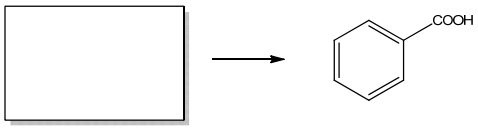
Planning a Reaction

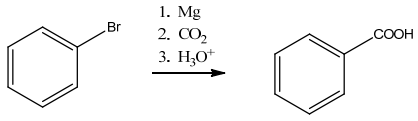
Proposing a Procedure

- Library
  - Primary literature
    - SciFinder Scholar
  - Secondary Literature
    - *Organic Syntheses*
    - *Fieser*
    - *Comprehensive Organic Transformations*



Case Study: Benzoic Acid

- Literature: Try a Grignard Reaction
- Well defined purpose
- Propose a reaction



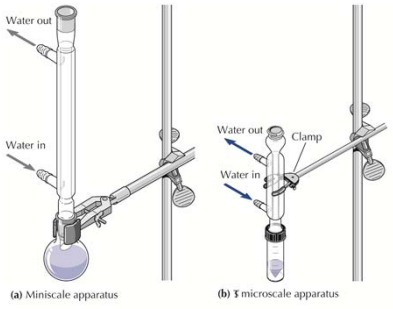
Done with the hard part—Right????

Considerations

- More left to consider than you think!
  - Scale of reaction
  - Solvent/amount of solvent
  - Glassware
    - Size
    - Inert atmosphere?
  - Order of reagents and addition
  - Temperature and reaction time
  - Isolation/purification of product

Scale of Reaction

- Macroscale: multigram
- Miniscale: 0.5g-10g
- Microscale: <0.5g
- Consider
  - Purpose
  - Further steps
  - Practicalities
  - Projected yield
- Apply to multistep synthesis

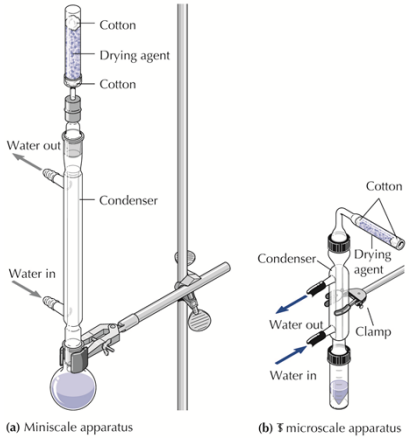


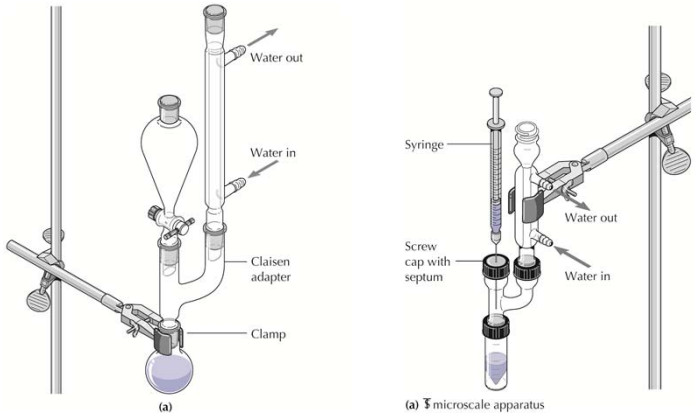
Solvent

- What solvent?
  - Solubility, protic/aprotic
- How much solvent?
  - Scale down: use proportionally more solvent
  - Scale up: use proportionally less solvent
  - Rule of thumb: 0.1M-0.5M
- Example: You are basing your reaction on a procedure that has 5 mmol of bromobenzene in 10 mL of ether solvent. If you are scaling down to 0.5 mmol starting material, how much ether should you use?

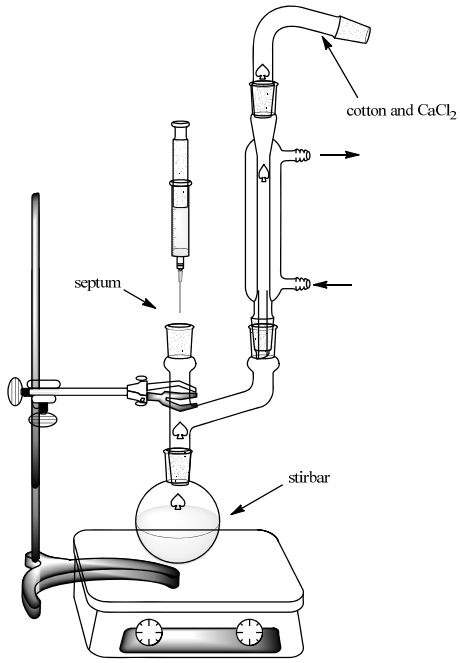
Glassware

- Size?
  - 1/2 to 1/3 full
- Heating/cooling?
- Anhydrous?
- Adding reagents?





- Which reagent first? How do we add gradually? Does it matter if we switch the addition funnel and reflux condenser?



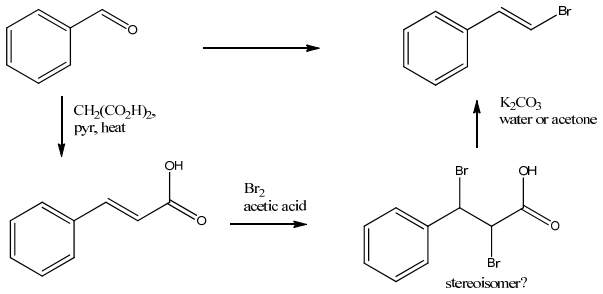
Heating:
Waterbath?
Sandbath?
Hotplate?

Cooling:
Icebath?
How long?

Reaction Isolation and Purification

- How would you determine reaction times if not given?
- Propose a workup.
  - Must consider solvent and other impurities, scale
- Propose a purification.
  - Must consider characteristics of impurities

Multistep Reaction



- Ideal multistep reaction is to make a valuable product from cheap commodity chemicals in high yield and purity, maintaining green chemistry principles