

# Safe and Convenient Procedure for Solvent Purification

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Received May 22, 1995<sup>⊗</sup>

**Summary:** This contribution describes a general method for the purification of solvents for use with air and moisture sensitive reactions. This procedure provides a nonhazardous alternative to distillations and vacuum transfers and does not require undue supervision or cooling, yet allows for the rapid collection of large quantities of extremely pure solvents on demand. Solvents are rigorously degassed in 18 L reservoirs and passed through two sequential purification columns. Protic contaminants are removed with activated alumina, while a supported copper catalyst is used to remove trace oxygen from hydrocarbons. The purification system is interfaced with either a glove box or Schlenk manifold for the anhydrous/anaerobic collection of solvents. Solvents purified by this method and tested with stock solutions of sodium benzophenone ketyl or titanocene dichloride/zinc dust are free of oxygen at least to the ppm level. Furthermore, this system may be used for the in-line purification of gases and is easily scaled down to provide a convenient method for the purification of deuterated solvents or other reagents.

## Introduction

Current methods for the purification of organic solvents include distillation and vacuum transfer from dehydrating/deoxygenating reagents such as sodium benzophenone ketyl, LiAlH<sub>4</sub>, NaK alloy, and CaH<sub>2</sub>.<sup>1,2</sup> Because of the extreme reactivity of the reagents, these procedures pose very serious explosion and fire hazards; this is true not only during the purification procedure but also when the spent materials are quenched for disposal. Distillations pose an especially dangerous fire hazard because of the presence of hot flammable vapors and heat/spark sources. Vacuum transfers are somewhat safer than distillation procedures, but are not convenient for high-boiling solvents or for purifying large volumes of solvent (>1 L). The procedure described herein provides a nonhazardous alternative that does not require undue supervision or cooling, yet allows for the rapid collection of large quantities of extremely pure solvents on demand. Stock solutions of sodium benzophenone ketyl or titanocene dichloride/zinc dust may be used to qualitatively assess the O<sub>2</sub> and protic contaminants. Coulometric methods are also available to test for water at the ppm level.<sup>3</sup> Solvents purified by this method are free of oxygen at least to the ppm level.

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<sup>⊗</sup> Abstract published in *Advance ACS Abstracts*, January 15, 1996.

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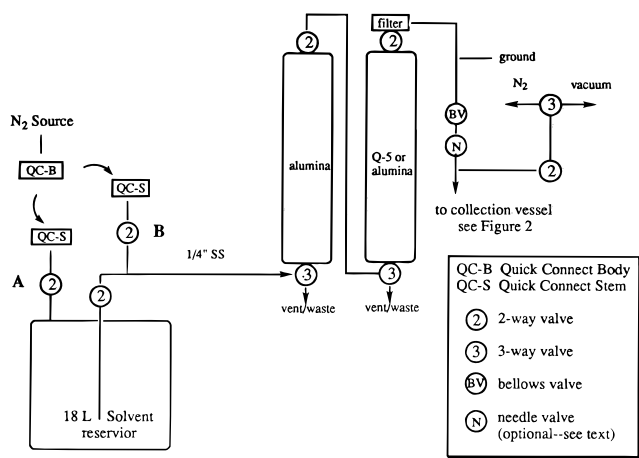
## Purification System

**General Outline.** Solvent reservoirs are sparged and pressurized with nitrogen (5–50 psig), and the solvent is passed through the two sequential purification columns. For all solvents, the first column is activated alumina, which removes polar impurities such as water, peroxides, and inhibitors (e.g., BHT). The second optional column is either another activated alumina column or a column of supported copper catalyst (Q-5), which removes trace O<sub>2</sub> to the ppm levels. If rigorously olefin-free hydrocarbon solvents are required, standard methods must be used to remove the olefins prior to use.<sup>1,2</sup> We have found that when HPLC grade reagents are used, upward of 400 L of solvent can be purified before regeneration of a set of columns is necessary. After column exit and before collection, the purified solvent is passed through an in-line filter (2–15 μm). Several collection systems have been developed. Two procedures include a Schlenk manifold for degassing and evacuating the void volume between the purification system and collection vessel. To avoid the construction of a vacuum system, the solvent may be plumbed directly into a dry box, dispensed directly into reaction flasks, or collected in receiving flasks (≥1 L) equipped with an oil bubble and septum port.

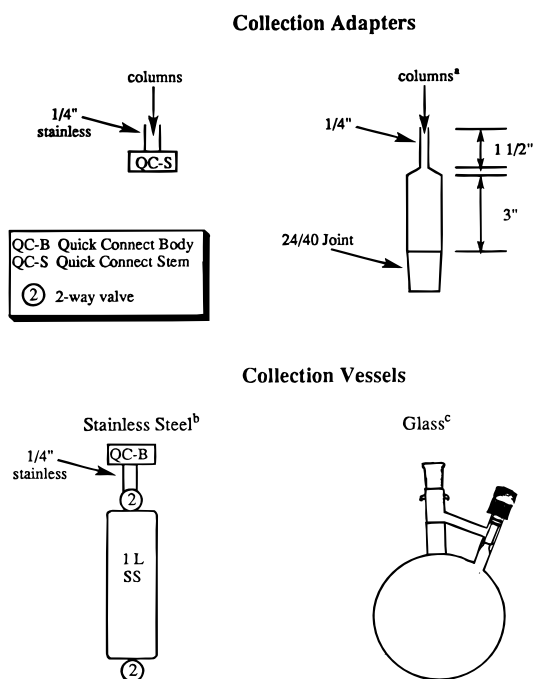
**Detailed Description.** Solvent reservoirs (18 L) may be rented prefilled with anhydrous solvent or purchased from Aldrich.<sup>4</sup> Reservoirs are filled with HPLC grade solvent on site. The accompanying columns (1–4 L capacity) are available from Whitey or may be constructed from stainless steel pipe, weld caps, and NPT nipples. LaRoche A-2 alumina (12 × 32) and Engelhard CU-0226S (formerly known as Q-5 reactant, a commercially available scavenger) are used as column packing. All tubing is 1/4 in. stainless steel with 1/4 in. stainless Swagelok fittings. Sample hardware is listed in the Experimental Procedures section. Quick connects and valves used with ethereal and halogenated solvents must have Kalrez or Teflon O-rings for long term operations.

A schematic diagram of the assembled system is shown in Figure 1. (**CAUTION!!** The setup in Figure 1 should be grounded to eliminate a spark source.) To maintain anaerobic and anhydrous conditions, the volume between the bellows valve and collection vessel is evacuated and back-filled with nitrogen several times. The collection vessel is under static vacuum before

(4) Solvents available in Kilo-Lab cylinders include acetonitrile, benzene, diethyl ether, dimethoxyethane, heptane, hexane, methylene chloride, pentane, tetrahydrofuran, and toluene. Empty cylinders are also available. Kilo-Lab cylinders are rated for 240 psi and have fusible plugs for overpressure situations.

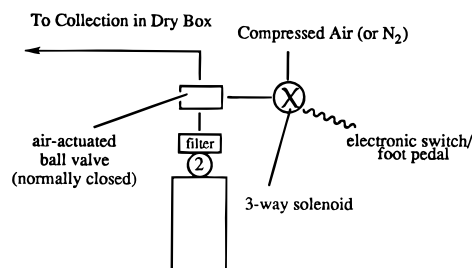


**Figure 1.** Solvent purification system. Degassing: Pressurize at B, vent to hood from A. Purging tubing with N<sub>2</sub>: Pressurize at B, vent to the three-way valve. Purification/collection: Pressurize at A.

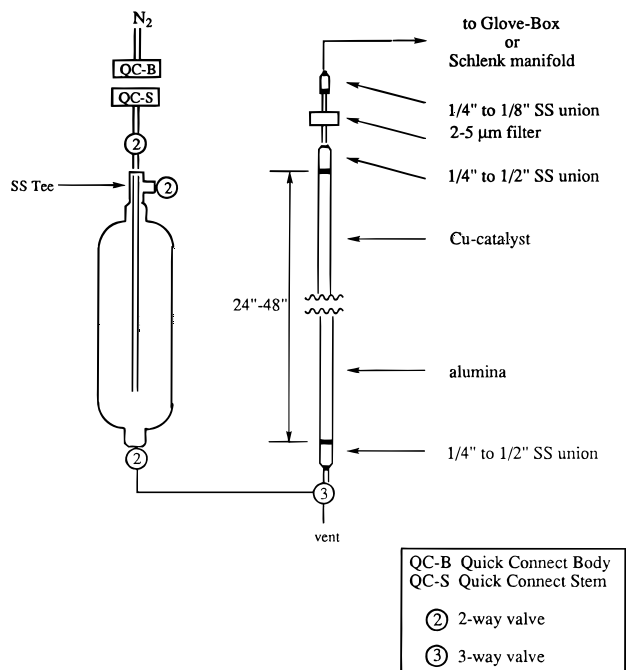


**Figure 2.** Collection adapters/vessels for use with Schlenk manifold. (a) A 24/40 adapter may be constructed of Pyrex or stainless steel and attached to the collection system with 1/4 in. Swagelok fittings. Teflon ferrules are used with glass adapters. (b) To aid in rapid draining of solvent in the glove box, a quick connect stem is attached to the top of the stainless steel vessel. (c) 1 L Straus flasks (Kontes 213210-1000) are ideal for solvent collection and storage.

opening the bellows valve. (In applications where the pressure exceeds 10 psig, a bellows valve and needle valve should be used in series.) Two types of collection vessels that may be used are shown in Figure 2. Stainless steel cylinders are convenient when there is a dry box available for draining and sealing the vessels. Glass collection vessels are convenient for use with a Schlenk line. (**CAUTION!!** Glass should not be used when the pressure exceeds 5 psig.) Installation of the vacuum manifold can be avoided by directly plumbing the solvent into a dry box. To maintain an air-tight seal into the dry box, the stainless steel tubing is fed through a drilled-out 1/4 in. Ultra-Torr fitting. To prevent the unattended accidental delivery of solvent in the box, an



**Figure 3.** Air-actuated control of solvent flow. (a) To open air-actuated ball valve: Depression of the foot pedal energizes the solenoid, which pressurizes and opens the air-actuated ball valve. To close ball valve: Disengagement of the foot pedal deenergizes/vents the solenoid, and the ball valve closes via a spring return.



**Figure 4.** Small scale purification system.

air-actuated ball valve with foot pedal control is installed between the columns and glove box (Figure 3).

A scaled-down version of this system can be used to purify small volumes of solvents, deuterated solvents, or frequently used reagents. The system can be built analogously to the preceding one by utilizing 1/8 in. tubing and a single smaller column (Figure 4). The reagent reservoir is a 1 L stainless steel sample cylinder. The dip-tube used for degassing is constructed from 1/4 in. stainless steel tubing and a drilled-through 1/4 in. Swagelok 1/4 in. male NPT adapter. Stainless steel tubing (1/2 in.) is used as the purification column, which is packed with alumina and the supported Cu catalyst.

## Experimental Procedures

**Column Activation.** The columns are packed with A-2 alumina or Q-5 reactant (supported copper redox catalyst) with plugs of glass wool at each end. Columns are heated<sup>5</sup> with a one- or two-zone heating mantle,<sup>6</sup> and the temperature is monitored with thermocouples. Alumina columns are activated at 375 °C for 6–8 h with a constant nitrogen purge

(5) Care should be taken during the activation step to prevent water vapor in the vent gas from condensing and running back into the column.

(approximately 2–25 L/min). The Q-5-packed columns are heated to 200 °C with a nitrogen purge (ca. 2–3 h), followed by activation with 5% hydrogen in nitrogen (ca. 25 L/min for 1–2 h); the temperature should not exceed 250 °C. Columns are cooled under nitrogen flow. The two-way valves recommended herein are not rated for the high temperatures of the exit gas and should be attached during nitrogen flow when the columns are cooled.<sup>7</sup> The columns are then isolated from the atmosphere and installed in the purification system.

**Reservoir Installation.** The entire system is purged with nitrogen through valve B prior to the first use of the columns (Figure 1). The two three-way valves at the bottom of the columns allow this to be done stepwise, so that air and moisture are not allowed to enter the activated columns. The solvent is degassed for 20 min with nitrogen through B while outlet A is vented to a hood. The nitrogen feed is then switched to A, and the tubing between the reservoir and columns is purged with a small amount of solvent before the solvent is introduced to the columns. The tubing between the reservoir and column is purged each time the solvent reservoir is changed or refilled. When the solvent is introduced into a dry, freshly activated alumina column, the column can become warm due to the heat of absorption.

**Solvent Collection.** When the purification system is in line with a glove box, solvent is collected by opening a two-way valve in the glove box while simultaneously opening the air-actuated ball valve. When a Schlenk manifold is used, the system is kept under dynamic vacuum (Figure 1: 2 open, 3 to vacuum) when not in use, and the collection vessel is attached under nitrogen purge (2 open, 3 to N<sub>2</sub>). Prior to collection, the vessel and void volume are evacuated/back-filled three times, and the collection vessel is left under static vacuum (2 closed). To collect solvent, BV and N are opened. Although stainless steel vessels may be completely filled, glass vessels should only be filled to three-fourths capacity to avoid overpressurization. When collection is finished, the vessel is back-filled with nitrogen (2 open, 3 to N<sub>2</sub>), and the collection vessel

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(6) Heating tape may also be used. For large columns at least two heating zones are needed with separate thermocouples and controls. We found it convenient to wrap the thermocouple between the column and heating mantle.

(7) Valves rated for higher temperatures are available at approximately 3 times the cost of the valves suggested (high-temperature two-way valve for use with hydrocarbons, Whitey 83KS4, with halogenated and ethereal solvents, Nupro SS-4BG). If these valves are used, they may be installed before column activation, and the columns may be cooled under dynamic nitrogen pressure with the exit valves closed.

is sealed and removed from the adapter under inert gas purge. The adapter is evacuated and the residual solvent is collected in the N<sub>2</sub> trap of the Schlenk manifold. The solvent may then be tested for trace protic contaminants and O<sub>2</sub>.

One or two drops of benzophenone ketyl in THF (without residual Na) are added to a small portion of solvent (3–5 mL) in the glove box. The persistence of a dark purple color indicates good solvent quality. If a glove box is not available, the solvent may be tested in a similar manner by using Ar-flushed syringes or cannulas. Solvents should be tested once the system is first constructed and each time the solvent reservoir is refilled. Solvents purified by these methods have been used in this laboratory in the synthesis of a variety of air and moisture sensitive compounds with no observed decrease in the purity or yield of the products.

**Column Regeneration.** When column performance deteriorates, the columns are removed from the purification system, blown dry of solvent, and disassembled, and the spent packing is disposed.<sup>8</sup> Reactivation is not recommended since it is difficult to remove all solvent residue, and upon heating they may react to form higher molecular weight products. Alumina columns that have been used to purify ethers should be washed with aqueous ferrous sulfate to destroy peroxides before disposal.<sup>1</sup> The packing material of columns used to purify gases can be reused by regeneration in the same manner in which they were initially activated. However, flammable gases need to be purged from the columns first.

**Sample hardware:** 18 L cylinders, outlet valves, and dip tubes, Aldrich Z14,888-1, Z14,886-5, and Z15,164-5, respectively; heating mantles from Glas-Col or LabGlas; 1 L cylinders, Whitey 304L-HDF4-1L-3.785L; three-way ball valves, Whitey SS-43XS4; two-way ball valves, Whitey SS 43S4; bellows valve, Nupro SS-4BG; in-line filters, Nupro SS-4FW-15; needle valve, Nupro SS-4H; quick connects (Swagelok), SS-QC4-D-400 and SS-QC4-B-400; QC series with Kalrez O-rings or QT series quick connects for ethereal and halogenated solvents; air-actuated valve, SS-42S4-131CS; three-way solenoid, ASCO 8314; foot pedal, HITREADLITE HT-52-S; nitrogen inlet flare fitting adapter for Kilo-Lab cylinders, SS-400-A-4ANF. Inexpensive 18 L cylinders equipped with all necessary valves are available from McMaster-Carr (refrigerant recovery cylinder No. 17305K74).

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(8) Any disposal practice must be in compliance with all federal, state/provincial, and local laws and regulations.