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Tutorial

# An Illustrated Guide to Schlenk Line Techniques

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ABSTRACT: Schlenk lines are versatile pieces of laboratory equipment that enable the safe and convenient manipulation of air- and moisture-sensitive compounds. First pioneered in 1913 by Wilhelm Schlenk, the apparatus and techniques used today have evolved considerably, allowing more challenging and sensitive synthetic chemistry to be carried out on a routine basis. This tutorial, which is based on *The Schlenk Line Survival Guide*, aims to showcase and explain the key technical aspects of Schlenk line chemistry through a series of illustrated guides. It is hoped that this practical guide provides a useful introductory resource and teaching tool for beginner Schlenk line users, as well as a convenient go-to aid for chemists of all proficiency.

Schlenk Line Techniques
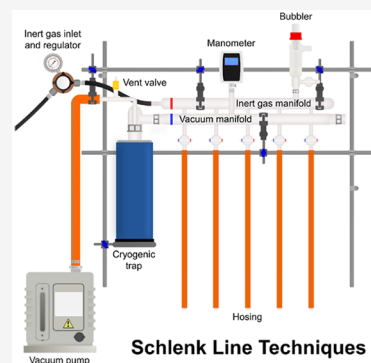
1. INTRODUCTION

The investigation of ketyl radical anions by Wilhelm Schlenk[1] in 1913 marks the birth of modern Schlenk line chemistry.[2] These compounds, which were described as being *"extraordinarily sensitive to air"*, required the use of *"completely dry ether under an air-free nitrogen atmosphere"* to enable their synthesis and characterization. This required specialist apparatus, which was detailed and illustrated in Schlenk's original manuscript, to perform sensitive filtrations with the strict exclusion of air.[2] Showcasing the immense utility of these early technical developments, Schlenk went on to discover organolithium compounds such as MeLi and PhLi in 1917,[3] reagents that are now ubiquitous in synthetic chemistry with extensive applications in industry and academic research.[4]

Schlenk lines and related apparatus are now commonplace in many synthetic chemistry laboratories, since they allow the safe manipulation of air- and moisture-sensitive species, which in turn grants access to new compounds with unprecedented structures, bonding, reactivities and properties. While the underlying basis of Schlenk techniques has not changed significantly in 100 years, there has been a constant improvement in the methodologies as well as the availability of both routine and specialized equipment. While leading books such as *"The Manipulation of Air-Sensitive Compounds"*[5] by Shriver and Drezdzon contain a wealth of detailed information regarding air-sensitive techniques, the introduction of updated, user-friendly, and accessible resources are essential to help facilitate the training of future generations of Schlenk line chemists.

There is often a gap between the skills introduced at the undergraduate level and those required at the postgraduate research level or in industry,[6,7] and this is particularly true for advanced synthetic skills such as Schlenk line techniques.

Training and guidance may also be limited by the lack of time or equipment and availability of knowledge from senior colleagues, or even by the hierarchical and often discriminatory nature of who receives access to quality training and resources. To help address these problems, *The Schlenk Line Survival Guide*[8] was launched in 2019; this is an open-access website that contains a library of detailed step-by-step guides and illustrations dedicated to Schlenk line chemistry. This tutorial aims to introduce readers to the fundamental aspects of Schlenk line chemistry, including safety considerations and routine techniques, while highlighting other key resources that focus on implementing Schlenk techniques into undergraduate laboratory courses. While these resources are no substitute for direct hands-on Schlenk line training, it is anticipated that they will be valuable prereading material or reference guides for both beginner and advanced Schlenk line users.

2. THE SCHLENK LINE

2.1. Introduction to the Schlenk Line. A Schlenk line (Figure 1a) is dual manifold system in which the vacuum manifold is connected to a vacuum pump, while the inert gas manifold is connected to a source of purified and dry inert gas (typically nitrogen or argon; see section 2.4 for details about Schlenk line setup and equipment selection). The two manifolds
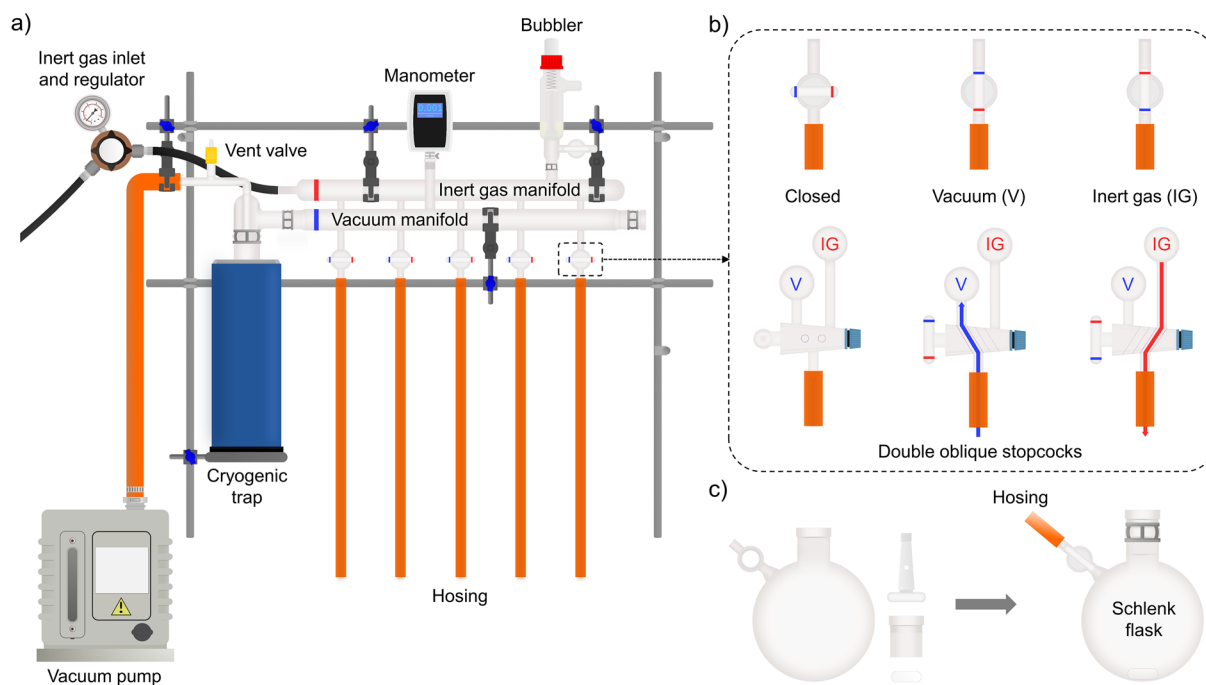
Figure 1. a) Typical Schlenk line. b) Front and side views of a double-oblique stopcock. c) Typical Schlenk flask before and after assembly.

Figure 2. Greasing and inserting a ground glass stopcock and stopper into a Schlenk flask. A hydrocarbon-based grease is shown for clarity.

have several ports which are interconnected via double-oblique stopcocks (Figure 1b) or Teflon taps, which allow sealed vessels (often referred to as Schlenk flasks or tubes depending on the shape) attached to the Schlenk line to be evacuated under vacuum or backfilled with inert gas. Schlenk flasks (Figure 1c) feature a gas inlet side arm (with a greased stopcock or greaseless Teflon tap) that can be attached to the Schlenk line using flexible hosing, alongside a standard ground glass joint to attach other glassware or to simply insert a stopper or septum. Schlenk lines may also be equipped with suitable ground glass adaptors to enable the direct attachment of appropriate glassware, without the needed for hosing. A slight overpressure of inert gas is employed, and this exits the Schlenk line through a bubbler (oil or mercury) which acts a pressure relief system, allows the gas flow rate to be monitored, and prevents the ingress of air back into the Schlenk line. A cryogenic trap (typically liquid nitrogen, -196 °C) is used to condense solvent vapors and other volatiles, which protects and prevents contamination of the vacuum pump. The vacuum manifold may be fitted with a manometer to measure the vacuum pressure: For a typical Schlenk line equipped with a rotary vane vacuum pump, a pressure between 10^{-2} and 10^{-4} mbar is often reached which is suitable for standard manipulations. Schlenk lines are often custom-made

for specific research laboratories, meaning that numerous designs and adaptations are possible depending on the intended applications.

Caution! Appropriate personal protective equipment (PPE) including eye protection, suitable gloves, and a lab coat must be worn when operating a Schlenk line (see section 3 for further safety considerations).

To begin using a Schlenk line, a clean and dry cryogenic trap is first attached to the Schlenk line ensuring that the ground glass joints are sufficiently greased. The trap is twisted to evenly coat the grease and then secured in place with a suitable clip. Cryogenic traps may instead be connected to the Schlenk line via greaseless O-ring joints. Ensure that the vent valve and all double-oblique stopcocks or Teflon taps are closed (or turned to inert gas if a vessel is already attached to the Schlenk line hosing). Turn on the vacuum pump, then wait 5−15 minutes for the trap and vacuum manifold to be evacuated before submerging the trap in a Dewar of liquid nitrogen—a manometer reading below 0.1 mbar is recommended to ensure there are no leaks within the Schlenk line assembly. The inert gas supply can now be opened and the Schlenk line is ready for operation; the inert gas supply can also be established independently of the vacuum for other applications (i.e., bubbling inert gas through a

solvent to degas it). To shut down a Schlenk line, first ensure that all Schlenk flasks and vessels connected to the Schlenk line are under inert gas and that all other stopcocks or Teflon taps are closed if not in use. Turn off the vacuum pump, remove the Dewar of liquid nitrogen from the trap, then open the vent valve to quench the vacuum and repressurize the vacuum manifold. Schlenk lines may have an additional Teflon tap to isolate the vacuum pump from the solvent trap and vacuum manifold. Allow the solvent trap to warm to room temperature before removing it from the Schlenk line and discarding of any collected solvent in an appropriate waste container.

2.2. Cycling Glassware onto the Schlenk Line. Glassware used for the manipulation of air- and moisture-sensitive compounds are typically dried in an oven prior to use (>100 °C, for a few hours or overnight) to remove residual solvent or adsorbed water. The stopcock and stopper are greased (using a length of silicone, hydrocarbon, or polyfluorinated-based lubricant) and inserted into the corresponding ground glass joints with twisting to ensure a smooth and uniform seal that is free of bubbles or streaks (Figures 2a−c). Only two-thirds of the stopper are greased to prevent excess grease from contaminating the inside of the flask. Appropriate nuts, O-rings, washers, and clips can be added to secure the stopcock and stopper in place (Figure 2d). The Schlenk flask is then connected to the Schlenk line hosing and evacuated under vacuum while it cools to room temperature. After a suitable amount of time (depending on the size of the flask, ∼5 min for a 100 mL vessel), the Schlenk flask is slowly backfilled with inert gas. This corresponds to a single "cycle", and this is repeated two more times to ensure complete removal of air and moisture from the reaction vessel. When connecting other vessels that are already sealed under inert gas, such as solvent ampoules (also called Schlenk bombs or solvent pods), shorter cycles are adequate to evacuate the Schlenk line hosing and side arm.

The process of performing numerous vacuum/inert gas cycles is akin to performing repeated extractions of an aqueous phase with organic solvents during a typical reaction workup. Assuming that a 100 mL reaction flask contains approximately 1 mmol of O_2 at room temperature and atmospheric pressure (∼1000 mbar), then an initial vacuum cycle down to 0.1 mbar will reduce the quantity of O_2 down to 1×10^{-4} mmol of O_2. Backfilling with inert gas and re-evacuating the flask down to 0.1 mbar again reduces the O_2 quantity down to 1×10^{-8} mmol, and a third vacuum/inert-gas cycle further lowers this to 1×10^{-12} mmol of O_2. This is several orders of magnitude lower than performing a single but longer evacuation down to 0.001 mbar, for example, and illustrates that even poor performing vacuum pumps can be sufficient to reach low partial pressures of O_2 after repeated vacuum/inert gas cycles.

2.3. Working Principles and Troubleshooting. It is important to understand and consider the following basic working principles that are required to correctly operate a Schlenk line, and to safely manipulate air- and moisture-sensitive compounds under an inert atmosphere. These include:

- Performing vacuum/inert gas cycles to remove air and moisture from oven-dried glassware
- Working with a slight positive pressure of inert gas
- Using dynamic vacuum to remove volatiles
- The use of flexible hosing to enable the versatile positioning of flasks
- Using greased ground glass joints or Teflon taps when applying vacuum

- Using rubber septa when manipulating liquids under an inert atmosphere

Beyond these working principles, it is also crucial to "know your own Schlenk line" to ensure that it is operating both smoothly and safely. This may include the following: (i) knowing the usual vacuum pressure; (ii) knowing what the vacuum pump sounds like; and (iii) knowing the typical inert gas flow rate and pressure. Being aware of these features will help to identify when there is a potential problem in the Schlenk line and how to properly address them.

The most common problem encountered when using a Schlenk line is poor vacuum pressures. This primarily suggests there is a compromised seal or small leak within the Schlenk line, which should be addressed immediately to prevent possible condensation of liquid oxygen into the liquid nitrogen trap. Low vacuum pressures are readily identified when using a manometer (pressures not reaching as low as typically observed) but also can be diagnosed if solvents are more difficult to remove under dynamic vacuum. Isolating and testing individual parts of the Schlenk line is often the most convenient way to identify the route of the problem. Cleaning and regreasing the ground glass double oblique stopcocks or replacing Teflon taps may be necessary to restore typical vacuum pressures. The vacuum pressure can also fail to get as low as expected if the solvent trap is blocked or needs to be topped up with cryogen to prevent evaporation of the condensed solvent. It may be necessary to shut down the Schlenk line, then thaw and empty the solvent trap to fix this problem. If the vacuum pressure is still poor after addressing these issues, then it may point toward a more serious concern with the vacuum pump (which would warrant maintenance or a full service by a trained professional), or more severe damage to the Schlenk line itself.

2.4. Schlenk Line Setup and Equipment Selection. Understanding *when* and *why* to use certain Schlenk line setups and pieces of equipment is perhaps as important as knowing *how* to perform key Schlenk line techniques. This section will detail the advantages and disadvantages of different setups and pieces of equipment which are commonly encountered in synthetic chemistry laboratories.

Schlenk lines and flasks are typically fitted with either ground glass stopcocks or Teflon taps which allow the connected glassware to be opened or closed to vacuum or inert gas. Double oblique ground glass stopcocks are considered safer to use than Teflon taps because it is not possible to simultaneously have a stopcock open to both vacuum and inert gas. They tend to be easier to use than Teflon taps and are therefore well suited for introducing and teaching Schlenk line techniques; often one or both sides of the stopcock head are marked with colored ink or tape to indicate which orientation corresponds to vacuum or inert gas (see Figure 1b). Double oblique stopcocks (and even regular single-holed ground glass stopcocks) are often manufactured specifically for each port on the Schlenk line to ensure the best seal—these may be called "mated" or "matched" ground glass stopcocks. For this reason, greater care is required when cleaning "mated" ground glass stopcocks and the use of base baths should be avoided as this will slowly etch the glassware and compromise the seal. Double oblique stopcocks must be evenly greased to ensure a good seal; this generally means that the vacuum pressure may not consistently reach as low values when compared to Teflon taps. The use of greased stopcocks may also not be compatible with certain reagents or conditions employed in a reaction, and furthermore they are not

recommended for the long-term storage of sensitive chemicals or anhydrous solvents since they are prone to seizing (i.e., freezing or locking).

Teflon taps typically hold better vacuum than ground glass stopcocks and avoid the use of grease to ensure a good seal. The main disadvantage of using Teflon taps on a Schlenk line is that it is possible to accidentally have both the vacuum and inert gas taps open simultaneously which can result in suck-back of the bubbler oil or the consumption (and potential condensation) of inert gas by the vacuum pump. Teflon taps are also prone to being overtightened which can damage the Teflon tap or the glassware. Nevertheless, Teflon taps are still recommended for more sensitive chemistry applications and for the long-term storage of solvents and reagents. It should be noted that Teflon taps will contract slightly when cooled, which may compromise the seal of flasks if placed in a fridge or freezer.

The choice of inert gas is also an important consideration for Schlenk line chemistry. Argon is a superior choice of inert gas since it is denser than N_2 and air, and therefore provides a protective blanket of gas making it more forgiving to use than N_2. Argon, however, is considerably more expensive than N_2 and can also condense at liquid nitrogen temperatures (Ar melting point = −189.34 °C; Ar boiling point = −185.848 °C; N_2 boiling point = −195.795 °C),[20] making it a potential safety hazard. N_2 is cheaper than Ar and is sufficiently inert for most Schlenk line applications but can still react with many low-valent transition metals[20] or even some main-group metals.[21,22] Prior to 1896, when Carl von Linde filed patents for the liquefaction and fractional distillation of air which made N_2 more readily available, notable chemists such as Frankland,[23,24] Beckmann,[25] Barbier,[26] and Grignard[26] quite remarkably performed air- and moisture-sensitive chemistry under atmospheres of H_2 and CO_2, gases that no organometallic or main-group chemist would consider to be inert!

Vacuum grease is a low-volatility lubricant which is used to provide a uniform and airtight seal between ground glass joints. Silicone grease is the most commonly used grease for Schlenk line chemistry and vacuum applications. It is cheap and widely available, has a good operating temperature range (−40 to +200 °C), but has limited chemical resistance and is prone to "creep" (i.e., undesirable spreading of the grease), and therefore it readily contaminates reactions and the resulting NMR spectra.[27] It is not recommended to be used for more permanent joints such as the double oblique ground glass stopcocks on Schlenk lines, but it is suitable for day-to-day operations using Schlenk flasks and vacuum traps. Hydrocarbon based vacuum greases (such as Apiezon or Leybonol) are "creep" resistant and are therefore recommended to be used for the double oblique ground glass stopcocks on Schlenk lines.[28] Hydrocarbon greases can be used for day-to-day operations but also is considerably more expensive when compared to silicone grease, and due to its solubility in aromatic hydrocarbon solvents, it can still easily contaminate reactions. Apiezon N is a fine grease which is best suited for fitted or moving joints on the Schlenk line such as double oblique ground glass stopcocks; it is also suitable for cryogenic temperature applications such as fitting liquid nitrogen traps. Apiezon M is often used for day-to-day operations such as Schlenk flask stopcocks or ground glass joints, while Apiezon H is employed for nonmoving ground glass joints or for high-temperature applications.[28] Polyfluorinated greases are made from PTFE (polytetrafluoroethane) or PFPE (perfluoropolyether) and therefore show excellent chemical resistance. They have a wide operating temperature range and

are insoluble in most organic solvents making them ideal for performing distillations and to generally avoid grease contamination. Polyfluorinated greases can also be used for day-to-day operations, but they are significantly more expensive than silicone grease and are also prone to "creep". The amount of grease used is another important consideration: Too much grease is likely to contaminate glassware and reactions or be expensive when using hydrocarbon or polyfluorinated greases, while too little grease will lead to a poor seal and risk seizing of joints. A thin strip of grease applied along one length of a ground glass stopcock or stopper is typically sufficient and twisting the male component several times will ensure a uniform seal. Ensure that the joints are suitably greased and mobile before being evacuated glassware under vacuum to avoid seized joints or leaks. Beyond greased ground glass joints (Figure 3a), nonmoving items of glassware may be connected by sealing the ground glass joints with vacuum wax (Figure 3b) or via greaseless O-ring ball and socket joints (Figure 3c).
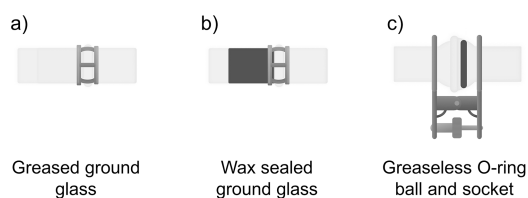

Figure 3. Commonly encountered joints for Schlenk line applications.

Flexible hosing or tubing allow Schlenk flasks and other glassware to be connected to the Schlenk line and manipulated under vacuum or an inert gas atmosphere. Many options are available, and they come in a range of materials, degrees of permeability and cost. Tygon tubing is made from a thermoplastic and exhibits many desirable characteristics such as transparency, lightweight, and chemical resistance. Because it is transparent, it is easy to see if the tubing is contaminated and needs to be replaced. Some plastic tubing may contain dioctyl phthalate as a plasticizer, and this can easily leach into reactions with solvent vapors and plague NMR spectra. Silicone tubing is also available but has limited chemical resistance and is less well suited for vacuum applications. Vacuum-grade rubber tubing is also frequently employed due to its high flexibility. Rubber tubing however is nontransparent and heavy when compared to plastic tubing and can become brittle over time. The advantages between plastic and rubber tubing is less clear-cut, and personal preference, availability, and cost are likely to decide which tubing is used.

Bubblers act as a one-way valve to allow the inert gas to exit the Schlenk line, while preventing atmospheric air and moisture into the inert gas manifold. Three main types of bubbler are used with Schlenk lines and each has their advantages and disadvantages. Oil bubblers (Figure 4a) are the most common bubbler employed in research and teaching laboratories due to their simplicity and low cost. They are filled with silicone or mineral oil, which have high chemical resistance. The major drawback of oil bubblers is their susceptibility to "suck back" when backfilling evacuated flasks with inert gas; this can cause oil to leak into the inert gas manifold unless a secondary vessel is placed between the inert gas manifold and oil bubbler. Alternatively, a one-way check valve that is rated to an appropriate pressure can be installed to prevent oil suck back. Another disadvantage of oil bubblers is the low inert gas pressure
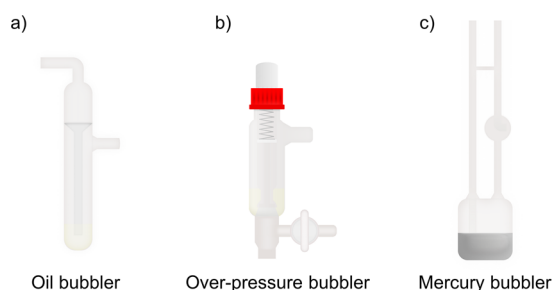
Figure 4. Typical bubblers used on Schlenk lines.

a) Oil bubbler
b) Over-pressure bubbler
c) Mercury bubbler

due to the low density of the oil; this means that the inert gas exiting the Schlenk line has to be restricted to increase the gas pressure to facilitate cannula transfers. Overpressure or pressure-relief bubblers (Figure 4b) are oil-based bubblers that contain a spring-loaded check valve; this prevents oil suck back and allows higher inert gas pressures to be safely reached. This is advantageous for performing cannula transfers and can also minimize inert gas usage. The disadvantage of overpressure bubblers is their high cost when compared to simple oil bubblers. Mercury bubblers (Figure 4c) work on a similar principle to oil bubblers but provide much higher inert gas pressures within the Schlenk line due to the high density of the liquid metal. Mercury bubblers are often over 76 cm in height (1 atm can support 760 mmHg; full length not shown in Figure 4c) which allows the inert gas manifold to be fully evacuated under vacuum, rather than being flushed or purged with inert gas. The major disadvantage of mercury bubblers is the health and safety issues concerned with handling mercury and disposing of waste. Mercury is also incompatible with many chemicals that may be used on the Schlenk line. Mercury bubblers should only be used in well ventilated fume hoods or when attached to an appropriate exhaust system; furthermore, an additional flask equipped with a gas inlet/outlet adapter can be employed to collect small beads of mercury that may exit the bubbler.

Another important consideration when performing Schlenk techniques is the correct use of support clamps. Schlenk lines are typically supported by lattice lab frames that are secured to the back wall of the fume hood. It is recommended to the secure the Schlenk line at a comfortable height, securing both the vacuum and inert gas manifold to prevent slippage or tilting. The clamps should be orientated such that the weight of the Schlenk line is supported by the bottom, nonmoving arm of the clamp. This same principle should also be applied to boss heads and when securing other glassware such as Schlenk flasks or distillation apparatus. It is also important to secure hosing and ground glass joints to glassware through the use of appropriate hose clamps, keck clips, rubber bands, or fork clamps; these are especially crucial when working with an overpressure of inert gas. Rubber septa can also be secured in place through the use of twisted copper wire, and stopcocks can be secured by using the supplied plastic washers, O-ring, and nuts.

3. Safety Considerations. *Caution! Appropriate personal protective equipment (PPE) including eye protection, suitable gloves and a lab coat must be worn when operating a Schlenk line.*

Schlenk line techniques allow chemists to safely handle dangerous and pyrophoric reagents on a routine basis, but they still pose many other risks that can be avoided with the correct technique and appropriate precautions. The main risks associated with Schlenk line chemistry include the condensation of liquid oxygen, implosion or explosion, handling pyrophoric

substances, or using sharp cannulas and needles. Risk assessments and appropriate training must be completed before operating a Schlenk line. Readers are directed to *The Safety Net*[29] for detailed safety information including a library of standard operating procedures.

Liquid oxygen may condense in the liquid nitrogen cold trap if a stopcock or Teflon tap on the Schlenk line is accidentally opened to air. Liquid nitrogen traps should therefore only be used where necessary, and alternative cryogenic traps (dry ice, −78 °C) should be considered. Liquid oxygen is a powerful oxidant and can react violently with many organic compounds including grease and solvents collected in the trap. The use of a manometer can help prevent liquid oxygen condensation by ensuring that the Schlenk line contains no leaks. It is important to regularly assess the status of the Schlenk line (primarily the stopcocks and taps) as well as the condition of hosing and connectors since these are common points of leaks and failure. In the event that liquid oxygen is identified or suspected in a solvent trap, the original cryogenic state should be immediately restored (vacuum pump on and liquid nitrogen Dewar raised). Do not remove the trap and allow the liquid oxygen to warm as this can lead to an explosion due to rapid expansion or reaction with organic substances. Provided the source of the leak has been identified and stopped, the liquid oxygen will slowly evaporate under dynamic vacuum, even at liquid nitrogen temperatures. For a complete and detailed standard operating procedure on how to deal with and help prevent liquid oxygen condensation, the reader is directed to *The Safety Net*.[29]

An explosion may occur if the inert gas pressure builds up within a closed system. This is generally prevented by using a bubbler which acts as a pressure relief system within the inert gas manifold of the Schlenk line. Pressure build-up can also occur if a reaction evolves a large volume of gas, for example when quenching pyrophoric substances[10] or $LiAlH_4$ work-ups; these should be performed controllably (often with appropriate cooling) and with an adequate source of pressure relief (e.g., a septum and bleed needle). Heating a reaction without a condenser, or unexpected thermal runaways, can also lead to pressure build-up within a Schlenk flask and inert gas manifold. Known exothermic reactions should be appropriately cooled using an ice bath or dry ice/acetone bath to prevent thermal runaways. Reactions that have been cooled to low temperatures (from 0 °C down to −78 °C) should be left open to the inert gas (and thus pressure relief) while warming back to ambient temperature. Since inert gas has a lower vapor pressure at lower temperature, the inert gas pressure will increase upon warming to ambient temperature. Manipulations under a dynamic flow of inert gas (nitrogen or argon) should never be cooled with liquid nitrogen since this will lead to condensation of the inert gas. In the event that this occurs, the flask should be left open to inert gas as it slowly warms to room temperature or turned to dynamic vacuum (to evaporate the inert gas) while maintained at liquid nitrogen temperatures. An implosion may occur if the Schlenk line or flask, which contains a crack or defect, is placed under dynamic vacuum. This may also lead to condensation of liquid oxygen in the solvent trap.

Pyrophoric substances, and the glassware and equipment used to manipulate and handle them, must be safely quenched prior to disposal and cleaning.[10] This is achieved by first suspending or dissolving the pyrophoric substance in toluene (a high boiling point aprotic solvent) under an inert atmosphere, cooling the flask in an ice bath or dry ice/acetone bath, and slowly adding isopropanol. Once all visible material has reacted, or when gas
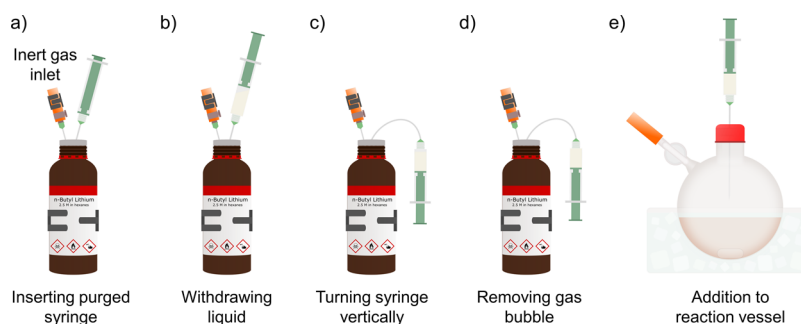
Figure 5. Using a syringe and needle to add an organolithium reagent to a Schlenk flask.

evolution cases, ethanol can be added, followed by methanol, and finally water. This should be stirred for a suitable period of time to ensure all pyrophoric material is fully quenched. After disposal of the solvent in an appropriate waste container, glassware should be thoroughly rinsed with water prior to contact with flammable organic solvents (e.g., washed with acetone or in a base bath). Syringes, needles, and cannulas used to transfer pyrophoric compounds should be quenched with a dilute (10−20%) isopropanol−toluene mixture immediately after use to quench residual material and prevent clogging. When dispensing large volumes (>20 mL) of pyrophoric reagents such as *n*-butyl lithium, it is recommended to directly cannula transfer the reagent into a graduated pressure-equalizing dropping funnel, or to select a suitable scale in which the whole reagent bottle is used for a single reaction. Always select an appropriately size syringe and needle gauge for the amount of liquid to be dispensed, and never use multiple syringe transfers to bypass the volumetric limit of a syringe. The death of Sheharbano Sangji in 2008 was in part due to the inappropriate selection and use of a syringe and needle when dispensing large volumes of *tert*-butyl lithium.[30]

A key aspect of Schlenk line chemistry is the purification and drying of organic solvents. Traditionally, this has been achieved through the use of solvent stills in which large volumes (>1 L) of solvent are refluxed over a suitable desiccant (typically alkali metals or metal hydrides) prior to distillation and collection. Solvent stills pose an enormous safety risk, however, and therefore have been ruled out of many synthetic laboratories and chemistry departments where possible. Solvent purification systems (SPS) are a safe and convenient solution for the purification and drying of organic solvents.[31] Using inert gas pressure, the organic solvent is passed through a series of columns: one containing activated alumina to remove water and protic contaminants, and one containing a supported copper catalyst to remove trace oxygen. The solvent is first degassed by bubbling inert gas through the solvent reservoirs, however it may also be necessary to degas the solvent after collection using the freeze−pump−thaw method (see section 4.5). The use of activated molecular sieves alone has also been shown to be sufficient to dry a range of organic solvents.[32] Water content can be quantitatively measured using a Karl Fischer apparatus or qualitatively assessed using the ketyl radical test.

4. SELECTED SCHLENK LINE TECHNIQUES

4.1. Transfer of Solvents, Liquids, and Solids. Schlenk line chemistry is typically based on solution-state methods (in contrast to vacuum line chemistry which often deals with reactive gases and volatile liquids using specialist equipment) and therefore the transfer of anhydrous solvents and liquid

reagents under an inert atmosphere constitutes a key technique. This can be achieved in two main ways: (i) using a syringe and needle or (ii) via cannula transfer. The former is convenient for the precise and quantitative transfer of liquid reagents or solvents, typically below 20 mL in volume, while the latter is best suited for transferring solutions from one vessel to another or for the approximate dispensing of solvents. Graduated pressure-equalizing addition funnels can also be employed to enable accurate dispensing of larger volumes (>20 mL) of solvents and liquid reagents. These processes are facilitated by the use of penetrable rubber septa; the stopper or Teflon tap on the Schlenk flask or ampoule is quickly replaced with an appropriately sized rubber septum under a positive pressure of inert gas and then replaced afterward to minimize exposure to atmospheric air and moisture. For a detailed report regarding the safe handling of cannulas and needles, the reader is directed to recent work by Chandra.[9]

A typical example in which a syringe and needle is used to measure and add a liquid reagent is the use of organolithium compounds such as *n*-butyl lithium. While these reagents are extremely air- and moisture-sensitive and even highly pyrophoric, they are commercially available in hydrocarbon solutions and stored under an inert atmosphere in a sealed bottle containing a penetrable rubber septum. Withdrawing the liquid from these sealed vessels requires an inert gas inlet to re-equalize the pressure and to prevent a partial vacuum; this could introduce atmospheric air and moisture through the compromised rubber septum and degrade the contents. It is common practice however to transfer commercially available air- and moisture-sensitive reagents to suitable storage flasks or ampoules to prevent decomposition during long-term storage. When using a syringe and needle to transfer liquid reagents, and particularly when dispensing pyrophoric substances, it is essential that an appropriately sized syringe and needle gauge is used (see section 3 for further safety details). Users must prepare quenching materials prior to handling pyrophoric reagents and have appropriate fire safety equipment on hand.

A clean short (40−60 mm) needle is first inserted into the Schlenk line hosing using an appropriate screw-thread (Luer-lock) adapter and hose clamp. The needle and hosing are purged with inert gas for 15−30 seconds before piercing the needle through the septum on the reagent bottle. The reagent bottle and hosing should be secured in place using clamps. The disposable syringe and long (100−120 mm) needle used to measure the reagent is first purged by piercing it through the rubber septum on the receiving Schlenk flask, withdrawing inert gas into the syringe, removing the needle from the septum, and then expelling the gas. The user must monitor the bubbler when withdrawing gas or liquid into the syringe: If the bubbler stops,
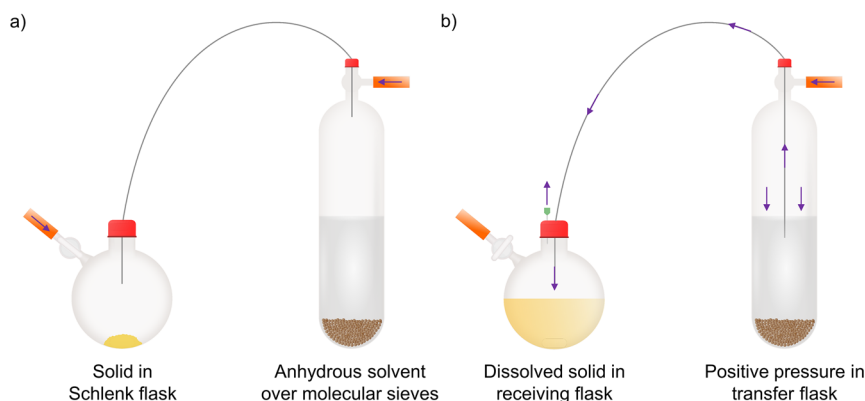
Figure 6. Cannula transfer for the addition of solvent to a Schlenk flask. The Teflon tap on the anhydrous solvent flask is replaced with a rubber septum once cycled onto the Schlenk line. Inert gas flow is marked with arrows.

then a local vacuum may have been introduced which compromises the inert gas atmosphere. This process is repeated two more times before carefully inserting the purged needle and syringe through the septum on the reagent bottle (Figure 5a). A slight excess of the liquid reagent is slowly withdrawn into the syringe (Figure 5b), and then the syringe is carefully turned vertically while keeping the needle in the reagent bottle (Figure 5c). The gas bubble is expelled (Figure 5d), and then the syringe plunger is depressed until the desired quantity of liquid is measured. The syringe and needle are removed from the reagent bottle, pierced through the septum on the receiving Schlenk flask, and slowly added (Figure 5e). It may be desirable to withdraw a small pocket of inert gas into the syringe to protect the reagent from exposure to atmospheric air or moisture during transfer from the reagent bottle to the Schlenk flask. After addition, the needle and syringe are removed and disposed into an appropriate sharps and waste container. For pyrophoric reagents, the needle and syringe should be quenched with isopropanol/toluene prior to disposal.[10] Gas-tight glass syringes fitted with nondisposable Luer-lock needles are frequently employed to accurately dispense solvents as this avoids potential leaching of organic compounds from disposable plastic syringes. These must be dried in an oven prior to use, akin to other glassware used to manipulate air- and moisture-sensitive chemicals.

Cannulas are long double-tipped needles made of stainless steel or PTFE; they are available in a range of lengths and gauges depending on the application. Cannulas are particularly suited for transferring larger volumes of solvents, solutions, or liquid reagents under an inert atmosphere. To perform a cannula transfer, the receiving and transfer vessels must first be under a positive pressure of inert gas and the ground glass or Teflon stoppers replaced with rubber septa. The cannula (typically predried in an oven) is inserted through the septum of the transfer flask (e.g., an anhydrous solvent ampoule) and into the headspace. The cannula is purged for 15−30 seconds with inert gas before being inserted through the septum on the receiving flask (Figure 6a). The cannula is lowered down into the solvent, then the stopcock on the receiving flask in closed, and a bleed needle (also called an exit or vent needle) is inserted into the septum on the receiving flask (Figure 6b). This establishes a pressure differential which will transfer the liquid from the transfer flask into the receiving flask (inert gas flow marked with arrows). Raising the height of the transfer flask, or lowering the height of the receiving flask, will help increase the rate of the cannula transfer. Once the desired volume of solvent has been

transferred, the cannula is raised above the liquid level, the stopcock on the receiving flask is opened to inert gas, and the bleed needle is removed. The cannula is then removed from the receiving flask and transfer flask, and the septa are replaced with the corresponding stopper or Teflon tap. This methodology can also be used to transfer slurries and suspensions provided a suitably bored cannula is employed.

In several circumstances, it may be more convenient to add solid reagents directly to the reaction flask instead of first dissolving it in a separate Schlenk flask and performing a cannula transfer. For less sensitive reactions involving air- and moisture-stable solids, it is often sufficient to simply add the solid through a powder funnel (to avoid it sticking to the greased ground glass joint) under a positive flow of inert gas. An inert gas blanket can also be employed; this is achieved by inserting the stem of an inverted funnel into the Schlenk line hosing and flushing inert gas over the Schlenk flask during the addition of the solid.[11] This method works best when using argon as an inert gas since it is denser than air and N_2 and is particularly useful for the portion wise addition of air- and moisture-stable solids.

The addition of sensitive solid reagents can be achieved by using a solid addition tube; these are similar to test tubes but typically contain a bend (~45°) and a ground glass male joint with can be sealed with a Schlenk cap, small round-bottomed flask, or a rubber septum. Solid addition tubes may also contain a gas inlet side arm with a ground glass stopcock or Teflon tap to control the inert gas atmosphere. The solid reagent is first added to the solid addition tube inside a glovebox, and this can then be cycled onto the Schlenk line (Figure 7a) then added to the reaction flask under a positive flow of inert gas (Figure 7b). Rotating the solid addition tube and gently tapping it will encourage the solid to enter the reaction flask (Figure 7c). This method is best suited for the addition of crystalline solids or salts (such as $ZnCl_2$)[12,13] that will not stick to the solid addition tube.
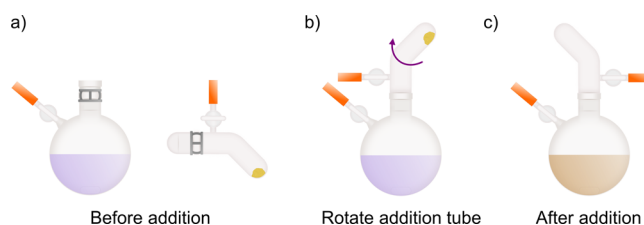

Figure 7. Using a solid addition tube to add sensitive solids to a reaction flask.

4.2. Refluxing. It is possible to perform a reflux under an inert atmosphere by simply fitting a condenser with a suitable gas inlet adapter. This can be cycled onto the Schlenk line by sealing the bottom of the condenser with a Schlenk cap or round-bottomed flask, which then replaces the stopper on the Schlenk flask under a flow of inert gas. During heating, the stopcock on the Schlenk flask should be closed to prevent condensation of the solvent into the gas inlet side arm, hosing, or inert gas manifold of the Schlenk line. If the heating process is expected to liberate corrosive or toxic gases (e.g., by using $SOCl_2$ as a solvent),[18] then an external bubbler can be attached to the reflux condenser. Here, the top of the condenser is fitted with a Drechsel head (gas inlet/outlet adapter) where the gas inlet is attached to the Schlenk line hosing, while the gas outlet is attached to a piece of hosing attached to the external bubbler (Figure 8a). The condenser is flushed with inert gas for 60
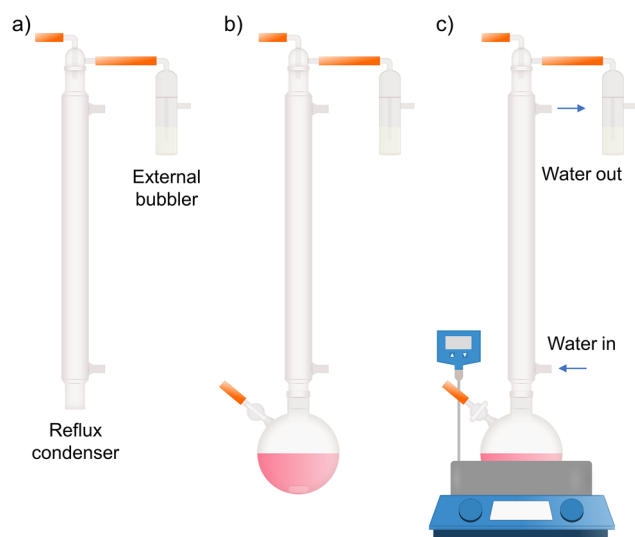

Figure 8. Refluxing under an inert atmosphere with an external bubbler.

seconds (since it cannot be sealed and evacuated) before being attached to the Schlenk flask (Figure 8b). The stopcock on the Schlenk flask is closed, the water-cooling lines are attached to the condenser (alternatively an air-free condenser can be used), and the flask is heated to reflux (Figure 8c). The inert gas flow rate, which can be monitored by the frequency of bubbling in the external bubbler, can be lowered once the desired temperature is reached, but it should be increased once the flask cools back to room temperature to prevent oil suck back.

It is generally recommended to not perform other reactions on the Schlenk line during a reflux to prevent contamination with solvent vapors. Reactions that require prolonged heating, and do not liberate gaseous byproducts, can be heated directly in Teflon-tapped ampoules without the need for a reflux condenser. Since this method does build up pressure within a sealed vessel, it is essential that the reaction vessel is suitable for such use. It is advised not to heat beyond the boiling point of the solvent unless specialist heavy-walled pressure vessels are used in tandem with a blast shield.

4.3. Inert Atmosphere Filtrations. Performing filtrations under strictly anaerobic and anhydrous conditions allows for the separation and isolation of sensitive compounds. This is a routine Schlenk technique which can be performed in two main ways: (i) cannula filtration or (ii) filtration through a frit. Both

methods can be used to either remove solids from a reaction mixture or to isolate a precipitated/crystallized product.

For cannula filtrations, a cannula in which one end contains a suitable filter attachment is used to separate the supernatant from the solid. This method is recommended in situations where the crystallized or precipitated solids readily settles out of solution; fine solids or suspensions on the other hand can easily block the filter cannula. For large crystals, it may be sufficient to simply decant off the supernatant using a long needle and syringe, or to perform a standard cannula transfer. Cannulas used for filtrations however should contain one end which is flat or suitably modified to allow a small glass microfiber filter to be secured to the cannula using PTFE tape (Figure 9a). First, a ∼10
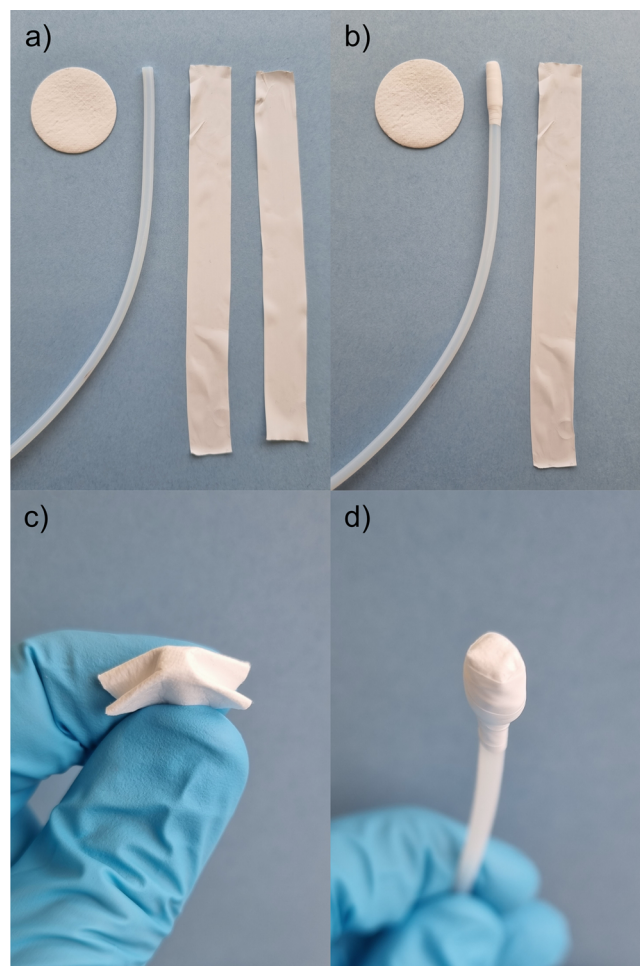

Figure 9. Preparing a filter cannula using PTFE tape and a glass microfiber filter.

cm length of PTFE tape is wrapped around a flat-ended cannula, making sure to not obstruct the hole (Figure 9b). A 125 mm diameter glass microfiber filter is then carefully folded around the cannula, ensuring that the filter remains flat and flush with the end of the cannula (Figure 9c). Finally, a second ∼10 cm length of PTFE tape is wrapped around the filter to secure it to the cannula (Figure 9d). The filter cannula is then stored in an oven prior to use. It is also possible to purchase premade filter attachments (available in different sizes and porosities) that connect to the cannula and can be secured in place using PTFE tape.

A cannula filtration is performed in a similar way to a cannula transfer, the primary difference being that the rubber septum which is to be inserted into the Schlenk flask for filtering must be fitted with the filter cannula prior to use. This is achieved by piercing the sharp end of the cannula through the bottom of the rubber septum and pulling it along so that the filter attachment is now close to the bottom of the septum. The stopper on the Schlenk flask containing the contents to be filtered is replaced with the septum and filter cannula assembly under a flow of inert gas. The cannula is purged for 15−30 seconds before inserting the sharp end of the cannula through a septum on a receiving flask that has previously been cycled onto the Schlenk line (Figure 10a). A bleed needle is inserted into the septum of the
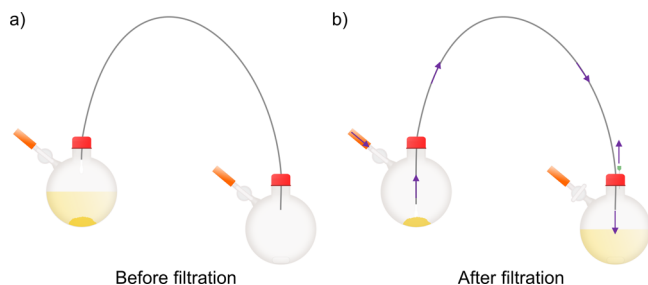

Figure 10. Performing a cannula filtration. Inert gas flow is marked with arrows.

receiving flask, the stopcock is closed, and the filter cannula is lowered into the supernatant to begin the filtration (Figure 10b). For cannula filtrations, it may be necessary to increase the inert gas overpressure and raise the height of the transfer flask to help speed up the filtration. Once the filtration is complete, the filter cannula is raised above the solids to allow any remaining filtrate to pass through the cannula. If necessary, it is possible to add additional solvent to the transfer flask to wash or extract the solids (by syringe or cannula transfer) and repeat the filtration. The stopcock on the receiving flask is opened to inert gas and the bleed needle is removed from the septum. The cannula is removed from the septum of the receiving flask and then from the transfer flask along with the septum and replaced with a greased stopper. This technique is also amenable to being performed at low temperatures by simply submerging the transfer flask in a suitable cooling bath. Hot filtrations using cannula filters may lead to undesirable crystallization or precipitation of solids within the cannula or on the filter paper and should therefore be used cautiously.

Filtrations using a glass frit are a powerful and versatile technique that can be used for numerous applications, including the following: (i) the removal of fine metal salts, often in tandem with a filtration aid such as Celite, or (ii) the isolation and washing of fine solids. The former will be explained in further detail below and further step-by-step practical examples [e.g., preparation of Li sand, synthesis of $P(SiMe_3)_3$, purification of $LiAlH_4$] which use the filter frit for different applications are available on *The Schlenk Line Survival Guide* website.[8]

A Schlenk flask equipped with a stir bar, a glass filter frit with a layer of Celite (predried in an oven), and Schlenk cap is greased, assembled, connected to the Schlenk line hosing, and evacuated under vacuum (Figure 11a). It is recommended to leave the assembly under vacuum for 30−60 minutes for the first cycle to ensure that the frit and Celite is thoroughly dried. The assembly is then carefully and slowly backfilled with inert gas to avoid disruption of the Celite: pulling vacuum from the receiving Schlenk flask side arm and then backfilling from the filter frit side arm (ensuring that the other stopcock is closed) is recommended. The Schlenk cap is replaced with a rubber septum and the reaction mixture to be filtered is transferred to the frit via cannula transfer (Figure 11b,c). The bleed needle is removed, and the stopcock on the filter frit is opened to inert gas. The cannula is left in place during the filtration since this facilitates any further washing/extraction steps. If the filter frit does not have an in-built gas inlet side arm, then it is essential to keep the cannula in place to provide a constant feed of inert gas. A pressure differential is required to initiate the filtration, which can be achieved by establishing a static vacuum in the Schlenk line hosing attached to the receiving flask (Figure 11d). This may have to be periodically refreshed to speed up the filtration. Once the filtration is complete, the stopcock on the receiving flask is opened to inert gas, the cannula is removed, and the filter frit is replaced with a greased stopper to allow further manipulations with the collected filtrate.

Alternatively, or if the reaction mixture is simply too thick to be transferred using a cannula, the filter frit assembly shown in Figure 11a can be rotated 180° and attached directly to the Schlenk flask containing the contents to be filtered. This is then carefully and slowly rotated 180° to pour the contents into the filter frit, being particularly careful to avoid pouring into the side arms and hosing. This method is not compatible with Celite however unless a bed of oven-dried glass wool is placed on top of the Celite to prevent it from falling into the transfer flask.

The methods outlined above can also be used to isolate and wash solids from a reaction mixture (no Celite is added to the
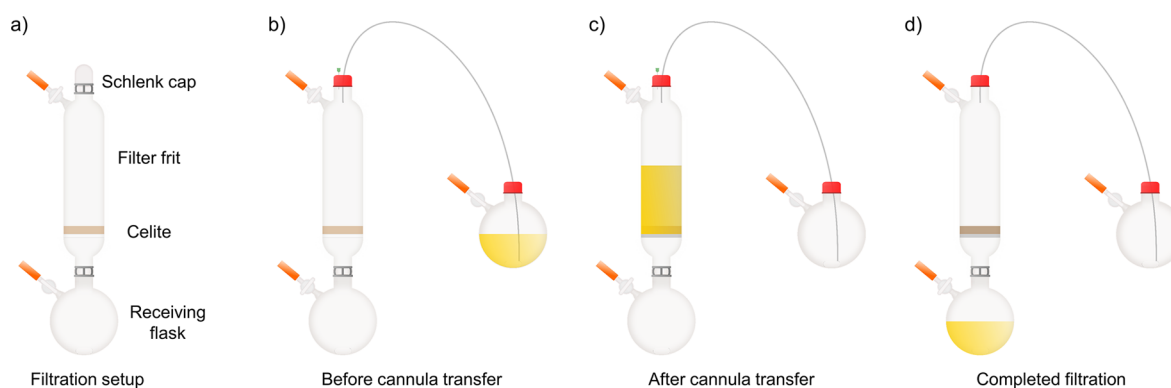

Figure 11. Performing a filtration through Celite using a frit for the removal of solids.

filter frit). After the filtration is complete (shown in Figure 11d), the cannula is removed, and the rubber septum on the filter frit is replaced with the Schlenk cap. The filter frit is detached from the receiving flask and capped at the bottom with a second Schlenk cap or round-bottomed flask, while the receiving flask is sealed with a greased stopper. Some filter frits may contain a built-in Teflon tap to directly seal the assembly after filtration. The solids collected on the filter frit can now be dried under vacuum and subsequently isolated in a glovebox (Schlenk flasks and other sealed greased glassware must be fully evacuated and under static vacuum to be cycled into the glovebox). Alternatively, if the filter frit does not contain a built-in side arm or gas inlet, then a suitable adapter or indeed another clean and precycled Schlenk flask can be attached to the bottom of the filter frit, which then allows the solids to be dried under vacuum. This method is very similar to the original procedure developed and reported by Schlenk in 1913[2] and subsequently used to isolate organo-lithium compounds in 1917.[3] More recently, the Hevia group have showcased the synthesis of useful organosodium reagents ("BuNa and NaTMP) through a series of detailed and annotated photographs, which take advantage of a filter frit to isolate, wash, and dry highly pyrophoric solids.[14]

An adaption of this technique is the use of swivel frits.[15] These are filter frits that contain a built-in pressure-equalizing side arm which allows the filtrate to be partially evaporated under a static vacuum such that fresh solvent condenses in the upper part of the apparatus and washes the filtered solids without requiring additional solvent. This technique is typically performed using a high-vacuum line, which avoids the use of hosing and rubber septa and instead relies on vacuum transfer techniques to quantitatively manipulate liquids and gases.[15]

4.4. Removing Solvent under Vacuum. Schlenk lines allow solvents and other volatiles to be readily removed under vacuum without exposing the reaction vessel to atmospheric air and moisture. The low pressures offered by rotary vane vacuum pumps means that even high boiling point solvents such as toluene can be removed at room temperature, which may be crucial for the isolation of temperature-sensitive compounds. When evaporating a small volume of solvent (>50 mL) or simply drying a compound under vacuum, the stopcock on the Schlenk flask is first closed, the stopcock on the Schlenk line is turned to vacuum, and then the stopcock on the Schlenk flask is slowly turned to vacuum, ensuring that the solution is adequately stirred to prevent bumping (i.e., rapid or uncontrolled bubbling/boiling).

A secondary external liquid nitrogen trap should be used when removing large volumes of solvents and is recommended when removing corrosive or reactive volatiles. Schlenk lines may also be equipped with a built-in secondary trap which allows larger volumes of solvent to removed without the need for an external trap. For solvents with freezing temperatures close to room temperature such as benzene or 1,4-dioxane, a dry ice/acetone bath (−78 °C) can instead be employed over liquid nitrogen to help prevent blockages in the external trap. The stopcock on the Schlenk flask is closed followed by the Schlenk line stopcock, and the flask is then detached from the Schlenk line hosing. An external trap (which consists of long vessel equipped with a Drechsel head type inlet/outlet adapter) is attached to the Schlenk line hosing, and the Schlenk flask is connected to the external trap with an additional piece of hosing. The external trap is then placed under vacuum (Figure 12a), then after a few minutes of being evacuated, the external trap is lowered into a Dewar of liquid nitrogen. Ensure that the manometer reading is
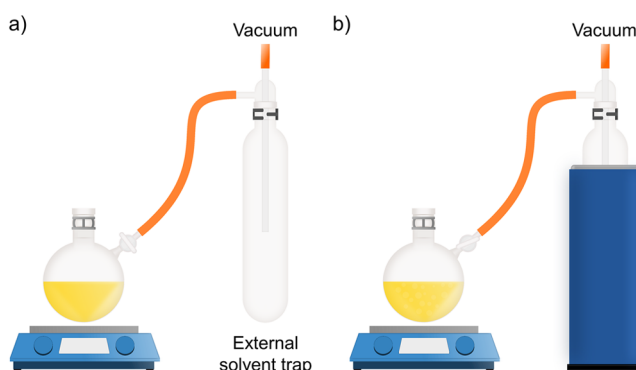
Figure 12. Removing solvent on the Schlenk line with an external trap.

sufficiently low (i.e., no leaks in the system) prior to lowering the external trap into the Dewar of liquid nitrogen. The stopcock on the Schlenk flask is carefully and partially opened to begin evacuating the flask (Figure 12b). Strong stirring is recommended during the removal of solvent to prevent bumping, and the external trap (as well as the primary trap on the Schlenk line) should be periodically topped up with liquid nitrogen. Once all the solvent has been removed, the stopcock on the Schlenk flask is closed followed by the stopcock connecting the external trap to the Schlenk line. The Schlenk flask can be disconnected from the hosing and then be cycled back onto the Schlenk line before being backfilled with inert gas for further manipulations. The external trap is removed from the Dewar of liquid nitrogen and disconnected from the Schlenk line hosing. The collected solvent and volatiles are allowed to thaw before being discarded into an appropriate waste container.

4.5. Freeze−Pump−Thaw and Other Degassing Methods. The freeze−pump−thaw (FPT) method is an effective way of degassing solvents, solutions, or liquid reagents. The Schlenk flask or ampoule containing the contents to be degassed is first sealed (by closing the stopcock or Teflon tap) and then cooled in a −78 °C dry ice/acetone bath (Figure 13a).
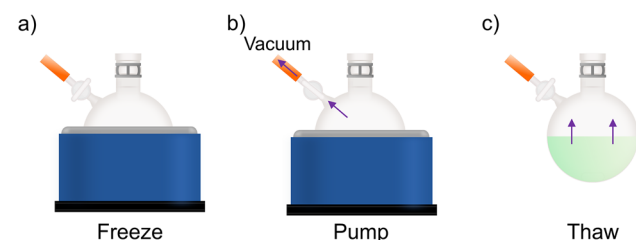
Figure 13. Degassing using the freeze−pump−thaw (FPT) method.

Cooling the solvent to low temperatures prevents or minimizes the amount of solvent that evaporates when placed under dynamic vacuum. Liquid nitrogen can be used to completely freeze the contents of the flask, but this may lead to condensation of liquid oxygen if there is a leak present while the flask is under static vacuum. Liquid nitrogen should therefore only be used for more valuable liquid reagents or deuterated solvents. Once all the liquid has cooled, the flask is placed under vacuum to evacuate the headspace, ensuring the flask is still in the cooling bath (Figure 13b). After several minutes, the flask is sealed and removed from the cooling bath (Figure 13c). As the liquid slowly warms or thaws, any dissolved gas will escape into the headspace of the flask. Avoid applying external heat (warm water bath or heat gun) to make this process

faster, since this risks cracking the flask and causing an implosion. This process is repeated two more times for a total of three FPT cycles; this ensures that all of the dissolved gas or any gas trapped within the frozen solid is removed. Once warmed back to room temperature after the final cycle, the flask can be backfilled with inert gas, or even a reactive gas such as H_2, CO, or CO_2. It is essential to never backfill a flask with inert gas (nitrogen or argon) while frozen in liquid nitrogen since this can lead to condensation of the inert gas, which, if the flask is then sealed, may result in an explosion as the temperature increases.

Other methods of degassing solvents include (i) sparging with inert gas and (ii) the boil-degas method. For sparging, inert gas is simply bubbled through the solvent for an appropriate amount of time to displace dissolved air and oxygen. For the boil—degas method, the solvent is placed under dynamic vacuum for an appropriate amount of time (with a suitable cryogenic trap) to remove dissolved gases. Both methods can be equally as effective as the freeze—pump—thaw method but do result in significant evaporative loss of the solvent, and therefore are only recommended for bulk organic solvents and should not be employed for degassing expensive deuterated solvents or volatile liquid reagents.

4.6. Distillations. The purification and drying of solvents or liquid reagents via distillation can be performed under anhydrous and anaerobic conditions in three main ways: (i) a simple distillation under inert gas; (ii) static vacuum distillation (often called vacuum transfer); or (iii) dynamic vacuum distillation. The choice of method is generally dictated by the scale and boiling point of the liquid, with dynamic vacuum distillation being the best choice for the purification of high boiling liquids, oils, or even low-melting or volatile solids (the latter is technically a sublimation).

For simple distillations under inert gas, the distillation apparatus is connected to the Schlenk line to provide a constant flow of inert gas. This can be connected through a vacuum takeoff adapter, or through the side arm of a Schlenk flask which is the recommended collection vessel. This method is best suited for the distillation of solvents and liquid reagents with boiling points below 150 °C. For solvents or reagents which will subsequently be used for the synthesis of air- and moisture-sensitive compounds, it is common to combine the purification with a drying step by stirring or refluxing over a suitable desiccant (drying agent) for a suitable period of time (a few hours to overnight) prior to distillation. It may be necessary to degas the resulting distillate prior to use via the freeze—pump—thaw method.

Static vacuum distillations (often called vacuum transfers) may also be employed for the purification and drying of solvents and liquid reagents, generally with boiling points below 150 °C. Three main factors influence the rate and thus practicality of performing static vacuum distillations: (i) the vapor pressure of the liquid; (ii) the quality of the vacuum; and (iii) the cross-sectional area of the distillation bridge. A pressure—temperature nomograph can be used to estimate the pressure at which a liquid will begin to boil at a given temperature (typically room temperature or lower); however, this does not necessarily consider the rate of evaporation or the fact that the liquid will cool significantly during evaporation. This technique is typically performed on Schlenk lines equipped with good rotary vane pumps (ultimate vacuum $\approx 10^{-2}$ to 10^{-4} mbar) or on high-vacuum lines[15] equipped with diffusion pumps (ultimate vacuum $\approx 10^{-4}$ to 10^{-7} mbar), which provide sufficiently low

pressures to readily distill solvents with boiling points below 150 °C at reasonable rates.

Static vacuum distillations are frequently used for the purification and drying of deuterated solvents to minimize evaporative losses but also may be used to purify and separate temperature sensitive or volatile compounds. Static vacuum distillations often employ custom-made greaseless vessels and distillation bridges which prevents grease contamination in the purified distillate. An oven-dried Teflon tapped ampoule with a 90° side arm, which is equipped with a stir bar, is cycled onto the Schlenk line using a suitable O-ring adapter. The ampoule is backfilled with inert gas and then the desiccant is added followed by the solvent (or liquid reagent); this can be introduced via syringe or cannula transfer or simply poured into the flask with a funnel under a flow of inert gas. The contents are then stirred overnight under an inert gas atmosphere; the flask can be sealed or periodically opened to the Schlenk line to release H_2 build-up (from the reaction of the desiccant with water or protic impurities). The contents are then degassed two times using the freeze—pump—thaw method. The ampoule is then connected to a greaseless distillation bridge (this may be built directly into the Schlenk or high vacuum line, or be a separate unit that can be connected to the Schlenk line hosing), and a second receiving ampoule is connected to the bridge and evacuated under vacuum (Figure 14a). Oven-dried glass wool is often placed
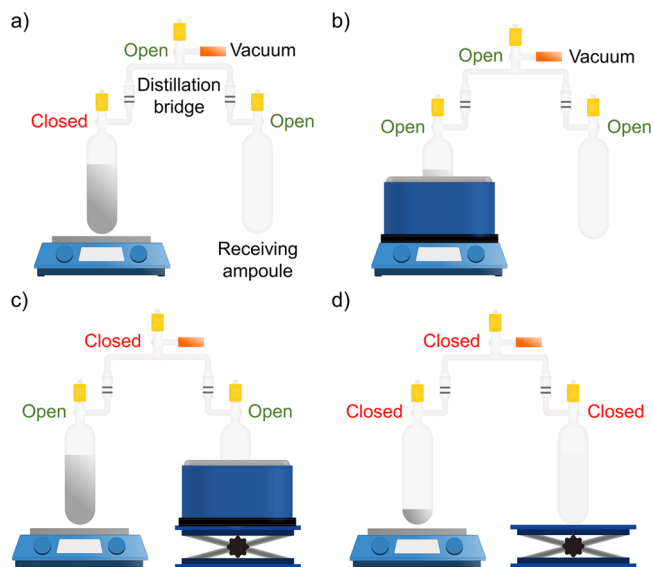
Figure 14. Performing a static vacuum distillation. Teflon taps are marked as open or closed for clarity.

within the distillation bridge or ampoule side arm to prevent solid desiccant from accidentally contaminating the purified distillate. The ampoule containing the liquid is cooled to −78 °C using a dry ice/acetone bath, and then evacuated under vacuum (Figure 14b). Liquid nitrogen cooling baths should be avoided where possible for vacuum transfers as this presents a significant risk of liquid oxygen condensation. Performing this third freeze and pump cycle while attached to the distillation bridge ensures that the best possible vacuum is established within the distillation apparatus. A manometer is beneficial here to confirm a suitable vacuum is established prior to beginning the distillation. The Teflon tap on the distillation bridge is closed, then the transfer ampoule is removed from the −78 °C cooling bath while the receiving ampoule is submerged in the −78 °C
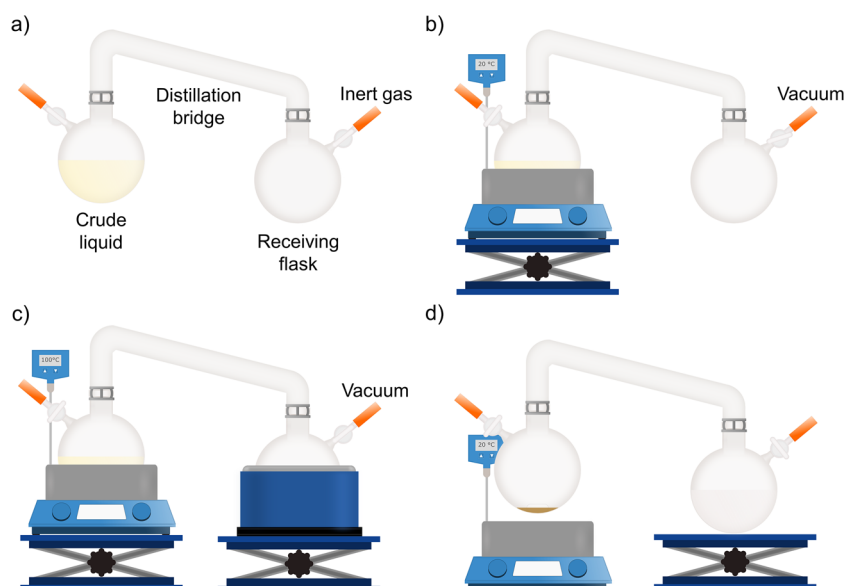
Figure 15. Performing a dynamic vacuum distillation.

cooling bath (Figure 14c). As the liquid slowly thaws, it will begin to evaporate under the reduced pressure and condense in the receiving flask at the lower temperature. It may be necessary to refresh the static vacuum periodically by closing the Teflon tap on the transfer ampule, then opening the Teflon tap on the distillation bridge to dynamic vacuum (ensuring a cryogenic trap is still in place). After several minutes, or until the manometer reading is sufficiently low, the Teflon tap on the distillation bridge is closed, and the Teflon tap on the transfer ampoule is slowly opened to continue the distillation. Once the distillation is complete, the Teflon taps on both ampoules are closed and the receiving flask is removed from the cooling bath (Figure 14d). The liquid in the receiving flask is allowed to thaw before being backfilled with inert gas (depending on the setup this may need to be first disconnected from the distillation bridge and then cycled back onto the Schlenk line). The freshly distilled liquid can now be transferred to a suitable flask for storage. The transfer ampoule is also cycled onto the Schlenk line and backfilled with inert gas, and then quenched with isopropanol/toluene to safely destroy the excess desiccant.[10]

Dynamic vacuum distillations are best suited for the purification of high boiling liquids (>150 °C) or low-melting solids. An oven-dried distillation bridge and receiving flask is greased, assembled, and cycled onto the Schlenk line (one end of the distillation bridge is sealed with a Schlenk cap) then attached to the distillation flask containing the crude liquid under a flow of inert gas (Figure 15a). The stopcock on the distillation flask is closed, and the flask is then lowered into a heating mantle or oil bath. With stirring (to prevent bumping and bubbling), the system is carefully placed under vacuum via the stopcock on the receiving flask (Figure 15b). This serves to degas the crude liquid and remove any residual solvent or volatile impurities. After several minutes, the temperature of the heating mantle (or oil bath) is slowly increased until the distillation begins. Since this method is generally used for nonvolatile compounds, an ice bath is often sufficient to cool the receiving flask and collect the distillate, but a dry ice/acetone bath can also be used if desired (Figure 15c). During the distillation, it may be necessary to insulate the distillation flask and part of the distillation bridge with aluminum foil, or to periodically encourage the distillation

along with a heat gun. Once the distillation is complete, the stopcock is closed on the receiving flask. The heating mantle (or oil bath) is lowered to allow the distillation flask to cool to ambient temperature, while the cooling bath is removed from the receiving flask to allow it to thaw or warm to ambient temperature (Figure 15d). The system is then slowly backfilled with inert gas, then the distillation bridge can be detached, and the receiving flask is sealed with a greased stopper for further manipulations on the Schlenk line. Dynamic vacuum distillations are employed for the purification of numerous air- and moisture-sensitive compounds including organophosphorus compounds [e.g., $P(SiMe_3)_3$][8] and transition-metal amides [e.g., $Fe\{N(SiMe_3)_2\}_2$].[16,17]

4.7. Preparing NMR Spectroscopy Samples on a Schlenk Line. Air- and moisture-sensitive samples to be analyzed by NMR spectroscopy can be readily prepared using Schlenk line techniques. NMR tubes used for sensitive samples typically contain a screw-thread Teflon tap (i.e., J. Young's) which ensures an airtight seal to prevent contamination by atmospheric air or moisture. Although it is often more convenient to prepare NMR samples inside of a glovebox, it may be desirable to add the deuterated solvent on a Schlenk line (to minimize solvent use in a glovebox or prevent contamination by other volatiles in the glovebox atmosphere) or to directly take an aliquot of the reaction mixture. NMR tube adapters that contain a gas inlet side arm, a ground glass joint (that can be sealed with a fresh rubber septum to avoid the use of grease) and a thermometer O-ring adapter (or a rubber septum drilled with a 5 mm hole) allow standard NMR tubes or J. Young's NMR tubes to be cycled onto the Schlenk line (Figure 16a) and for liquids (a deuterated solvent or the reaction mixture) to then be added via cannula transfer or using a syringe and needle (Figure 16b). The Teflon tap (or a tapered rubber bung when using standard NMR tubes) is then added under a positive flow of inert gas to seal the NMR tube (Figure 16c).

Solvent can be removed directly from NMR tubes under vacuum by using the tapered glass adapters that are supplied with J. Young's NMR tubes. The J. Young's taps are hollow, allowing the NMR tube to be opened or closed to vacuum or inert gas while connected to the Schlenk line hosing (Figure 17).
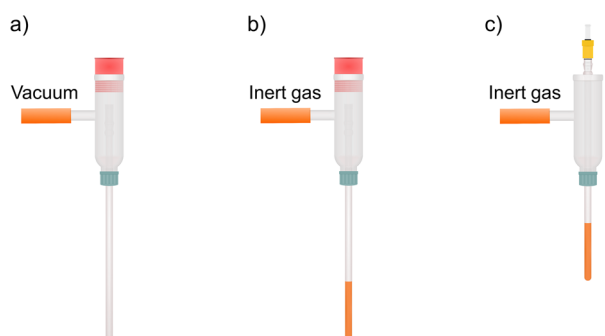
Figure 16. Cycling an NMR tube onto the Schlenk line and adding a solvent or reaction aliquot to the tube under an inert gas atmosphere.
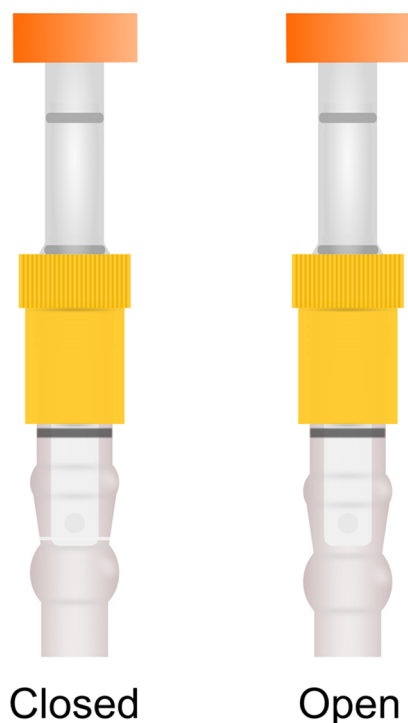

Figure 17. Illustration of closed and open NMR tubes equipped with a J. Young's Teflon tap and connected to the Schlenk line hosing.

To remove solvent from a J. Young's NMR tube, it is first connected to the Schlenk line hosing using the tapered glass adapter and placed under vacuum. The contents of the NMR tube are cooled (or frozen) in a dry ice/acetone bath (-78 °C) or a Dewar of liquid nitrogen. The Teflon tap is opened (by twisting anticlockwise until the white band is no longer observed) to evacuate the headspace in the NMR tube. After 30−60 s, the tap is sealed, and the contents of the NMR tube are carefully thawed and warmed to room temperature. This represents one freeze−pump−thaw (FPT) cycle, which helps prevent bumping while removing the solvent under dynamic vacuum. The freeze and pump cycle is repeated but now the Teflon tap is kept opened while under dynamic vacuum, and removed from the cooling bath. As the NMR tube warms to room temperature, the solvent will slowly evaporate. Holding the NMR tube at an angle with gentle agitation helps to increase the surface area to facilitate evaporation of the solvent. It may be necessary to close the Teflon tap and repeat this process if the solvent removal becomes uncontrolled. Once all visible solvent has been removed, the NMR tube is kept under dynamic

vacuum for several minutes to remove all volatile material. The NMR tube can then be backfilled with inert gas ready for further manipulations on the Schlenk line or in a glovebox.

The freeze−pump−thaw method can be used to degas NMR tubes which can subsequently be backfilled with a reactive gas such as H_2, CO, or CO_2. Calibrated gas bulb assemblies can be used to add stoichiometric amounts of a condensable gas,[15] or backfilling while cooling the evacuated NMR tube to different temperatures enables higher pressures of gas to be achieved within the NMR tube once it is sealed and comes to room temperature (e.g., introduction of 1 atm of H_2 at -196 °C gives approximately 4 atm of H_2 at room temperature).[19] This technique should only be used with J. Young's NMR tubes that are suitable for high-pressure operations, and the NMR tube must be carefully thawed behind a blast shield in case of an explosion.

5. PEDAGOGY AND OTHER RESOURCES

A number of pedagogical resources have been published in chemical education research journals which introduce under-graduate students to Schlenk line techniques.[33,34,43−47,35−42] These experiments help to showcase key aspects and advances in organometallic chemistry such as the preparation of transition-metal complexes,[33,35−38,41,42,47] ligand synthesis,[45] or perform-ing ubiquitous catalytic reactions such as cross-couplings,[40,45,46] hydrogenations,[39] or ring-closing olefin metathesis.[34] Some Schlenk line techniques, including the safe use of needles and syringes for the handling of pyrophoric reagents, or even cannula transfers for solvent addition, can be performed simply with an inert gas inlet or balloon.[44]

Due to time and equipment restrictions, however, the full arsenal of key Schlenk line techniques is rarely taught at the undergraduate level. This generally means that students are trained on an *ad hoc* basis as part of a research project which may follow a less structured and organized approach, while also putting undue pressure on the student (e.g., to obtain high yields or new results). The development and implementation of dedicated Schlenk line training programs, as part of a taught undergraduate or postgraduate research course, would be highly beneficial; this could include tailored experiments that focus on learning a variety of key Schlenk line techniques and identifying when to employ each of them. It is hoped that this guide and the other available resources highlighted within, help to facilitate the training of new Schlenk line users.

The Schlenk Line Survival Guide[8] contains step-by-step illustrations and guides for all techniques covered in this tutorial review. In addition, it contains further details regarding Schlenk line equipment, assembly, cleaning, troubleshooting, and much more, and it is frequently updated with new guides and useful information. Other publications and resources that focus on the synthesis of air- and moisture-sensitive reagents, precursors, and catalysts are also available, many of which contain photographic step-by-step guides.[14,48] A number of books[5,49,50] and other resources[51] detailing Schlenk line techniques and other advanced protocols such as vacuum line methods have been published; however, it should be noted that many of these resources are outdated and have access tolls (i.e., subscription and site licenses), and are therefore not well suited for teaching and training purposes.

6. CONCLUSIONS AND OUTLOOK

Over 100 years after Schlenk's initial report, Schlenk line techniques have become an indispensable method for the safe handling and manipulation of air- and moisture-sensitive compounds. This tutorial provides a user-friendly overview of key technical aspects of Schlenk line chemistry through a series of detailed illustrated guides. This includes basic Schlenk line operating procedures and routine techniques such as the transfer of liquids, inert atmosphere filtrations, degassing, removal of solvents, and distillations. It is anticipated that these guides will be a useful introductory reading and training resource for beginner Schlenk line users, as well as a convenient go-to aid for chemists of all proficiency.

In the bigger picture beyond Schlenk line chemistry, it is hoped that this tutorial inspires and motivates other researchers to create their own high quality open education resources to supplement and aid scientific research. While this may not always be feasible, researchers are encouraged to be fully transparent in their published experimental methods and provide accurate details to ensure the results can be replicated by others.

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Notes

Caution! *The guides provided herein are an education resource and are no substitute for direct and hands-on Schlenk line training. Never operate a Schlenk line alone; ensure that a senior student, postdoctoral researcher, technician, or PI is in the lab to supervise and to assist in the case of an emergency. Appropriate risk assessments alongside necessary training courses (e.g., fire extinguishing, gas cylinder safety) must be completed before operating a Schlenk line. The specific techniques and guides presented in this tutorial review are based on the author's own opinion which have been established from training and experience in numerous main-group and organometallic chemistry laboratories around the world. Alternative methodologies and techniques may be employed by different users depending on personal preference and available equipment.*
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