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Organic Laboratory Assessment Experiment

Student Name:_____

TA Name: _____

Date:_____

This Extra Credit *Organic Laboratory Assessment Experiment* must be completed in-class and this booklet can not be removed from the laboratory. **You have 2.5 hours to complete this work. At the end of the 2.5 hours you must hand in this booklet, your lab notebooks and then sign in your drawer. If you finish early you must stay in lab and quietly wait till time is up to sign-in your drawer.**

You can use the information in this handout and your previous write-ups in your laboratory notebooks to help you complete this assessment. You will be provided all other equipment/glassware and reagents. Write in pen only and in this booklet only. **Talking is not allowed in this lab. You will lose all extra credit points if you talk.**

Grading scheme:
1. If you attend the lab and write your name on the booklet and return it to your TA without having performed any of the work in the assessment you will receive a maximum of 2 points extra credit.
2. If you attempt the lab assessment experiment and corresponding write-up you will receive a maximum of 18 more extra credit points depending on how well you performed. *Note: the maximum possible total for this assessment is 20 extra credit points.*

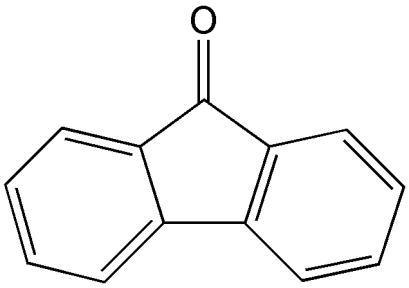
TA INITIAL and the time that the booklet is handed in:	

Sample 1

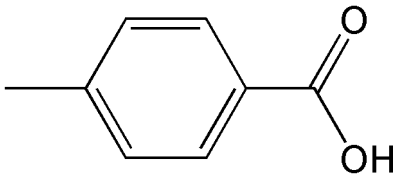
Organic Laboratory Assessment Experiment
Booklet Index

The Problem

You are issued with a sample mixture containing 50 mg *p*-toluic acid and 50 mg 9-fluorenone (structures are shown below). Your task is to design and carry out the separation and isolation of these two compounds. Describe the method you develop to solve this problem in a flowchart. Carry out the method and record your observations, procedures and results in the same way that you did this semester in your lab notebook. In your results you should report the melting point and calculate percentage recovery for each compound. Lastly, write a discussion and conclusions section describing the chemistry concepts that you employed to design and carry out your method (of separation and isolation for the two compounds), you may include chemical equations in this section. Submit the two isolated compounds in labeled vials for inspection to your TA.



9-fluorenone



p-toluic acid

Physical Properties of Reagents					
Compound	MW	Amount	m.p. (°C)	b.p. (°C)	*density* (g/cm^3)
9-fluorenone	180.19	50 mg	83.5		
p-toluic acid	136.15	50 mg	180		
diethyl ether	74.12	~4 mL-6 mL		35	0.7184
2 M HCl					
6 M HCl					
3 M NaOH					
6 M NaOH					
Na_2SO_4		~300 mg per drying procedure			

Experimental Procedure <u>Start</u>

Your starting point: Add 4 mL of diethyl ether to the vial containing the mixture of 50 mg *p*-toluic acid and 50 mg 9-fluorenone. Cap the vial and vortex the mixture to dissolve the solids.

The rest of the procedure is up to you as stated in **The Problem** section. You are provided with two acid solutions of different strengths and two base solutions of different strengths. In addition, you will need litmus paper to verify the approximate pH of your solution at each step of your protocol. It is also a recommendation that you do not add more than 2 mL at a time of any reagent to your vial. Also, note the density of water is 1.0 g/cm^3.

Flowchart

Flowchart con't

Procedures	Observations

Procedures	Observations

Procedures	Observations

Results

Discussion and Conclusions

Discussion and Conclusions con't

A copy of the pre-assigned reading from your MAYO lab textbook (pp 72-83, 5th Edn: liquid-liquid extraction, separation of acids and bases, salting out, drying of the wet organic layer) for this *Assessment Experiment* is given below as reference materiel.

Extraction

Liquid–Liquid Extraction. The more common type of extraction, liquid–liquid extraction, is used extensively. It is a very powerful method for separating and isolating materials at the microscale level. It is operationally not a simple process, so attention to detail is critical.

There are several important criteria to consider when choosing a solvent for the extraction and isolation of a component from a solution:

- The chosen extraction solvent must be immiscible with the solution solvent.
- The chosen extraction solvent must be favored by the distribution coefficient for the component being extracted.
- The chosen extraction solvent should be readily separated from the desired component after extraction. This usually means that it should have a low boiling point.
- The chosen organic extraction solvent must not react chemically with any component in the aqueous mixture being extracted.

NOTE. The aqueous phase may be modified, as in acid–base extractions, but the organic solvent does not react with the components in the aqueous mixture. See Experiments [4B, 4C], pp. 146–150.

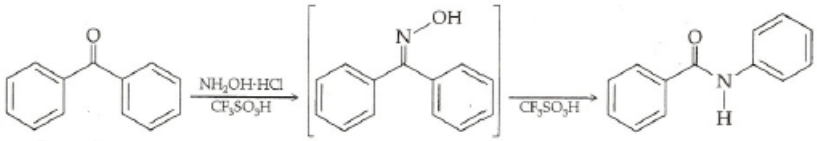
Microscale Extraction. A capped conical vial or a stoppered centrifuge tube is the best container for most microscale extractions, but a small test tube may be used. Note that a conical vial and a centrifuge tube have the same inner shape. This shape has the advantage that as the lower phase (layer) is withdrawn by pipet, the interface (boundary) between the two liquid phases becomes narrower and narrower, and thus easier to see, at the bottom of a conical container. This is not the case for a test tube. The centrifuge tube has the added advantage that if a solid precipitate must be separated or an emulsion broken up, it can easily be done using a centrifuge.

A good rule of thumb is that the container to be used for the extraction should be *at least three times the volume of liquid* you wish to extract.

Regardless of the container used, in any liquid–liquid extraction, the two immiscible solvents must be completely mixed to maximize the surface area of the interface between the two and allow partitioning of the solute. This can be accomplished by shaking (carefully to avoid leakage around the cap), using a Vortex mixer, or by adding a magnetic spin vane and then stirring with a magnetic stirrer.

Another important rule in the extraction process is that you should *never discard any layer until the isolation is complete.*

Let us consider a practical example. Benzanilide can be prepared by the in situ rearrangement of benzophenone oxime in acid solution:



Benzophenone — Benzophenone oxime — Benzanilide

The benzanilide is separated from the reaction mixture by extraction with three 1.0-mL portions of methylene chloride solvent.

NOTE. Saying, for example, "extracted with three 1.0-mL portions of methylene chloride" means that three extractions are performed (one after the other, each using 1.0 mL of methylene chloride) and the three methylene chloride extracts are combined.

A microscale extraction process consists of two parts: (1) mixing the two immiscible solutions, and (2) separating the two layers after the mixing process.

1. Mixing. In the experimental procedure for the isolation of the benzanilide product, methylene chloride (1.0 mL) is added to the aqueous reaction mixture contained in a 5.0-mL conical vial (or centrifuge tube). The extraction procedure is outlined in the following steps:

Step 1. Cap the vial.

Step 2. Shake the vial gently to thoroughly mix the two phases (careful!)

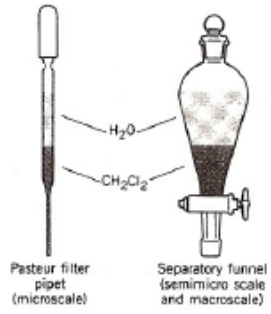


Figure 5.14 Extraction devices.

NOTE. The mixing may be carried out using a Vortex mixer or magnetic stirrer—see previous discussion.

Step 3. Carefully vent the vial by loosening the cap to release any pressure that may have developed.

Step 4. Allow the vial to stand on a level surface to permit the two phases to separate. A sharp phase interface should appear.

NOTE. For safety reasons it is advisable to place the vial in a small beaker to prevent tipping. If a volatile solvent such as ether is used, it is advisable to place the vial or centrifuge tube in a beaker of ice water to prevent loss of solvent during the transfers.

2. Separation. At the microscale level, the two phases are separated with a Pasteur filter pipet (a simple Pasteur pipet can be used in some situations), which acts as a miniature separatory funnel. The separation of the phases is shown in Figure 5.14.

A major difference between macro and micro techniques is that when microscale volumes are used, as just discussed, the mixing and separation are done in two parts. When macroscale volumes are used in a separatory funnel, mixing and separation are both done in the funnel in one step. The separatory funnel is an effective device for extractions with larger volumes, but it is not practical for microscale extractions because of the large surface areas involved.

Benzanilide is more soluble in methylene chloride than in water. Multiple extractions are performed to ensure complete removal of the benzanilide from the aqueous phase. The methylene chloride solution is the lower layer because it is more dense than water. The following list outlines the general method for an organic solvent more dense than water.

NOTE. (a) One technique is to hold the pipet across the palm of the hand and squeeze the bulb with the thumb and index finger. (b) Remember to have an empty tared vial available in which to place the separated phase. (c) A pipet pump (Figure 5.15) may be used to replace the bulb. One advantage with using a pipet pump is the dispensing of liquids in a more controlled fashion.

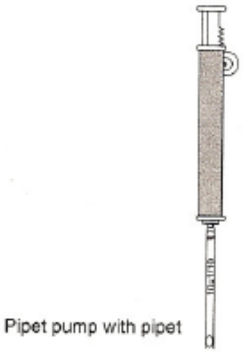


Figure 5.15 Pipet pump with pipet. (Reprinted with permission of John Wiley and Sons, Inc. from Szafran, Z.; Pike, R. M.; Foster, J. C. Microscale *General Chemistry Laboratory*, 2nd ed., p. 36. 2003.)

The recommended procedures are shown in Figures 5.16 and 5.17.

Step 1. Squeeze the pipet bulb to force air from the pipet.

Step 2. Insert the pipet into the vial until it is close to the bottom. Be sure to hold the pipet vertically.

Step 3. Carefully allow the bulb to expand, drawing only the lower methylene chloride layer into the pipet. This should be done in a smooth, steady manner so as not to disturb the interface between the layers. With practice, you can judge the amount that the bulb must be squeezed to just separate the layers. Keep the pipet vertical. *Do not tip the pipet back and allow liquid to enter the bulb! Do not suck liquid into the bulb!*

Step 4. (Step 4 is not shown in the figure.) Holding the pipet vertical, place it over and into the neck of an empty vial (as shown in Fig. 5.16, Step 2), and gently squeeze the bulb to transfer the methylene chloride solution into the vial. A second extraction can now be performed after adding

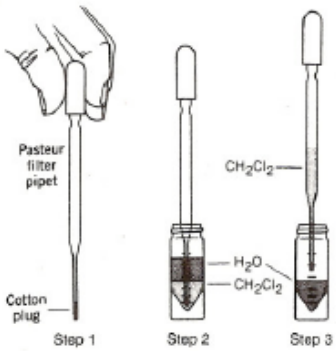


Figure 5.16 Pasteur filter pipet separation of two immiscible liquid phases; the more dense layer contains the product.

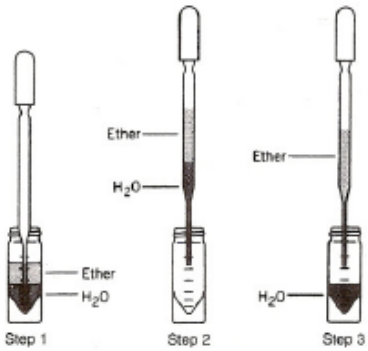


Figure 5.17 Pasteur filter pipet separation of two immiscible liquid phases; the less dense layer contains the product.

another portion of methylene chloride to the original vial. The procedure is repeated. Multiple extractions can be performed in this manner. Each methylene chloride extract is transferred to the same vial—that is, the extracts are combined. The reaction product has now been transferred from the aqueous layer (aqueous phase) to the methylene chloride layer (organic phase), and the phases have been separated.

In a diethyl ether–water extraction, the ether layer is less dense and thus is the upper layer (phase). An organic reaction product generally dissolves in the ether layer and is thus separated from water-soluble byproducts and other impurities. The procedure followed to separate the water–ether phases is identical to that described above for methylene chloride–water systems, except that here the top layer (organic layer) is transferred to the new container. The following list outlines the general method for an organic solvent less dense than water (refer to Fig. 5.17).

Step 1. Squeeze the pipet bulb to force air from the pipet and insert the pipet into the vial until it is close to the bottom. Then, draw **both** phases slowly into the pipet. Keep the pipet vertical. *Do not tip the pipet back and allow liquid to enter the bulb! Do not suck liquid into the bulb!* Try not to allow air to be sucked into the pipet, as this tends to mix the phases in the pipet. If mixing does occur, allow time for the interface to re-form.

Step 2. Return the aqueous layer (bottom layer) to the **original** container by gently squeezing the pipet bulb.

Step 3. Transfer the separated ether layer (top layer) to a new tared vial.

Separatory Funnel—Semimicroscale and Macroscale Extractions. A separatory funnel (Fig. 5.14) is effective for extractions carried out at the semimicroscale and macroscale levels. The mixing and separation are done in the funnel itself in one step. Many of you may be familiar with this device from the general chemistry laboratory. The same precautions as outlined above for microscale extraction should be observed here.

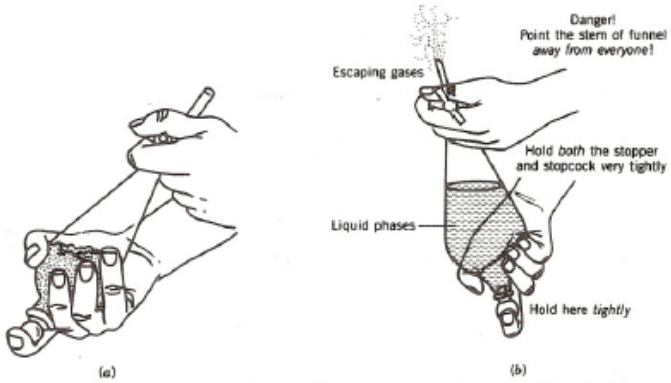


Figure 5.18 (a) Correct position for holding a separatory funnel while shaking. (b) Correct method for venting a separatory funnel.

NOTE. The funnel size should be such that the total volume of solution is less than half the total volume of the funnel. If the funnel has a ground-glass stopcock and/or stopper, the ground-glass surfaces must be lightly greased to prevent sticking, leaking, or freezing. If Teflon stoppers and stopcocks are used, grease is not necessary because these are self-lubricating.

Step 1. Close the stopcock of the separatory funnel.

Step 2. Add the solution to be extracted, after first making sure that the *stopcock is closed*. The funnel should be supported in an iron ring attached to a ring stand or rack on the lab bench.

Step 3. Add the proper amount of extraction solvent (about one-third of the volume of the solution to be extracted is a good rule of thumb) and place the stopper on the funnel.

Step 4. Remove the funnel from the ring stand, keeping the stopper in place with the index finger of one hand, and holding the funnel in the other hand with your fingers positioned so they can operate the stopcock (Fig. 5.18*a*).

Step 5. Carefully invert the funnel (make sure its stem is pointing up, and not pointing at you or anyone else). Slowly open the stopcock to release any built-up pressure (Fig. 5.18*b*). Close the stopcock and then shake the funnel for several seconds. Position the funnel for venting (make sure the stem is pointing up, and not pointing at you or anyone else). Open the stopcock to release built-up pressure. Repeat this process 2–4 times. Then, close the stopcock and return the funnel upright to the iron ring.

Step 6. Allow the layers to separate and then remove the stopper.

Step 7. Place a suitable clean container just below the tip of the funnel. Gradually open the stopcock and drain the bottom layer into the clean container.

Step 8. Remove the upper layer by pouring it from the top of the funnel. This way it will not become contaminated with traces of the lower layer found in the stem of the funnel.

When aqueous solutions are extracted with a *less dense solvent*, such as ether, the bottom, aqueous layer can be drained *into its original container*. Once the top (organic) layer is removed from the funnel, the aqueous layer can then be returned for further extraction. Losses can be minimized by rinsing the original container with a small portion of the extraction solvent, which is then added to the funnel. When the extraction solvent is denser than the aqueous phase (e.g., methylene chloride), the aqueous phase is the top layer, and therefore is kept in the funnel for subsequent extractions.

Continuous Liquid–Liquid Extraction. Continuous extraction of liquid–liquid systems is also possible and particularly valuable when the component to be separated is only slightly soluble in the extraction solvent. The advantage of using continuous extraction is that it can be carried out with a limited amount of solvent. In batchwise extractions a prohibitive number of individual extractions might have to be performed to accomplish the same overall extraction. Specialized apparatus, however, is required for continuous liquid–liquid extraction.

Two types of continuous extraction apparatus are often used to isolate various species from aqueous solutions using less dense and more dense immiscible solvents (e.g., diethyl ether and methylene chloride) (Fig. 5.19).

The extraction is carried out by allowing the condensate of the extraction solvent, as it forms on the condenser on continuous distillation, to drop through an inner tube (see Fig. 5.19*a* in the case of the less dense solvent) and to percolate up through the solution containing the material to be extracted. This inner tube usually has a sintered glass plug on its end, which generates smaller droplets of the solvent and thus increases the efficiency of the procedure. The extraction solution is then returned to the original distilling flask. Eventually, in this manner, the desired material, extracted in small increments, is collected in the boiling flask and can then be isolated by concentrating the collected solution. This method works on the premise that fresh portions of the less-dense phase are continuously introduced into the system, and it is often used in those instances where the organic material to be isolated has an appreciable solubility in water. In the case of a more dense extraction solvent (see Fig. 5.19*b*) the system functions in much the same fashion, but in this case the inner tube is removed and the condensed vapors percolate directly through the lighter phase (the phase to be extracted) to form the lower layer. This layer can cycle back to the distillation flask through a small-bore tubing connection from the bottom of the receiver flask to the distillation flask. Continuous liquid–liquid extraction is useful for removing extractable components from those having partition ratios that approach zero. Note that this method requires a very long period of time.

Separation of Acids and Bases. The separation of organic acids and bases is another important and extensive use of the extraction method. The distribution coefficients of organic acids and bases are affected by pH when one of the solvents is water. An organic acid that is insoluble in neutral water (pH 7) becomes soluble when the water is made basic with an aqueous sodium hydroxide solution. The acid and the sodium hydroxide quickly react to form a sodium carboxylate salt, $RCO_2^-Na^+$. The salt is, of course, ionic and therefore it readily dissolves in the water. Thus, the acid–base reaction reverses the solubility characteristics of a water-insoluble organic acid.

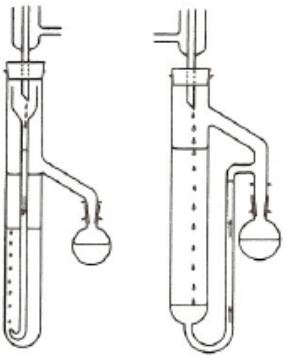
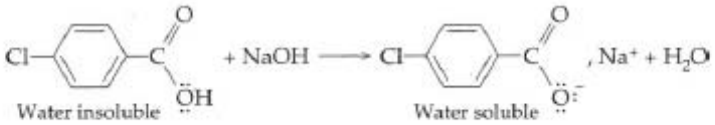
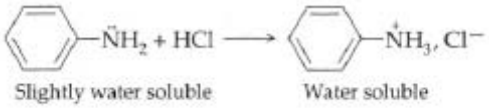
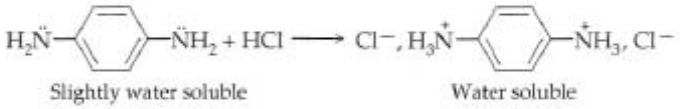


Figure 5.19 Early designs for single-stage extractors: (a) Kutscher–Steudel extractor; (b) Wehrli extractor.

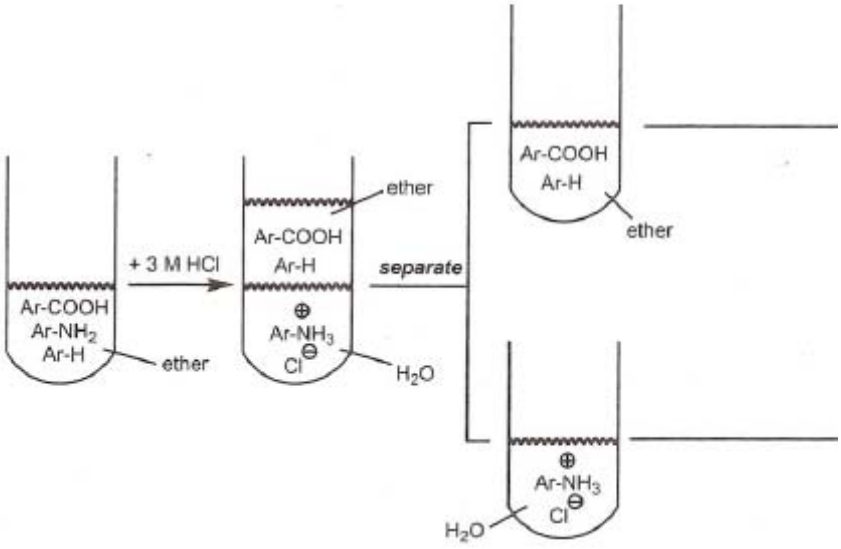


The water phase may then be extracted with an immiscible organic solvent to remove any impurities, leaving the acid salt in the water phase. Neutralizing the water layer with hydrochloric acid (to pH ≤ 7) reprotonates the carboxylate salt to reform the carboxylic acid, and causes the purified water-insoluble organic acid to precipitate (if it's a solid). In a similar fashion, water-insoluble organic bases, such as amines (RNH_2), can be rendered water soluble by treatment with dilute hydrochloric acid to form water-soluble hydrochloride salts (e.g., Experiment [23]).





Extraction procedures can be used to separate mixtures of solids. For example, the flow chart below diagrams a sequence used to separate a mixture made up of an aromatic carboxylic acid ($ArCO_2H$), an aromatic base ($ArNH_2$), and a neutral aromatic compound (ArH). Aromatic compounds are discussed here simply because they are likely to be crystalline solids.



In this example, we assume that the organic acid and base are solids. If either or both were liquids, an additional extraction of the final acidic aqueous or alkaline solution with ether, followed by drying and concentration, would be required to isolate the acidic or basic component.

Salting Out. Most extractions in the organic laboratory involve water and an organic solvent. Many organic compounds have partial solubility in both solvents. To extract them from water, the partition coefficient (between the organic solvent and water) can be shifted in favor of the organic layer by saturating the water layer with an inorganic salt, such as sodium chloride. Water molecules prefer to solvate the polar ions (in this case sodium and chloride ions), and thus free the neutral organic molecules to migrate into the organic phase. Another way to think of this is to realize that the ionic solution is more polar than pure water, so the less polar organic molecules are less soluble than in pure water. Forcing an organic material out of a water solution by adding an inorganic salt is called *salting out*.

Salting out can also be effectively used for the *preliminary drying* of the wet organic layer that results from an extraction process. (Diethyl ether, in particular, can dissolve a fair amount of water.) Washing this organic layer with a saturated salt solution removes most of the dissolved water into the aqueous phase. This makes further drying of the organic phase with solid drying agents easier and much more effective (see Drying Agents below).

Solid–Liquid Extraction

The simplest form of solid–liquid extraction involves treating a solid with a solvent and then decanting or filtering the solvent extract away from the solid. An example of this technique (see Experiment [11A]) is extracting usnic acid from

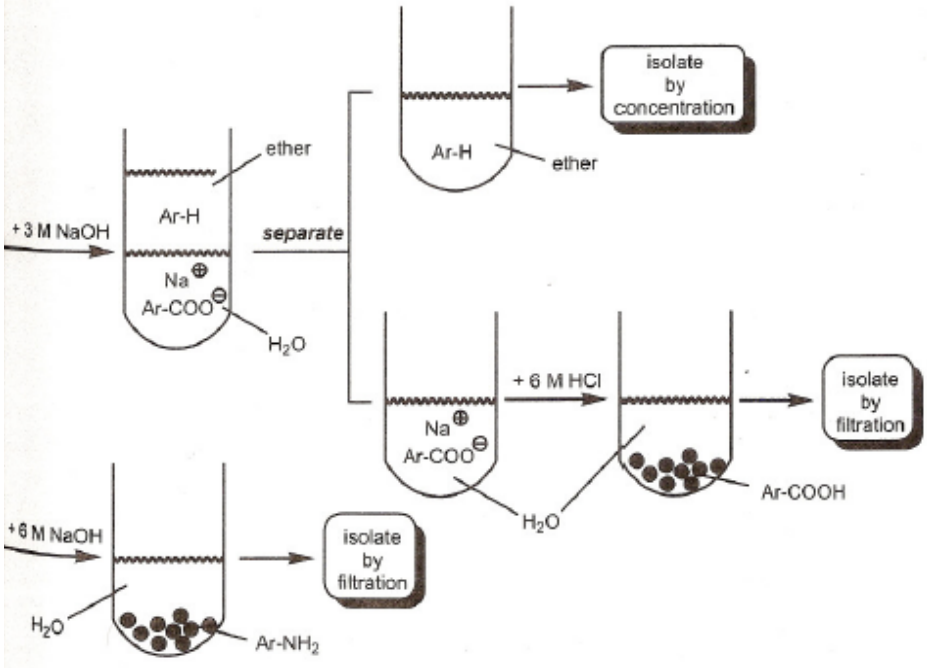


Figure 5.20 A solid–liquid continuous extraction apparatus.

its native lichen with acetone. This type of extraction is most useful when only one main component of the solid phase has appreciable solubility in the solvent. The extraction of caffeine from tea (see Experiment [11B]) is another example of this method; it is accomplished by heating the tea in an aqueous solution of sodium carbonate. This approach works well because the water swells the tea leaves and allows the caffeine to be extracted more readily.

Microscale extractions of trimyristin from nutmeg, and cholesterol from gallstones, have been described.[5] Diethyl ether was used as the solvent in both cases. A packed Pasteur pipet column was used for filtering, drying (nutmeg experiment), and decolorizing (gallstone experiment).

Herrera and Almy described a simple continuous extraction apparatus (Fig. 5.20).[6] The apparatus is constructed from a 50-mL beaker and a paper cone prepared from a 9-cm disk of filter paper (nonfluted), which rests on the lip of the beaker. A small notch is cut in the cone to allow solvent vapor to pass around it. The extraction solvent is placed in the beaker; the solid material to be extracted is placed in the cone. A watch glass containing 2–3 g of ice is placed on top of the assembly to act as the condenser and to hold the paper cone in place. As the ice melts, the water is removed and replaced with fresh ice. The beaker is heated on a hot plate in the hood (some solvent evaporates during the extraction process and may need to be replaced). The concentrated solution collected in the beaker is then cooled and the solid product is isolated by filtration or is recrystallized. This system needs to be attended at all times, but works reasonably well for brief extractions.

Various apparatus have been developed for use when longer extraction periods are required. They all use what is called a *countercurrent process*. The best-known apparatus is the Soxhlet extractor, first described in 1879 (Fig. 5.21).[7] The solid sample is placed in a porous thimble. The extraction-solvent vapor, generated by refluxing the extraction solvent contained in the distilling pot, passes up through the vertical side tube into the condenser. The liquid condensate then drips onto the solid, which is extracted. The extraction solution passes through the pores of the thimble, eventually filling the center section of the Soxhlet. The siphon tube also fills with this extraction solution and when the liquid level reaches the top of the tube, siphoning action returns the thimbleful of extract to the distillation pot. The cycle is automatically repeated many times, concentrating the extract in the distillation pot. The advantage of this arrangement is that the process may be continued automatically and unattended for as long as necessary. The solvent is then removed from the extraction solution collected in the pot, providing the extracted compound(s). Soxhlet extractors are available from many supply houses and can be purchased in various sizes. Of particular interest to us is the microscale variety, which is effective for small amounts of material and is now commercially available.[8]

Drying Agents

Organic extracts separated from aqueous phases usually contain traces of water. Even washing with saturated salt solution (see Salting Out above) cannot

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[5]Vestling, M. M. *J. Chem. Educ.* **1990,** *67,* 274.
[6]Herrera, A.; Almy, J. *J. Chem. Educ.* **1998,** *75,* 83.
[7]Soxhlet, F. *Dinglers Polytech. J.* **1879,** *232,* 461.
[8]Microscale Soxhlet equipment is available from ACE Glass, Inc., 1430 Northwest Boulevard, Vineland, NJ 08360.

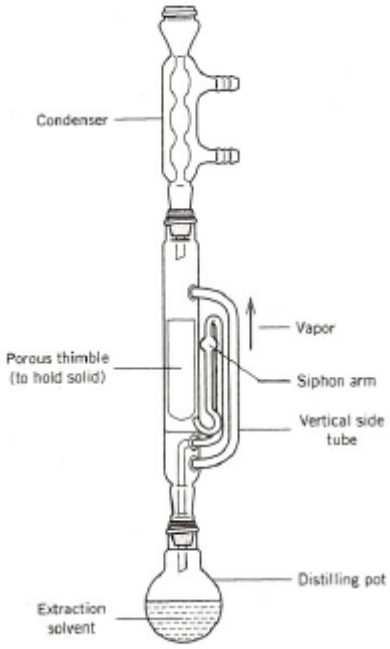


Figure 5.21 Soxhlet extractor.

remove all of the water. Organic extracts must therefore be dried to remove any residual water before the solvent is evaporated or further purification is performed. Organic extracts can be conveniently dried with an anhydrous inorganic salt, such as magnesium sulfate, sodium sulfate, or calcium sulfate. These salts readily absorb water and form insoluble hydrates, thus removing the water from the wet organic phase. The hydrated solid can then be removed from the dried solution by filtration or by decanting (pouring) the solution away from the solid. Although many drying agents are known, not every drying agent can be used in every case. The ideal drying agent should dry the solution quickly, have a high capacity for water, cost little, and not react with the material being dried.[9]

Table 5.5 summarizes the properties of some of the more common drying agents used in the laboratory.

Make sure that the solid drying agent is in its *anhydrous* form. Sodium sulfate is a good general-purpose drying agent and is usually the drying agent of choice at room temperature. Use the granular form, if at all possible.

Magnesium sulfate is supplied as a fine powder (high surface area). It has a high water capacity and is inexpensive; it dries solutions more quickly than does sodium sulfate. The disadvantage of magnesium sulfate is that the desired product (or water molecules) can become trapped on the surface of the fine particles. If it is not thoroughly washed after separation, precious product may

[9]Quantitative studies on the efficiency of drying agents for a wide variety of solvents have been reported. See Burfield, D. R.; Smithers, R. H. *J. Org. Chem.* **1983**, *48*, 2420, and references therein. Other useful information can be found in Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 5th ed.; Elsevier: New York, 2003, and in Ridduck, J. A.; Bunger, W. B.; Sakano, T. K. *Organic Solvents, Physical Properties and Methods of Purification*, 4th ed.; Wiley: New York, 1986.

Table 5.5 Properties of Common Drying Agents

Drying Agent	Formula of Hydrate	Comments
Sodium sulfate	$Na_2SO_4 \cdot 10H_2O$	Slow to absorb water and inefficient, but inexpensive and has a high capacity. Loses water above 32 °C Granular form available.
Magnesium sulfate	$MgSO_4 \cdot 7H_2O$	One of the best. Can be used with nearly all organic solvents. Usually in powder form.
Calcium chloride	$CaCl_2 \cdot 6H_2O$	Relatively fast drying, but reacts with many oxygen- and nitrogen-containing compounds. Usually in granular form.
Calcium sulfate	$CaSO_4 \cdot \frac{1}{2} H_2O$	Very fast and efficient, but has a low dehydration capacity.
Silica gel	$(SiO_2)_m \cdot nH_2O$	High capacity and efficient. Commercially available t.h.e. SiO_2 drying agent is excellent.[a]
Molecular sieves	$[Na_{12}(Al_{12}Si_{12}O_{48})] \cdot 27H_2O$	High capacity and efficient. Use the 4-Å size.[b]

[a] Available from EMD Chemicals, 10394 Pacific Center Court, San Diego, CA 92121.
[b] Available from Sigma-Aldrich, Inc., 940 West Saint Paul Ave., Milwaukee, WI 53233.

be lost. Furthermore, it is usually more difficult to remove a finely powdered solid agent, which may pass through the filter paper (if used) or clog the pores of a fine porous filter. A smaller surface area translates into less adsorption of product on the surface and easier separation from the dried solution.

Molecular sieves have pores or channels in their structures. A small molecule such as water can diffuse into these channels and become trapped. The sieves are excellent drying agents, have a high capacity, and dry liquids completely. The disadvantages are that they dry slowly and are more expensive than the more common drying agents.

Calcium chloride is very inexpensive and has a high capacity. Use the granular form. Do not use it to dry solutions of alcohols, amines, or carboxylic acids because it can react with these substances.

Calcium sulfate is often sold under the trade name of Drierite. It is a somewhat expensive drying agent. Do not use the blue Drierite (commonly used to dry gases) because the cobalt indicator (blue when dry, pink when wet) may leach into the solvent.

The amount of drying agent needed depends on the amount of water present, on the capacity of the solid desiccant to absorb water, and on its particle size (actually, its surface area). If the solution is wet, the first amount of drying agent will clump (molecular sieves and t.h.e. SiO_2 are exceptions). Add more drying agent until it appears mobile when you swirl the liquid. A solution that is no longer cloudy is a further indication that the solution is dry. Swirling the contents of the container increases the rate of drying; it helps establish the equilibrium for hydration:

$$\underset{\text{Anhydrous solid}}{\text{Drying agent} + nH_2O} \rightleftharpoons \underset{\text{Solid hydrate}}{\text{Drying agent} \cdot nH_2O}$$

Most drying agents achieve approximately 80% of their drying capacity within 15 min; longer drying times are generally unnecessary. The drying agent may be added directly to the container of the organic extract, or the extract may be passed through a Pasteur filter pipet packed with the drying agent. A funnel fitted with a cotton, glass wool, or polyester plug to hold the drying agent may also be used.

As for the most common question asked with this technique—Is this "dry"?—you should be encouraged to have in your lab a series of flasks which contain a set quantity of solvent and drying agent. The difference with each flask within the series is the percentage of water which allows for a visual comparison of what is and what is not "dry."

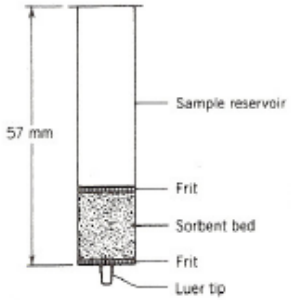


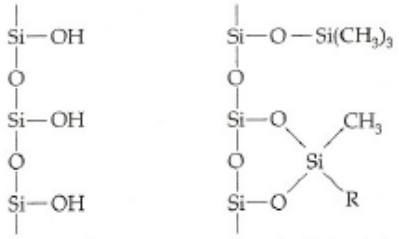
Figure 5.22 Polyethylene solid-phase extraction column.

Solid-Phase Extraction

In the modern research laboratory, the traditional liquid–liquid extraction technique may be replaced by the solid-phase extraction method.[10] The advantages of this newer approach are that it is rapid, it uses only small volumes of solvent, it does not form emulsions, isolated solvent extracts do not require a further drying stage, and it is ideal for working at the microscale level. This technique is finding wide acceptance in the food industry and in the environmental and clinical area, and it is becoming the accepted procedure for the rapid isolation of drugs of abuse and their metabolites from urine. Solid-phase extraction is accomplished using prepackaged, disposable, extraction columns. A typical column is shown in Figure 5.22. The columns are available from several commercial sources.[11]

The polypropylene columns can be obtained packed with 100–1000 mg of 40-μm sorbent sandwiched between two 20-μm polyethylene frits. The columns are typically 5–6 cm long. Sample volumes are generally 1–6 mL.

The adsorbent (stationary phase) used in these columns is a nonpolar adsorbent chemically bonded to silica gel. In fact, they are the same nonpolar adsorbents used in the reversed-phase high-performance liquid chromatography (HPLC). More specifically, the adsorbents are derivatized silica gel where the —OH groups of the silica gel have been replaced with siloxane groups by treating silica gel with the appropriate organochlorosilanes.



Silica surface — Chemically bonded silica surface

[10]For a description of this method see Zief, M.; Kiser, R. *Am. Lab.* **1990,** *22* 70; Zief, M. *NEACT J.* **1990,** *8,* 38; Hagen, D. F.; Markell, C. G.; Schmitt, G. A.; Blevins, D. D. *Anal. Chim. Acta* **1990,** *236,* 157; Arthur, C. L.; Pawliszyn, J. *Anal. Chem.* **1990,** *62,* 2145; Dorsey, J.; Dill, K. A. *Chem. Rev.* **1989,** *89,* 331; Zubrick, J. W. *The Organic Chem Lab Survival Manual,* 7th ed., Wiley: New York, 2008; Simpson, N. J. K, Ed. *Solid-Phase Extraction: Principles, Techniques and Applications,* Marcel Dekker: New York, 2000; "Solid Phase Extraction." Retrieved March 19, 2009 from www.sigmaaldrich.com/analytical-chromatography/sample-preparation/spe.html.

[11]These columns are available from Analytichem International, J. T. Baker, Inc., Supelco, Inc., Aldrich Chemical, Waters Associates and Biotage (a Division of Dyax Corp).