

## STANDARD EXPERIMENTAL TECHNIQUES

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*Introduction.* How carefully you handle material is a part of your culture as a chemist, and will have a long-lasting consequence on your success. It will dramatically affect your results, including yields, and thus your ability to finish a total synthesis or any other project. Thus, the overall technique is really the first place to start as an experimentalist. Use a funnel while transferring a solution from flask to flask. Rinse your flask several times. Rinse your funnel several times. Rinse your tapered glass joint. Do not be easily satisfied with your handling methods. Keep your work place organized and clean. {MOVIE}

1. **Inert Atmosphere:** Reactions that require an inert atmosphere are carried out in glassware flame-dried under vacuum and back-filled with dry argon or nitrogen. This is done on our vacuum manifolds. The vacuum source for these manifolds is only for flame-drying reaction glassware, and NOT for drying compounds, if there is no cold trap attached. We use a separate manifold for drying final products or reagents. It is important to follow these instructions in order to have reliable reaction set-up.
2. **Septa.** Septa should only be used to cover reactions that require only a short period of time (< 6 hr). All overnight or longer reactions should use 3-way stopcocks or yellow caps. Septa are very permeable to oxygen!
3. **Analysis.** Thin-layer chromatography (TLC) is probably the most important analytic technique available to you. It is inexpensive, and very rapid. It allows analysis within ~5 min directly from your reaction mixtures.

TLC should be performed very accurately. Do not be satisfied with sloppy TLCs.

In your analysis of a reaction, if you observe a spot at the baseline ( $R_f$  0.0), make every effort to find conditions where this spot is seen at  $R_f$  at least 0.2 or more by increasing solvent polarity. If you see a spot at the front ( $R_f$  1.0), make every effort to record an additional TLC where this spot is seen at  $R_f$  at least 0.8 or lower by decreasing solvent polarity.

Thus, in many cases I will expect to see several high-quality TLCs for any given new reaction.

4. **Quenching reactions.** Clearly, *proper quenching techniques are critically important for success of a reaction.* In many cases, all product may be lost because of improper quenching and isolation procedure. Always think carefully about the exact details of quenching, and consider what by-products are formed and get familiar with their general properties, especially inorganic compounds (solubility, reactivity, toxicity etc.). **Plan ahead.**

General guidelines are provided here.

a. Grignard reactions are usually quenched by addition of saturated aqueous ammonium chloride at 0 C followed by warming to rt.

b. DIBAL reactions: very conveniently quenched by first adding saturated aqueous Rochelle's salt (sodium potassium tartrate), then dilution with your extraction solvent, then stirring until two easily separable clear layers are formed, typically 2 hr. No hard to handle gels are observed with this procedure.

c. Cuprate reactions are quenched by adding a 9:1 v/v mixture of saturated aqueous ammonium chloride and conc. ammonia, and stirring at rt for 2 hr until clear blue solution is formed.

d. Many reactions are conveniently quenched with saturated aqueous sodium bicarbonate. BUT THINK WHAT YOU ARE TRYING TO ACHIEVE, AND WHAT PROCESS YOU WOULD LIKE TO HAPPEN upon quench. It is extremely useful to consult the wisdom of published experimental procedures from ours, or well-established groups in case you are carrying reaction for the first time and are not familiar with the quench procedure.

5. **Extraction solvents.** If your compound is soluble in hexane this is surely the best choice since it is inexpensive and will not dissolve water. Ether is a bad choice - it is dangerous to distill, and dissolved large amounts of water (4%). Instead of ether, try to use hexane-ethyl acetate mixtures (3:1), or pure ethyl acetate for polar compounds. Dichloromethane is a good choice for certain reactions (usually those that use DCM as the reaction solvent).

6. **Drying of organic layer.** Usually, drying of the organic layer is achieved by filtering through a sintered funnel filed with anhydrous sodium sulfate. Place a piece of cotton on top to stabilize the solid phase. (See picture on the next page).

7. **Evaporation.** Obviously, make sure that the tapered glass joints on your rotary evaporator and flask are always rinsed and clean.

8. **Purification.** Distillation, recrystallization, or chromatography: refer to appropriate chapters.

9. Final drying is carried out on specially designated high vacuum manifold. Make sure the trap is filled with isopropanol-dry ice in order to protect the high-vacuum pump.

10. **Always**, the reaction is concluded by obtaining analytical data:  $^1\text{H}$  and  $^{13}\text{C}$  NMR and mass-spectroscopy.

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