Hints for success in the lab…
…or how to run three experiments per day

Nearly every experiment occurs in 6 distinct phases:

1. Planning
2. Setting it up
3. Monitoring
4. Quench and workup
5. Purification
6. Characterization

1. Planning

- **Constantly think about alternate transformations, reaction conditions, different routes**

  "If I could make the oxime, then I could get to the nitrile."

- **Pull several papers on a transformation and look at multiple experimental procedures**

  Do a forward search. Try to classify information into groups: Nearly all $LiAlH_4$ reactions occur in ether solvent. Pull the original reference.

- **Read the current literature and think about how it could help your project**

  "Could this method help in my substrate?"

- **Plan your experiment before you set it up, ideally the night before**

  Know what you are testing, and what scale is appropriate!
  Scale up by 3x. Test reactions on 10% (or less) of your stash.

- **Oven dry glass, get reagents on your bench, calculate amounts**

  Do we have enough hydrazine? **PURIFY YOUR REAGENTS!!!**

2. Set Up

- **Arrive at lab early, ready to go.**

  Get in, get a reaction on. Set one up before you go to class. Then set up another later.

- **Make sure it's air/water free**

  Invert the septum, use an out-gas bubbler to ensure inert atmosphere, rotovap SM down from PhH (3x)

- **Use proper technique**

  Make solutions for small amounts, distill your solvent + reagents (night before), cannula transfer, HAVE SOMEONE WATCH YOU SET IT UP!

- **Use purified reagents**

  Check them by NMR! Use EROS to find original report of preparation – this will include purification. Use Perrin's book.

- **Reaction still doesn't work?**

  Run a control experiment (known substrate) to check your technique.

3. Monitoring

- **TLC the reaction immediately**

  TLC after 1-5 min, after 1 hour, 5 hours, etc. and right before quench!
  Just because "they" say it takes 48 h means NOTHING!!!

- **Monitor by NMR or other method**

  Remove an aliquot via syringe, conc, and NMR. The intake of H_2 can be monitored. Watch the color. Use an immersion thermometer.

- **Do a mini-workup**

  TLC shows nothing? Remove an aliquot, quench in a vial, add solvent, TLC organic layer

- **Try multiple TLC solvent conditions and stains**

  There's more than hex:EtOAc and vanillin! 2,4-DNP, I_2 vapor, etc.

- **Keep a beautiful notebook**

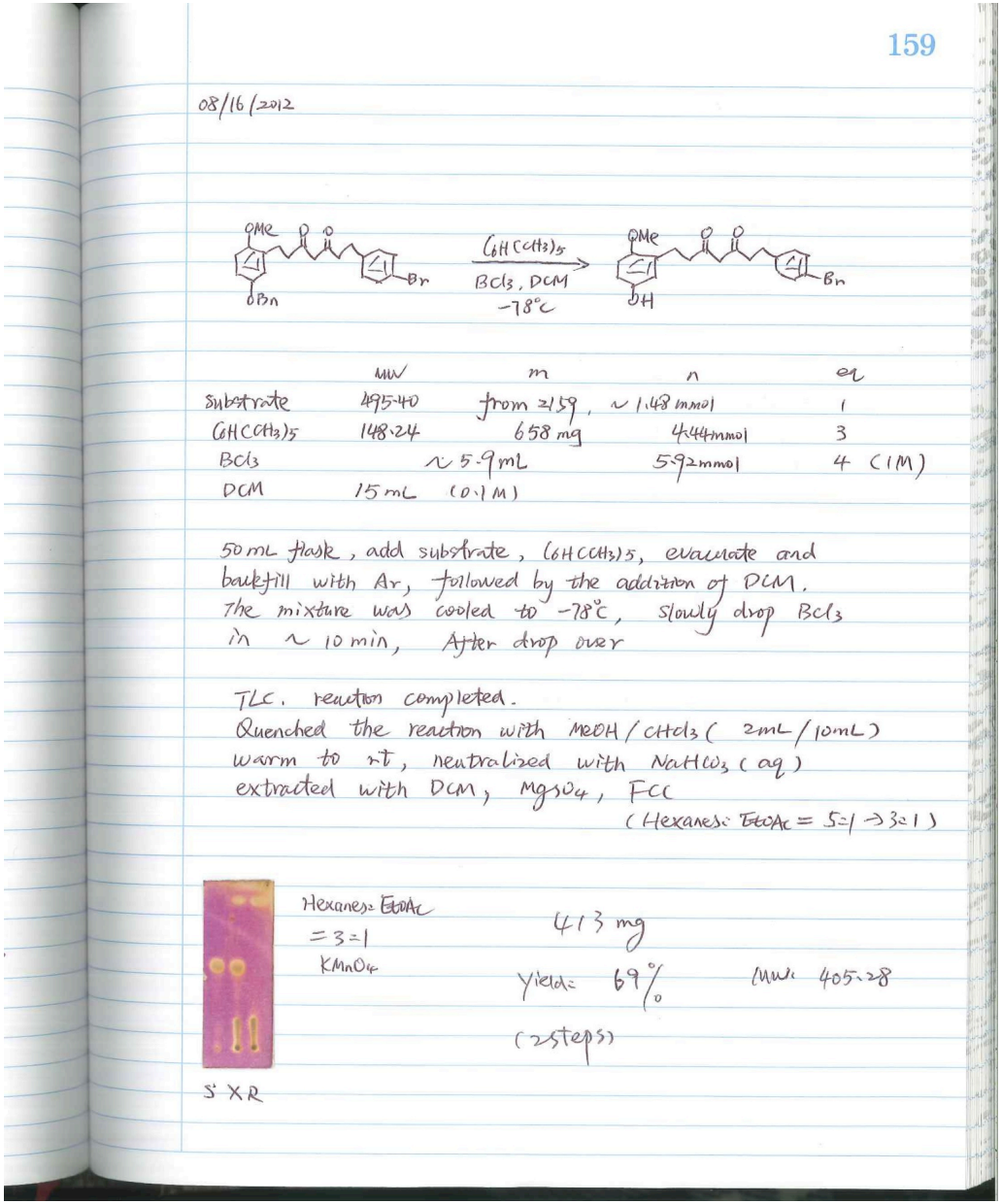
  See next slide…

Check your last 10 notebook pages

…ask yourself, do they look like this?

Remember:

Date
Reaction
Reagents w/ stoich. & molarity
Procedure
Yield (%)
TLC
Spectrum in the binder



4. Quench and workup

- **Quench at rt or below**

  Can quench a reaction at –78 °C with a reagent or H_2O

- **It often takes time to sequester the inorganic byproducts**

  You have to stir DIBAL workups for a long time to complex Al

- **Follow your workup by TLC**

  TLC looked good, but the yield is low? Is your product in the aqueous layer? Do you really need to extract 3x… or should you really extract 10x?

- **Check literature for workup conditions**

  How does one remove Cu in the sep funnel? Black aq and org layers? A white NMR cap will float between layers.

- **Get a crude mass and NMR the crude material**

  Did it decompose on the column? How much mass came out of the organic layer? This CAN ONLY be answered if we have a crude mass.

5. Purification

- **Avoid chromatography, esp. difficult chromatography, esp. early in route**
  Distill, kugelrohr, recrystallize, filter, change the work up, test different reaction conditions, try different TLC conditions

- **Silica is NOT inert!**
  Alumina, florisil, reverse phase, HPLC. Check for decomp on silica using a 2D-TLC, add Et_3N to your eluent, add pH 7 buffer to silica

- **Practice improving your technique**
  A 5 cm silica gel column should take you 30 minutes or less from pulling the column off the rack to putting your product on the rotovap

- **Isolate the byproducts and the starting material ("decomp" doesn't exist)**
  Is it really the starting material? What else came out of the reaction?

- **Don't use squirt bottles after chromatography**
  If you're working on less than a gram, your squirt bottle will give you trash in your NMR. Septa, caps, pipette bulbs, etc. are organic chemicals

6. Characterization

- **Don't wait**

  As soon as it's clean, get a ^{1}H, ^{13}C NMR, DEPT90, DEPT 135, then TLC the NMR tube, then concentrate 10% into a vial for MS, then use the other 90% to get an IR.

- **Don't store your compound on the bench**

  Freeze it in PhH. Put it in the –78 freezer.

- **Get the EtOAc out**

  Rotovap your sample down from $CDCl_3$ to remove solvent peaks. Add a stirbar to a thick oil when you pump on it (careful – it will bump).

- **Characterize as you go and "Over-Characterize"**

  Overall, this will save you massive amounts of time.
  Get extra data to be confident of structure… don't get fooled!

- **Type up experimentals as you go**

  The time-saving alternative to Facebook and YouTube!

Final Thoughts

The single best complement you can receive as an experimental scientist, is hearing that you have "good hands" from a skilled experimentalist.

Few people realize that it's not about your "hands" or some mysterious skill.

With proper control experiments, clean reagents, attention to detail, you will spend less time working on things that don't work… that is, you will be able to "cut bait" on reactions that don't work and try new ones.

We conduct FAR TOO MANY experiments multiple times, only to find out in the final attempt that certain byproducts are forming, and then move on

If you practice efficiency, focus, and managing your time you WILL be much more productive and successful.

It's not personal: 90% of new experiments fail. Don't take it personally.