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Schlenk Lines Transfer of Solvents

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Overview

Source: Hsin-Chun Chiu and Tyler J. Morin, laboratory of Dr. Ian Tonks—University of Minnesota Twin Cities

Schlenk lines and high vacuum lines are both used to exclude moisture and oxygen from reactions by running reactions under a slight overpressure of inert gas (usually N_2 or Ar) or under vacuum. Vacuum transfer has been developed as a method separate solvents (other volatile reagents) from drying agents (or other nonvolatile agents) and dispense them to reaction or storage vessels while maintaining an air-free environment. Similar to thermal distillations, vacuum transfer separates solvents by vaporizing and condensing them in another receiving vessel; however, vacuum transfers utilize the low pressure in the manifolds of Schlenk and high vacuum lines to lower boiling points to room temperature or below, allowing for cryogenic distillations. This technique can provide a safer alternative to thermal distillation for the collection of air- and moisture-free solvents. After the vacuum transfer, the water content of the collected solvent can be tested quantitatively by Karl Fischer titration, qualitatively by titration with a Na/Ph_2CO solution, or by ^1H NMR spectroscopy.

Principles

Purified solvents that are both moisture- and oxygen-free are needed in diverse fields of chemistry, from small molecule synthesis to advanced materials applications.[1-3] For example, butyllithium, which is commonly used in organic synthesis and as an anionic polymerization initiator, is water-reactive and trace water in solvents can greatly affect the actual reagent concentration. Similarly, many inorganic and organometallic compounds, in particular low valent or coordinatively unsaturated metals, are often highly reactive toward water and oxygen and require the use of air-free manipulations in addition to dry and deoxygenated solvents.[4] Employing a Schlenk line or high vacuum line allows for the proper manipulation of such compounds that are air and/or moisture sensitive, and vacuum transfer is one method for rigorously drying and degassing solvents.

The Schlenk line and corresponding glassware was initially developed by the chemist Wilhelm Johan Schlenk as a tool to synthesize and manipulate the triphenylmethyl radical as well as organosodium and organolithium compounds.[4] Schlenk lines have been widely adopted by synthetic chemists, and there are several commercially available designs. A Schlenk line typically consists of twin glass manifolds (one for vacuum, one for inert gas) with 4–6 valved ports, and thick-walled rubber tubing leading from the ports to various reaction apparatus.[5,6] Most commonly, the manifold valves are either greased ground glass or PTFE stopcocks that allow for a seamless transition between inert gas/vacuum, while the thick-walled rubber tubing is either butyl rubber or Tygon brand tubing. In general, there are tradeoffs in ease of maintenance versus air-free quality (rates of outgassing and/or gas permeability) when choosing between various types of valve construction or tubing type, and different applications necessitate different degrees of quality.

The vacuum manifold is connected to a vacuum pump. A cryogenic trap (often liquid nitrogen, 77 K, or dry ice/acetone slurry, 195 K) is located between the vacuum manifold and the pump in order to prevent solvents or other harmful materials from entering the vacuum pump.[8] Many research groups employ a two-trap design, wherein the first trap is used for solvent removal and the second trap for pump protection; in general this design provides superior protection for the vacuum pump during routine operation. The inert manifold is connected to a pressure-regulated inert gas source (N_2 or Ar) that has been passed through moisture/oxygen scrubbers and is vented through an oil bubbler to keep the line pressure slightly above atmospheric pressure.

A high vacuum line consists of the same twin manifold design, but uses a diffusion pump placed between the manifold and vacuum pump to generate a significantly higher vacuum (down to 10^{-7} torr). The diffusion pump works by refluxing heavy oil or mercury to produce a high-speed jet of vapor, which then directs molecules down the throat of the pump. Additionally, high vacuum lines forego the use of thick-walled rubber tubing and primarily use glass-on-glass connections to connect equipment, which minimizes gas diffusion into the system. In general, Schlenk lines are used for operations that require cannula transfers, counter-flow methods, or fractional distillations, while high vacuum lines are used for quantitative gas condensations or extremely air-sensitive reactions; however, either could be used for most applications depending on the users' personal preference.

Vacuum transferring is a common technique for transferring solvents from vessel-to-vessel while maintaining an air-free environment. This technique is commonly encountered while drying/purifying organic solvents for air-free reactions as a method for separating solvent from desiccant; however, it can be generally applied to the capture or separation of any volatile compound within a mixture. In a general sense, vacuum transfers are cryogenic distillations and operate under the same physical principles as standard thermal distillations. Their main advantage over traditional distillations is that they are not heated, substantially reducing the risk of fire or explosion when working with flammable or peroxide forming solvents. While only bulb-to-bulb vacuum transfers are presented here, it is possible to separate multiple components via successive cryogenic trappings with more elaborate setups.

Three main factors dictate the rate (and practicality) at which one can cryogenically vacuum transfer a volatile component: (1) the vapor pressure of the volatile (higher is better); (2) the quality of the vacuum (lower is better — thus, high vacuum lines are preferred over Schlenk lines); and (3) the length/diameter of the distillation pathway (short length, wide diameter is better). In order to maximize vacuum transfer efficiency, solvents will be first degassed using the freeze-pump-thaw technique, and then vacuum transferred to a storage vessel through a specialized U-shaped bridge tube connected to a high vacuum line or Schlenk line with *only* glass-on-glass connections. This technique can allow for the transfer of high-boiling solvents such as toluene and dioxane with relative ease.

Procedure

1. Using Schlenk Lines

1 Start Up

1. Make sure that all working ports on the manifold are closed, and that all joints are properly greased with high vacuum grease.
2. Attach the solvent trap(s) to the vacuum line, and seal by turning on the vacuum pump. **NOTE:** Each vacuum pump has its own "unique" sound when air is actively being pumped out of the system. It is important to "get to know" the regular sounds that your vacuum makes while pumping and while under full vacuum.
3. Place vacuum-sealed dewars around the solvent trap(s) and fill the dewars with liquid nitrogen (best) or dry ice/acetone slurry (*only* for low vapor pressure solvents — risk of vacuum pump damage) to cryogenically protect the vacuum pump.
4. Turn on the regulated inert gas flow, and adjust the flow by watching the rate at which the bubbler bubbles. (An approximate flow rate of 5 bubbles per 10 s is ideal)
5. Connect desired apparatus to a manifold port using thick rubber tubing or directly using standard taper glassware.
6. Clear the headspace (and potentially the apparatus) of residual air and moisture by performing 3 vacuum/inert gas backfill cycles: (1) open the reaction port to vacuum, wait for full vacuum, and then close the reaction port to vacuum; (2) *slowly* open the reaction port to inert gas, and then wait until the bubbler begins to bubble again. Rapidly opening the port to inert gas may result in air being sucked into the system through the bubbler. Close the reaction port to inert gas. (3) Repeat 3 times total.

2 Shut Down

1. Close off all manifold ports, and turn off the inert gas flow.
2. Remove the solvent trap dewar(s). ***CAUTION:*** *if a blue liquid is present in the trap upon removal, it is possibly liquid oxygen (B.P. -183 °C), which can condense at liquid nitrogen temperatures (B.P. -196 °C) and can form explosive mixtures with organic compounds or cause a rapid pressurization explosion in a closed system upon warming.[7] In the case where liquid oxygen is present, immediately replace the dewar in order to keep the trap cold, close the fume hood sash, and inform others of the situation. Leave the trap up and the system under vacuum, and leave it to slowly warm up and evaporate. Condensing liquid oxygen may be avoided by ensuring the manifolds no leaks and by limiting vacuum exposure to ambient atmosphere. A similar event can take place with liquid argon (B. P. -186 °C), and care should be taken to not pump significant volumes of argon through an LN_2 trap.*
3. Turn off vacuum pump and vent the system to ambient atmosphere by opening the solvent trap vent (if applicable) or a port on the main vacuum manifold.
4. Remove the solvent traps, and dispose of any trapped volatiles into the appropriate waste container.

2. Drying Hydrocarbon Solvents/Reagents

> ***CAUTION:*** *Sodium metal reacts violently with water. Ketyl radicals are dangerously incompatible with some solvents, in particular halogenated solvents. Proper references should be consulted prior to choosing an appropriate desiccant for a given solvent. Follow the guidelines in Purification of Laboratory Chemicals.[8-9]*

1 Preparation of a "Solvent Pot" – 5 g Ph_2CO per liter of solvent.[10]

1. See **Figure 1** for needed glassware. Under inert atmosphere, measure approximately 1 cm[5,6] Na metal (wire or chunk), cut it into smaller pieces, and place the pieces into a 500-mL round-bottom flask with a 24/40 standard taper neck joint.
2. Weigh approximately 1.25 g of Ph_2CO and place it into the 500 mL round bottom flask with the sodium.
3. Place a heavy duty stir-bar into the 500 mL round bottom flask, then seal the flask using a 180° 24/40 adapter that has been greased with a minimal amount of heavy duty high vacuum grease. Place a Keck clip over the joint to ensure a sturdy connection.
4. Remove the flask from the glovebox and evacuate on the Schlenk/high vacuum line as described in Section 1.2.6. Seal the 180° adapter and remove the flask from the line while it is under vacuum.
5. Attach a funnel to the top of the solvent pot (*do not use grease!*) and fill the funnel with the desired solvent. Using a long needle attached to a nitrogen line, bubble nitrogen through the solvent to partially degas it.
6. While maintaining nitrogen bubbling, slowly open the 180° adapter to introduce solvent into the solvent pot. When the solvent level in the funnel approaches the 180° adapter, close the adapter and remove the funnel. ***NOTE:*** *Solvent can be introduced in other ways, with varying degrees of air-free rigorousness. Commonly, users may choose to fill the pot while open to air and degas more later, or may choose to fill the pot with pre-dried solvent directly taken from a solvent purification system.*
7. Stir the solvent pot for several hours, during which time the solution will turn deep purple indicating the formation of the sodium benzophenone ketyl radical. In the case that the pot does not turn deep purple, degas the solution (Section 2.2) and stir again.

2 Freeze-pump-thawing to degas solvent

> ***CAUTION:*** *Liquid nitrogen is commonly used to "freeze" solvents for freeze-pump-thaw cycles. It is highly recommended not to use liquid nitrogen unless absolutely necessary and upon consultation with supervisors. Cooling a closed system to liquid nitrogen temperatures greatly increases the chance of condensing liquid oxygen if there is a leak in the system. Furthermore, the large temperature gradient increases the chance of glass breaking due to thermal shock. In almost all cases, -78 °C is sufficient to cool a system for degassing with minimal solvent loss.*

1. Start up the Schlenk or high vacuum line (Section 1.1) and attach the solvent pot to the manifold (Section 1.1.6).

2. Use dry ice/acetone cooling bath to cool down the contents of the pot to -78 °C. This may freeze the solvent depending on its freezing point. ***NOTE:*** *A common misconception of "freeze-pump-thaw" is that the solvent must be frozen to degas it. This is untrue; in fact it is easier to degas a cold liquid than a frozen solid because gas will get trapped in the solid matrix.*
3. If the freezing point of the solvent is above -78 °C and the solvent is frozen, open the solvent pot to vacuum by opening the 180° adapter in order to remove the gas headspace in the pot. Wait for the system to return to full vacuum, and then close the solvent pot to vacuum.
4. Allow the solvent pot to return to room temperature, and observe if any bubbles are forming in the solid/liquid mix. If bubbles are present, the solvent is not fully degassed and steps 2.2.2–2.2.4 should be repeated. Typically three "freeze-pump-thaw" cycles are sufficient for degassing.
5. If the freezing point of the solvent is below -78 °C and the solvent has a low vapor pressure at -78 °C, then instead of performing steps 2.2.3 and 2.2.4, the solvent pot can be opened to vacuum for approximately 5 min (or until bubbling stops) to degas the system. After 5 minutes, close the 180° adapter. A small amount of solvent may be lost to the vacuum pump trap.
6. If the freezing point of the solvent is below -78 °C and the solvent has a higher vapor pressure at -78 °C, two options are available: perform steps 2.2.3 and 2.2.4 and cool with liquid nitrogen instead of the -78 °C bath (less solvent loss, more inherent risk), or perform step 2.2.5 for shorter periods of time (more solvent loss, safer).

3. Vacuum transferring solvents/chemicals

1. Dry a 500-mL receiving Straus flask and a U-shaped vacuum transfer bridge in a drying oven (125 °C) for at least 1 h.
2. Attach the Straus flask and solvent pot to the U-shaped bridge and grease all joints lightly with grease. Attach the U-shaped bridge to the vacuum line. ***NOTE:*** *This heavy system should be supported by lab jacks and Keck clips to prevent it falling off of the line and breaking. Vacuum from the manifold may not be enough to hold it on the line.*
3. Evacuate the system as described in step 1.1.6.
4. Degas the solvent pot as described in section 2.2.
5. Close off the top U-bridge valve to close off the vacuum transfer setup from dynamic vacuum. The system should now be under static vacuum with the Straus valve open and the solvent pot 180° adapter closed.
6. Use a lab jack to raise a -78 °C acetone/dry ice to cool the receiving Straus flask. ***CAUTION:*** *Cooling a closed system with liquid nitrogen is dangerous, as there is a significant chance of condensing liquid oxygen if there is a leak. While it may be faster to vacuum transfer at liquid nitrogen temperatures, it is not worth the tradeoff in safety. This practice is banned in our laboratories. If a solvent can't be vacuum transferred at a -78 °C, it is suggested to use a better vacuum or consider thermal distillation.*
7. Turn on magnetic stirring to stir the solvent pot, then **slowly** open the stopcock of the 180° adapter on the solvent pot, so that the liquid in the solvent pot will not rapidly boil over into the U joint.
8. Shortly, solvent should begin condensing in the receiving flask. Wait until the solvent pot is almost dried or the desired amount of solvent has been collected. Close the stopcock on the receiving Straus flask and the valve on the solvent pot, which can be refilled or used again.
9. If the solvent pot freezes during transfer, close the Straus flask valve and allow the solvent pot to warm to room temperature before continuing.
10. If the vacuum transfer is extremely slow or slows down, re-degas the system by following the protocols in section 2.2.

4. Testing the collected solvent in a nitrogen glovebox

1 Preparation of the ketyl solution

1. Weigh out 0.137 g of Ph_2CO and more 0.028 g of Na metal in a 20 mL vial.
2. Add 20 mL of THF to the vial and a small stirbar, then cap the vial and stir overnight. This should generate a deep purple solution of 0.0337 M Na/Ph_2CO ketyl radical with a small excess of Na remaining at the bottom of the vial.

2 Titration of the collected solvent

1. Pipette approximate 4 mL of the solvent to be tested into a 4 mL vial.
2. Use a Pasteur pipette to carefully drop a *single* drop of purple Na/Ph_2CO THF solution in to the vial.
3. Gently stir the vial with a *clean* pipette tip and analyze the resulting color. Solvent that is 10 ppm H_2O or less should remain pale purple. (*Not blue)*
4. If the solvent will react with Ph_2CO radical (*e.g.* halogenated solvents such as dichloromethane), test the solvent with Karl Fischer titration or, in the case of deuterated solvents, [1,2,3]H NMR spectrometry.

Results

The picture was taken of the vacuum transfer in progress (**Figure 2**) and after the Na/Ph_2CO titration titration was performed (**Figure 3**).

Solvents collected via this method have been tested by ketyl titration. **Figure 3** shows the common possible outcomes of the ketyl test. The purple color in (a) indicates < 10 ppm H_2O in the solvent; while the blue and colorless solutions indicate a wetter solvent that needs further purification prior to use with water sensitive applications.

Figure 1. Glassware needed to make a ketyl pot and perform a vacuum transfer to a Straus flask. (a) Funnel for adding solvent to ketyl pot; (b) 500-mL round-bottom flask; (c) 180° adapter; (d) 500-mL Straus flask; (e) vacuum transfer bridge.

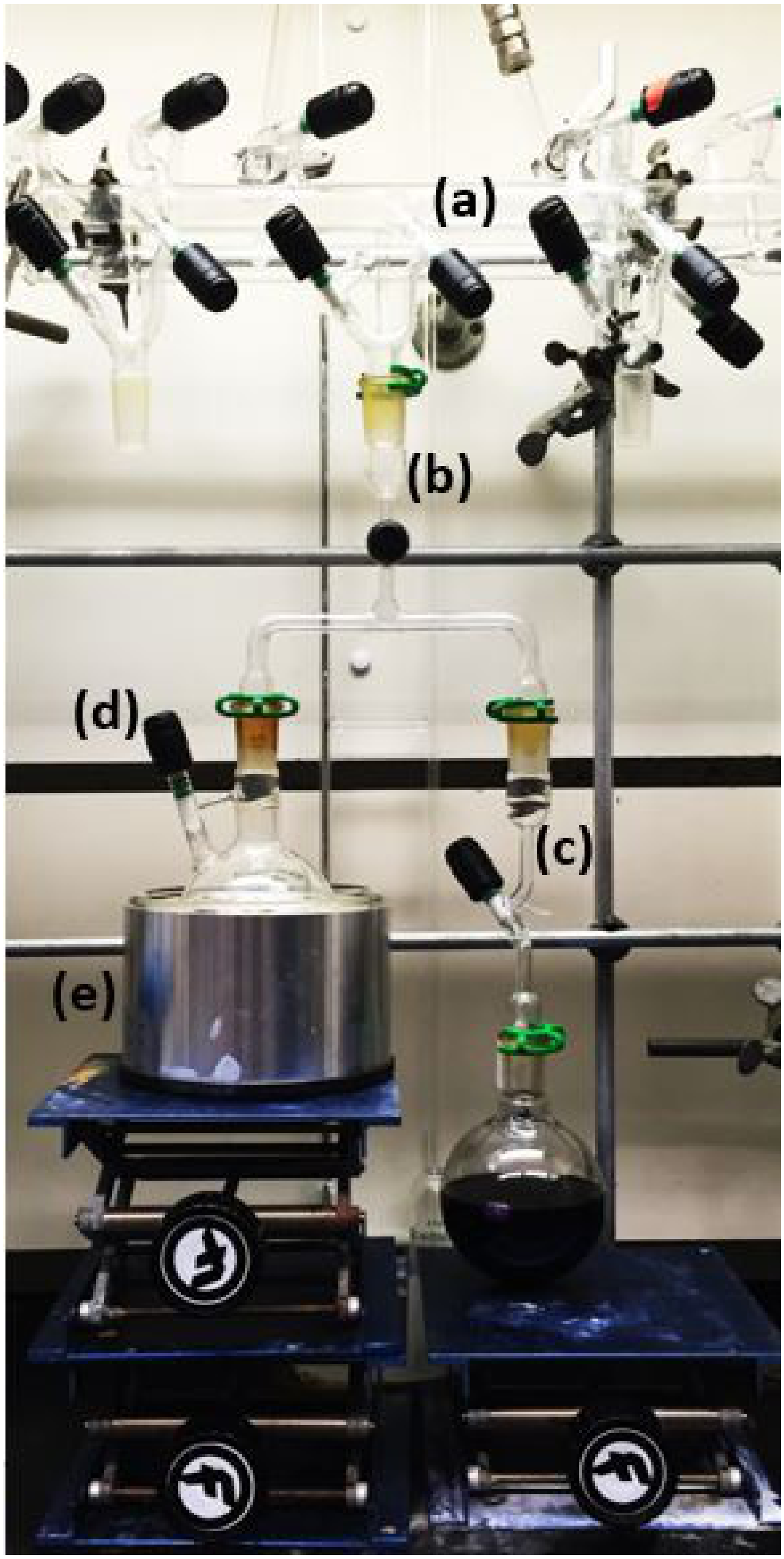

Figure 2. Setup of vacuum transfer: (a) the high vacuum line, (b) the transfer bridge, (c) the solvent pot with 180° adapter, (d) the receiving Straus flask, and (e) cooling bath.

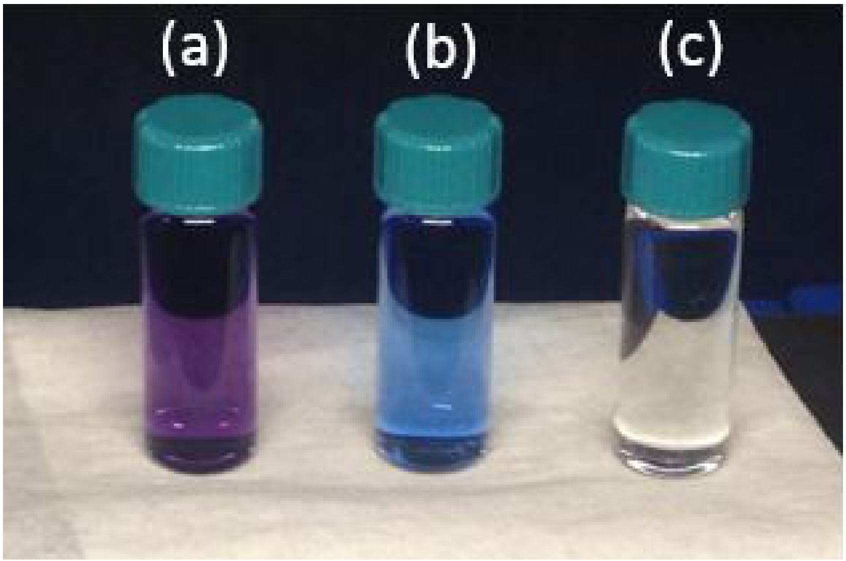

Figure 3. Collected solvent after titration of the ketyl solution. (a) purple indicates < 10 ppm H_2O, while (b) blue and (c) colorless require further purification.

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