiment you will be carrying out an EAS reaction akin to a Friedel-Crafts alkylation. But instead of the standard F-C conditions — alkyl chloride and AlCl_3 — you will be generating the electrophile by the reaction of an alcohol with a strong acid.

The reaction that you will be carrying out is the di-*tert*-butylation of *para*-dimethoxybenzene with a mixture of acetic acid and sulfuric acid solvent. The latter also functions as the catalyst. The electrophilic *tert*-butyl cation will be generated by the reaction of *tert*-butyl alcohol with sulfuric acid. The product, 1,4-di-*tert*-butyl-2,5-dimethoxybenzene, will precipitate as it is formed, and it will be isolated, dried, and purified by recrystallization from a mixture of CH_2Cl_2 and CH_3OH .

Your pre-lab prep should include determination of the quantities of reagents needed to make a theoretical yield of 7.0 g of the product. *p*-Dimethoxybenzene is the limiting reagent. Determine the stoichiometric ratio of *t*BuOH needed (i.e. 1 equiv? 2 equiv? How many moles is

that?), and then plan on using a 20% excess. *t*BuOH melts at 25°C, so you may find the bottle full of solid or full of liquid, depending on the temperature of the lab. If the compound is solid, it's easy enough to melt a little. So assume that you'll be working with *liquid*, and determine the volume that you'll need. Plan on using *about* 3 ml of acetic acid (HOAc) and 5 ml of sulfuric acid (H₂SO₄) for every gram of dimethoxybenzene you start with. Note carefully the word "about". Solvents don't need to be measured to the hundredth of a ml. Your TA will check your calculations. If you mess it up or get silly with the sig figs you'll have stand in the corner for 30 min, so be sure to do this correctly.

Procedure. *As you go, record in your notebook what you actually did and what you observed. This should be written in enough detail that someone else can follow and repeat the procedure using just your notebook write-up.* In contrast to the document you're reading, which contains advice, warnings, and various bits of prodding to get you to think about certain things, *your* write-up will focus on reporting the relevant data and facts. For example, "45 ml of water was added, causing formation of a red-purple needle-like solid. This was filtered by suction..."

Place your *p*-dimethoxybenzene in a 125-ml Erlenmeyer flask (the easiest way to do this is to tare the flask, then weigh the solid directly into it. You might consider including a suitable funnel in the tare. Alternatively, you can omit the funnel, but then be sure to clean all the spilled solid off of the balance, the countertops, your shoes, etc. ***In the fume hood***, add the *tert*-butyl alcohol and acetic acid, and place the mixture in an ice-water bath to cool. Put a thermometer in this solution. Swirl the flask periodically to encourage dissolution of any solid that remains. Don't use the thermometer as a stirring rod.

Carefully measure the sulfuric acid into a separate *dry* Erlenmeyer. (What size? Use your judgment — normally a flask that ends up about 30 to 60% full is about right, depending on what you need to do with it — add more stuff? Swirl vigorously? Just think ahead.) **Caution: sulfuric acid is highly corrosive — do not get it on your skin, and do not drip or spill it. Clean up any drips, drops, or splatters promptly, or sooner.** Put this flask in the ice-water bath to cool.

Clamp the 125-ml Erlenmeyer (still in the ice bath), and mount an addition funnel (cleverly disguised as a separatory funnel) directly above it, with the tip below the rim of the flask. Carefully add the chilled H₂SO₄. Watch that you don't get ice bath droplets into anything.

While gently swirling the Erlenmeyer (loosen the clamp if necessary), slowly add the sulfuric acid from the addition funnel. The addition should take about 5 to 10 min. Keep an eye on the temperature, and try to control the addition rate so that it stays below 15°C.

By the end of the addition there should be a considerable amount of solid product. The next step is to dilute the mixture with water, but adding water to concentrated acid generates lots of heat, so this could easily get out of hand. A common way to carry out such a dilution is to keep the rxn mixture in the ice bath and carefully add crushed ice to the flask. Ten or 15 pieces should do the trick. Check that the flask is still cool to the touch. If so, carefully add water to bring the total volume to about 80 ml.

(Deionized water or tap water? The former is essentially just water; the latter is water with dissolved salts. Is there a reason to add a random amount of dissolved stuff to your reaction mixture? So when a procedure calls for “water”, that means just water. If the procedure requires water with something dissolved in it, it will say that, e.g. “5% aq NaHCO₃”, or 1M aq HCl.)

Continue to cool the reaction mixture as necessary. When it is at room temp or below, collect the product by suction filtration. Use the glass fiber filter circles. (Standard filter paper will get eaten by the acid.) Press the filter cake with a spatula and apply suction for an additional minute or two, then release the vacuum, rinse the solid with 5 ml of cold methanol, and reapply suction. Repeat this process to rinse with two more 5-ml portions of cold methanol.

There is likely still residual water in your solid at this point, and it would take too long to let it air-dry. Instead, transfer the solid to a clean Erlenmeyer. (Q: What size? A: Read ahead and figure it out. Q: Is it okay if it's wet? A: If you're going to recrystallize the solid from water, then it doesn't matter; if you're going to dry it, then introducing more water is counterproductive, eh? Just think ahead...)

In the fume hood, dissolve the solid in about 10 ml of dichloromethane (aka methylene chloride). Now, you may see droplets of water, or your solution might be cloudy due to lots of microdroplets, or water may be dissolved in the solvent. It doesn't matter — we just want to get rid of it. Dry the solution with anhydrous MgSO₄. (Q: How much? A: Enough to remove all the water. Q: How can you tell? A: Recall that we did this last semester. What happens when you

add a drying agent to a wet solution?) After a few minutes you can filter off the drying agent. Recover the product residue by rinsing with a little solvent.

Now we need to get the product to crystallize. It's so soluble in CH_2Cl_2 that we can't play the usual game with temperature to get it back out of solution. (If there were no other option, cooling with dry ice might induce crystallization, but...) The product is much less soluble in methanol, and because methanol is miscible with CH_2Cl_2 , we can do a variation on the mixed-solvent crystallization. The added benefit of using this solvent pair is that CH_2Cl_2 boils at a lower temperature than CH_3OH , so we can remove most of the CH_2Cl_2 , effectively changing the solvent composition all the way from pure dichloromethane to nearly pure methanol. If you didn't look the bps up before lab, you can find them posted on the back wall by the GC room.

Add about 20 ml of methanol, insert a boiling stick (easier to remove than a stone), and heat the solution on a steam bath *in the fume hood* to drive off dichloromethane until crystals start to form. Then let the crystallization proceed at room temp. When the crystals decide that they're finished crystallizing, place the flask in ice to encourage more to come out of solution. Collect the solid in the usual manner and rinse with a little cold methanol.

The crystals should air-dry within a few min. Determine the yield (mass and %) and measure the melting point. Remember, you need to control the temperature so that it's no more than about 1°C per min through the melting range or the thermometer and sample may not be at the same temperature!

Clean-up. Be sure to thoroughly rinse all the droplets of sulfuric acid out of the addition funnel. All waste solutions go in the liquid waste container. The used drying agent and filter paper go in the solid waste container.

Write-up. Turn in your duplicate notebook pages with your clear and concise procedural write-up, including your reported yield and mp. In a few sentences, discuss the implications of these results. Is the yield reasonable? Very low? Over 100%? Is the mp too high? Too low?

Adapted from *Organic Experiments, 7th Edition*, L.F. Fieser and K.L. Williamson; D.C. Heath, Lexington 1992; Experiment 37: Friedel-Crafts Alkylation of Dimethoxybenzene, pp. 359–362.