

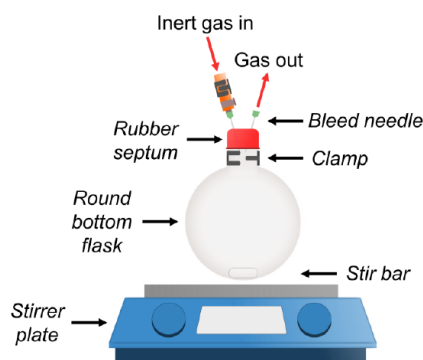
3: Performing Sensitive Reactions without a Schlenk Line

Whilst Schlenk lines and Schlenk flasks are the ideal equipment to ensure that reactions are free of air and moisture, it is still possible to perform air- and moisture-sensitive reactions without the need for specialist equipment. This is especially true when the products of the reaction are not particularly air- and moisture-sensitive but the reagents or catalysts used for the reaction are. In these cases, it is often sufficient to use a round bottom flask fitted with a rubber septum, and to have an inert gas inlet, either from an inert gas manifold or simply a balloon filled with inert gas.

A representative reaction (the synthesis of *N*-aryl amidines from secondary amines and benzonitriles – adapted from [here](#)) is used as an illustrative guide, but each step can be modified depending on the reaction conditions required and nature of the reagents.

Step 1

An oven-dried round bottom flask equipped with a magnetic stir-bar is fitted with a rubber septum and clamped securely. A bleed needle is added followed by the inert gas inlet needle, and the flask is flushed for several minutes (depending on the volume) to remove air. *Note: If using a Schlenk line and Schlenk flask then the reaction vessel would instead be [cycled](#) onto the line prior to use.*



Flushing a round bottom flask with inert gas prior to use.

Step 2

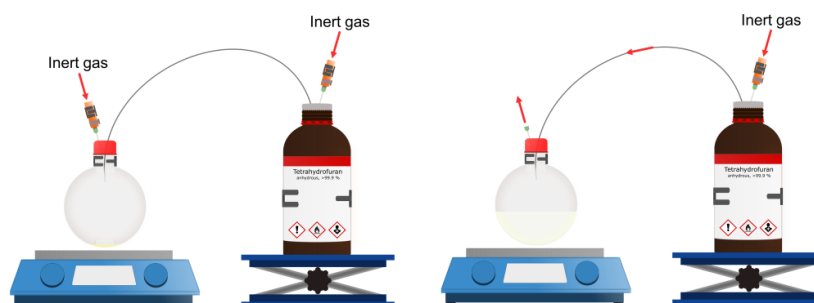
Once the reaction flask has been flushed with inert gas, the bleed needle is removed from the septum. For the addition of liquid reagents (aniline in this specific case), the syringe and needle is first [purged](#) three times with inert gas (this is recommended even for non air- and moisture-sensitive reagents) and then the required quantity of liquid reagent is added. For solid reagents, it is recommended to add the required quantity of solid to the flask prior to flushing with inert gas.



Addition of liquid reagents to the flask.

Step 3

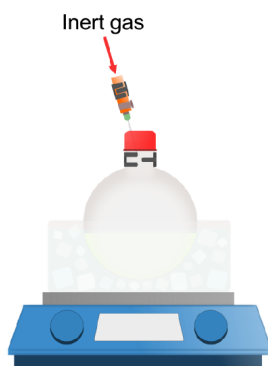
Anhydrous solvent (commercially available bottle equipped with a rubber septum) is added to the reaction flask. This can be achieved via [cannula transfer](#) (as illustrated below) or more conveniently by using a [syringe and needle](#).



Addition of anhydrous solvent via cannula transfer.

Step 4

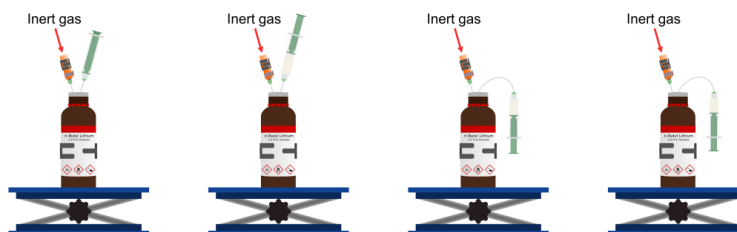
The reaction flask is cooled to 0 °C in an ice bath. *Note: This is specific to the reaction.*



Cooling the reaction in an ice bath.

Step 5

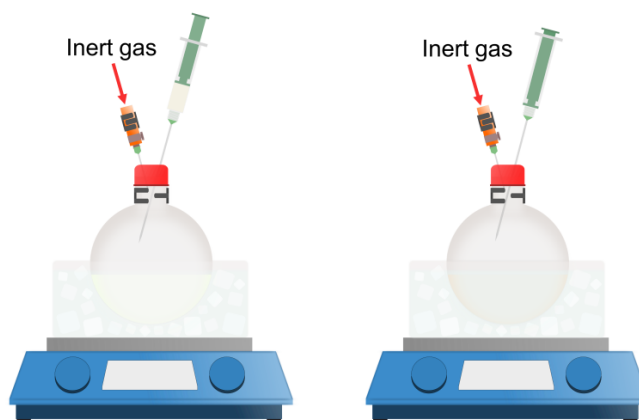
n BuLi is dispensed from the reagent bottle using a syringe and needle (see [here](#) for full details). *Note: n BuLi is prime example of a reagent that requires air and moisture free conditions for its safe handling, whilst the final product obtained after hydrolysis or electrophilic quenching may not be sensitive.*



Dispensing n BuLi from the reagent bottle.

Step 6

The n BuLi is added dropwise to the reaction flask.



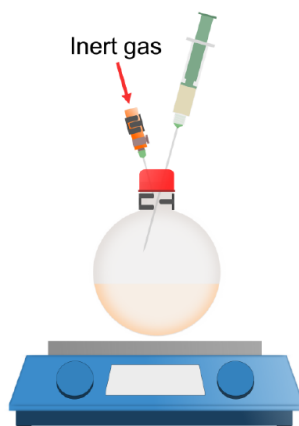
Dropwise addition of $n\text{BuLi}$ to the reaction flask.

Step 7

The reaction flask is removed from the ice bath and allowed to stir for 1 hour at room temperature. *Note: If an inert gas balloon is used, it may be necessary to manually release excess pressure from the reaction flask using a bleed needle.*

Step 8

The third liquid reagent (benzonitrile in this specific case) is slowly added to the reaction flask using a syringe and needle.



Addition of a liquid reagent.

Step 9

The reaction is stirred at room temperature for 1 hour. The gas inlet is carefully removed, followed by the rubber septum, and the reaction is quenched with ice water. The product (*N*-phenyl benzamidine in this specific case) is obtained after work-up and recrystallisation.

Tip, Tricks and Safety Notes

- When handling large quantities of pyrophoric reagents, it is strongly advised to use a Schlenk line and rigorously dried Schlenk flasks to ensure that reactions are free of air and moisture, and therefore performed as safely as possible.
- It may be convenient to add air sensitive solids such as catalysts or strong bases to the reaction flask using a glovebox. The flask can be removed from the glovebox fitted with the rubber septum to ensure it remains sealed and free of air and moisture.
- If the reaction is not sensitive to moisture, it may be sufficient to degas the solvent by **sparging** (bubbling inert gas through the solvent) directly in the reaction flask prior to use. Even if anhydrous solvent is used, it may be beneficial to sparge the solvent with inert gas for 5-10 minutes prior to the addition of reagents.

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