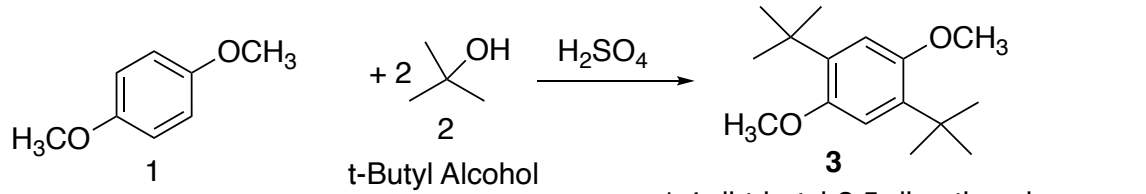
# Friedel-Crafts Alkylation of 1,4-Dimethoxybenzene




1
1,4-dimethoxybenzene
mw=138 g/mol

2
t-Butyl Alcohol
mw = 74.1 g/mol
Density = 0.79g/mL
mp = 26°

**3**
1,4-di-t-butyl-2,5-dimethoxybenzene
mw=250 g/mol
mp = 80-120 range

## General Issues with Electrophilic Aromatic Substitution Reactions

### 1. Polysubstitution

Aromatic substitutions always involve the issue of how many substitutions will occur. Will reaction stop after one substitution? Will it proceed to give a second substitution? Will it proceed further to give a third substitution? In today's experiment the reaction does not stop after a single substitution, but proceeds on to a second. However, it does basically stop after the second substitution and does not proceed appreciably to a third or fourth substitution. Influential factors are electronic and steric:

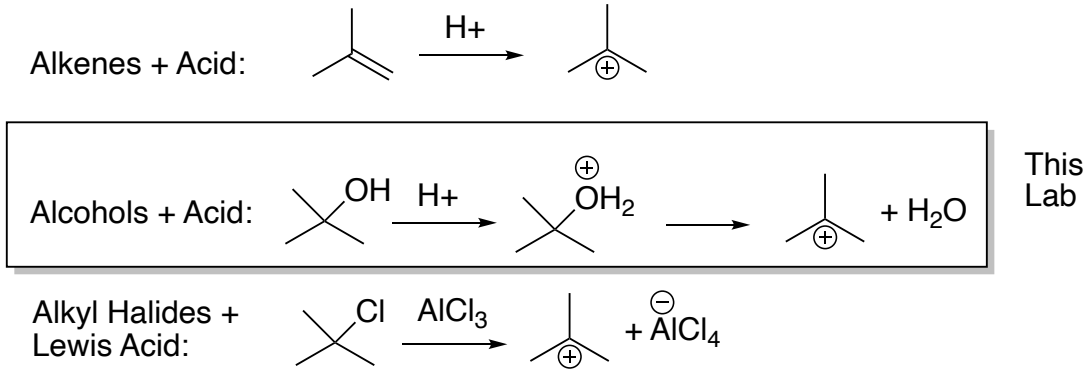
- Electronics: are new substituents electron donating or electron withdrawing? Will they stabilize or destabilize the cation involved in subsequent substitutions? As a result will they activate or deactivate toward subsequent substitution?
- Steric: are new substituents large enough to obstruct further substitution?

### 2. Position of Substitution: Ortho, Meta, or Para To a Pre-existing Substituent?

Relative to a pre-existing substituent (or several of them…), will a new substitution occur ortho, meta, or para? Electronic and steric factors are again influential. In today's experiment, for example, after the first t-butyl group is attached, why does the second t-butyl group go where it does?

### 3. Generation of the Electrophile

All electrophilic aromatic substitution reaction mechanisms require a strong electrophile, usually cationic. In today's experiment, the active electrophile is the t-butyl cation. For a general alkylation, in which an alkyl cation is required, there are several alternate precursors. Ours will use the alcohol, which under protonation can lose water and produce the 3° carbocation which can then add to the aromatic ring.



**Reaction Procedure:**

1. Weigh out 1.50 g of 1,4-dimethoxybenzene and place in a 125-mL Erlenmeyer flask containing a stir bar.
   - Note: For calculations, this will be the limiting reagent.
2. Measure out 3.10 mL of warm t-butyl alcohol into a syringe, and inject into the Erlenmeyer flask. (Note: t-butanol freezes at 26ºC, so it's best to handle it somewhat warm so it stays liquid. If it has much chance to cool off, it may solidify and complicate delivery.)
   - Note: This is a substantial surplus of t-butanol. There is lots more than two equivalents relative to the aromatic substrate.
   - So, for theoretical yield calculations, this is NOT a factor for limiting reagent.
   - This also means that there must be some reason why substitution quits after adding two t-butyl groups, and for some reason will NOT add a third t-butyl group.
3. Measure out 5 mL of acetic acid from a buret. You can deliver this directly into your Erlenmeyer, or else drain it into a small flask/beaker and pour it in. Acetic acid is smelly, so delivering it directly in the hood is a good way to reduce smells in the lab. If you do transfer via a small flask/beaker, rinse that out pretty quickly in the hood so that the lab doesn't smell too much like vinegar.
4. Cool the Erlenmeyer flask in an ice-water bath on a stir plate, and adjust to get steady stirring.
5. Drain 10 mL of concentrated sulfuric acid from a buret into your separatory funnel. Note 1: Make sure the stopcock on your separatory funnel is not open! Note 2: Sulfuric acid is a very strong acid; you do not want any to touch your skin or clothes.
6. Position your separatory funnel above your Erlenmeyer flask, and then drop in the sulfuric acid <u>very slowly</u>, drop by drop, over a period of 5-7 minutes into the continuously stirred solution. Keep the Erlenmeyer flask in an ice-water bath throughout.
7. After addition of the sulfuric acid is complete, remove the cold bath and continue stirring at room temperature for 20 minutes to allow completion of the reaction.
8. During this 20-minute wait, rinse the separatory funnel with the residual sulfuric acid with tap-water. You can drain into the sink. This is also a good time to write up your lab report, including stoichiometry calculations, procedure and observations, and post-lab questions.

**Isolation of the Crude Product:**

9. Add some ice to the Erlenmeyer flask to dilute the sulfuric acid, swirling the flask as you do so. (One of the functions of the ice is to absorb some of the heat that is produced when sulfuric acid and water mix.) Then add ice-cold water to a total volume of 75 mL or more, swirling vigorously as you add.
10. Use a scoopula or micro-spatula to swirl and stir the mixture for at least two minutes.
11. At this point, you should have a lot of crystal that formed. Because the desired product has so many carbons, it has very low solubility in water, so adding all the water basically crashes most of the the product from solution.
12. Filter the solution using a Buchner funnel.
13. Rinse thoroughly with another 70 mL of ice-cold water. (The function of the water is to make sure all the sulfuric acid, acetic acid, and t-butanol is washed away from the product.)
14. Take the Buchner funnel off of the filter flask, and pour the water down the drain. Then reattach the Buchner funnel.
15. Rinse with a 5-mL portion of ice-cold methanol
16. Rinse again with a second 5-mL portion of ice-cold methanol. (The methanol washes away some organic impurity and also functions to remove much of the water.)
17. Measure your crude mass
18. Save a small portion of the crystals for a crude melting point.

**Recrystallization of the Crude Product:**

19. The main batch of crystals should be purified by recrystallization. Use methanol as your main solvent. Use your experience in recrystallization in order to figure out how to do this. Remember, you want to dissolve the solid in a minimum of hot solvent. So, if your solvent is boiling hot and your crystals still won't dissolve, what should you do? Add more solvent! Conversely if you think you have too much/too good solvent, what should you do? Either boil some off, or add some water (one drop at a time) to reduce the solubility and approach saturation. (Mixed solvent technique).
20. Use your experience to guide your filtration and washing of the crystals.
21. Pour the methanol from the filter flask into the alcohol waste container in the hood.
22. Let the crystals vacuum dry for at least 8-10 minutes before getting mass yield and taking melting point. When you take your melting point of the recrystallized material, also take a melting point of the crude material in order to compare so you can see whether recrystallizing actually helped.
23. Take a H-NMR of the product. To run an NMR on a solid, stab the tube into the crystal, like you do to get some solid into a melting point tube. Remember that for an H-NMR of a liquid you put in one or two drops; so, try to put in enough solid that would be comparable to a drop of liquid. Note: Students routinely put in <u>too little</u> solid! Remember that most of the space in a solid crystal is just air. So, compared to a drop of liquid you'd like to have 5 times as much volume of a solid. If your tube is maybe $1/10^{th}$ full, that will be good for this week. Dilute to about 1/3 depth with D-chloroform. Note: The NMR is for instructor's grading purposes, just to see how clean your material is. You don't need to explain it in your lab report.

**Caution:** Safety Note: Concentrated sulfuric acid is <u>very</u> potent and will dissolve you, your clothes, your papers, or anything else it touches! Avoid pouring; try to use burets/pipets exclusively, or as much as possible. Rinse your glassware thoroughly with water after usage. Acetic acid is smelly, so avoid exposing this outside of the hood.

**Cleanup:** If an aqueous acid waste bottle is out, put your original solution (following filtration) into that. If not, dilute the original solution with water, neutralize with sodium carbonate (expect it to fizz!), and pour down the drain.

Pour the methanol from the recrystallization into the organic waste container.

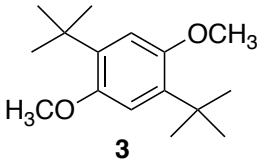
**Lab Report:**

Standard synthesis lab report format. Data must include the crude and recrystallized melting points; the crude and purified mass yield and percent yield; and the H-NMR.

**Questions:**

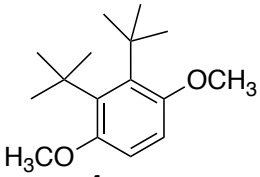
1. Draw a detailed mechanism for the formation of t-butyl-2,5-dimethoxybenzene. (In other words, for the first alkylation, but not the second…).
(draw this on the back side or on a different sheet).

2. The actual dialkylation product is 1,4-di-t-butyl-2,5-dimethoxybenzene. Why is this isomer preferred rather than the alternative isomer 1,2-di-t-butyl-3,6-dimethoxybenzene?




**3**

Does Form.




**4**

Doesn't form. Why?

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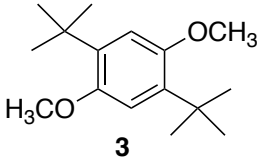
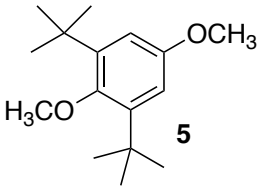



**3**

Does Form.




**5**

Doesn't form. Why?

4. From your actual calculations, how many moles of t-butyl alcohol did you use, and how many moles of 1,4-dimethoxybenzene did you use? [The major product involves only two moles of t-butyl alcohol adding per mole of 1,4-dimethoxybenzene. The following questions relate to why you added more than one, but not more than two…]

5. Why do you think you <u>did not</u> stop after just a single alkylation? In other words, why were you able to add two t-butyls, not just one?

6. Why do you think you <u>did</u> stop after two alkylations? In other words, why were you able to add two t-butyls, but did not continue on to add a third t-butyl group at least to some of your molecules, even though there was still a lot of t-butyl alcohol left at the end?

7. You used t-butanol and acid to generate the t-butyl cation used to form 1,4-di-t-butyl-2,5-dimethoxybenzene. Suggest two organic precursors other than t-butanol that could be used as precursors for t-butyl cation?