[MUSIC - CLAUDE DEBUSSY, "DEUX ARABESQUES"]

PROFESSOR: Reaction work-up 1-- extracting, washing, and drying. As all chemists quickly learn, it is very rare for a chemical reaction to provide only the one compound that you're looking for. Even highly selective reactions generate the desired product as a crude mixture, containing byproducts and underreacted starting materials and reagents.

Liquid-liquid extraction is the most common technique for separating a compound from a complex mixture. In an extraction, you can take advantage of differing solubilities to selectively separate the different components. By carefully planning out an extraction and washing sequence, otherwise known as a work-up, the desired product can usually be separated from the unwanted impurities. This video will illustrate the proper technique involved in working up a reaction.

In an ideal world, each chemical reaction in the laboratory would provide only the desired product in its pure form. In reality, the product is almost always generated as part of a messy mixture of byproducts and side products. In short, garbage.

Liquid-liquid extraction is a useful technique used to isolate the desired compound from a complex mixture. In an extraction, the mixture is partitioned between two immiscible solvents in a separatory funnel, otherwise known as a "sep" funnel. The key is that the two solvents are mutually insoluble, so they form two distinct layers. One of the solvents is almost always water, and the other is an organic solvent of your choice.

The different components of the mixture are selectively distributed in one solvent or the other, depending on their different solubilities. In this way, you can take advantage of differing solubilities to selectively transport solutes from one layer to another. In most cases, but not all, neutral organic molecules prefer the organic phase, while charged molecules and inorganic salts prefer the aqueous layer.

By carefully planning out an extraction and washing sequence, otherwise known as a reaction work-up, the desired compound can usually be separated from most of the unwanted impurities. This brings up an important point. What is the difference between an extraction and a wash? These terms describe similar, but fundamentally different, operations.

An extraction involves pulling the desired compound out of a mixture of compounds. Whereas, in a wash, you are pulling unwanted impurities away from the desired product. In other words, you always keep the extracts, and trash the washes. This might sound confusing, but it will hopefully become clear as we continue.

The first step in an extraction and washing sequence-- once you have decided on the appropriate solvents, of course-- is filling the sep funnel. It is a good idea to use an iron ring and a nice, cushy cork ring to safely support the sep funnel. Before you add any solvent, close the stopcock, and place a clean, dry flask under the sep funnel. This will prevent you from dumping precious material all over the dirty bench. The flask will save you if the funnel leaks, or the stopcock somehow opened itself.

When the stopcock is safely closed, and the flask is in place, pour your two solvents into the sep funnel. Use a sep funnel large enough that you don't fill it more than 3/4 full. If it is too full, you won't be able to efficiently mix the solvents.

This brings us to the next step-- mixing and venting. It is important to mix the two solvents very well. This increases the contact surface area and allows the distribution of solutes to occur very rapidly.

But use caution-- mixing will frequently cause pressure to build up inside of the sep funnel. Pressure buildup is especially common when you are using particularly volatile solvents, like diethyl ether, or compounds that can generate gas, like sodium bicarbonate. Under acidic conditions, sodium bicarbonate will release gaseous carbon dioxide.

Before any vigorous mixing, it is a good idea to gently swirl and invert the sep funnel. Then, invert the sep funnel, holding the stopper tightly. Allow the liquid to drain away from the stopcock, and point the tip of the sep funnel away from yourself and other people. Slowly open the stopcock to allow venting.

Now, you're ready to really mix it up. Hold the sep funnel firmly, and shake it vigorously for several seconds. Once again, invert the funnel and vent it carefully. Repeat the shaking and venting until you no longer hear gas escape when you open the stopcock. Then, set your funnel down, and let the layers settle. Ideally, two layers with a nice, clean interface should form very quickly.

Unfortunately, things don't always go so smoothly. A thick, cloudy layer, called an emulsion, can sometimes form between the two solvent layers. An emulsion is a colloidal mixture of the two solvents, and is frequently caused by the presence of fine particles in the solution.

Getting rid of an emulsion can take some time, so if you know that you are likely to generate one, your best bet is to take pains to prevent it ahead of time. For example, gently swirling and inverting your sep funnel will rarely cause an emulsion to form. You will have to spend more time mixing because swirling is not as efficient as shaking, but it may be worth it.

Don't worry, if you unwittingly generated a monster emulsion, you still have a few options. First, you can just sit and wait. It might clear itself up, even if it takes a few hours.

If you don't have all day to finish your extraction, try swirling the mixture gently, and stirring the emulsion with a glass rod. If this doesn't work, add several milliliters of saturated sodium chloride solution to the funnel, and swirl to mix. The sodium chloride increases the ionic strength of the aqueous layer and decreases the solubility of the organic solvent in the water. As a last resort, you may need to use vacuum filtration to filter your entire mixture through a pad of Celite.

When you are carrying out an extraction and washing sequence, it is very important that you keep track of which layer is which, and what compounds are dissolved in each layer. This means that you constantly need to be asking yourself, which layer is on the top? Which layer is on the bottom?

One way to keep track of this is to know something about the densities of the solvents you are using. In every case, the solvent with the lowest density will be on top. And the solvent with the highest density will be on the bottom. This is helpful because you can generally assume that dilute aqueous solutions have a density around 1 gram per milliliter, similar to water.

The organic solvent will be in the top layer if it has a density less than 1 gram per milliliter, such as hexane, diethyl ether, or ethyl acetate. The organic solvent will be the bottom layer if it has a density greater than 1 gram per milliliter, such as methylene chloride or chloroform. But be careful-- high concentrations of solutes can sometimes drastically affect the density of a solvent.

If you're having trouble figuring out which layer is which, you may need to perform a quick solubility test. Take a couple of drops of the layer in question, and add them to a small amount of water in a test tube. If the drops dissolve without turning the water cloudy, then the drops were from the aqueous layer.

If the solution turns cloudy, or the drops form an insoluble layer on the bottom, or an insoluble layer on the top, then the drops are from the organic layer. But even if you think you know which layer is which, do not discard any of the layers until you are absolutely sure that you have isolated all of the material.

Once you have a good idea of where your material is, it's time to separate the layers. Before you do anything, place a clean, dry labeled beaker under the sep funnel, and remove the stopper. If you don't do this, you'll have some trouble getting any liquid to drain. With the stopper off, open the stopcock, and allow the bottom layer to drain into the beaker. Take it slow when you get near the interface, so that you can close the valve precisely in between the two layers.

Once you have drained the bottom layer, you have a few options. If you still need to perform a wash or an extraction with the top layer, then leave it in the funnel. Pour in the second solvent, and proceed to mix and vent. If you are done with the top layer, then pick up the funnel, and pour it into a second clean, dry labeled beaker.

Here is a little bit of sep funnel etiquette to follow. When you are separating the layers, always drain the bottom layer through the stopcock, and pour the top layer through the top. This will minimize recontamination of your material.

Before we move on to proper post extraction procedures, let's walk through a sample reaction work-up, similar to one you might use in the laboratory. Let's say that you performed an acylation reaction to generate phenyl acetate. At the end of the reaction, you were left with a solution containing a lot more than the material you were looking for. So what do you do?

First, you know that phenyl acetate is soluble in diethyl ether, and that diethyl ether is insoluble in water. Therefore, in your work-up, you will use diethyl ether as the organic layer, and wash it with different aqueous solutions to remove the impurities. Now, it is time to plan out the washes.

It is important that you use what you know about the impurities to decide on appropriate aqueous washes for your mixture. Keep in mind that the washes should only be 10% to 50% of the volume of the solution that you are washing. And make sure to repeat each wash two or three times to wash away as much of the impurities, as possible.

Your crude mixture contains acetic acid, a fairly strong acid, and two weak bases-- triethylamine and DMAP. To get rid of the acetic acid, you need to wash the solution with a mild base that will deprotonate the acid and pull the charged acetate ion into the aqueous layer. Saturated sodium bicarbonate works very well for this purpose.

Add the sodium bicarbonate solution and mix well. Make sure that you vent frequently to release the carbon dioxide gas that is generated. Finally, drain away the aqueous solution that now contains the sodium acetate, and repeat the wash two more times.

To get rid of the weak bases-- triethylamine and DMAP-- you need to wash with a dilute solution of a strong acid that will protonate the bases and pull them into the aqueous layer. A 10% aqueous solution of HCL works well for this. Once again, add the wash, and mix and vent well. Drain the aqueous layer containing the protonated amines, and repeat two more times.

So far, this looks like a pretty effective reaction work-up. But there is one more thing to keep in mind. Water is slightly soluble in ether-- not to a large extent, but there is some water hanging around in the organic layer. One way to pull some of the water out is to wash it with saturated sodium chloride, otherwise known as brine. The high ionic strength of the salt solution decreases the solubility of the aqueous layer in the ether, effectively washing away some of the water.

Voila. Now that you have done all you can with your sep funnel, it's time to dry your organic layer even more with the drying agent. Magnesium sulfate is one popular drying agent because it is quick and effective. It is also a very fine powder, so take care that you don't leave any of your desired material absorbed onto the surface when you discard it. Keep in mind that magnesium sulfate is also slightly acidic. So it may not be suitable for use with compounds that are sensitive to acid.

To dry the organic layer with magnesium sulfate, add a small amount of the powder and swirl. Incrementally add more drying agent, and swirl until you get the snow globe effect. There should be free, unclumped powder in the flask, even after letting it sit for a few minutes.

Sodium sulfate is another common drying agent. Although it is slower than magnesium sulfate, it is effectively neutral. And, in its granular form, will absorb less of your desired material onto its surface. Drying the organic layer with sodium sulfate is similar to using magnesium sulfate, except you may need to look a bit closer to see whether there is free, unclumped drying agent in the flask.

It is also a good idea to let the solution dry for 5 or 10 minutes before removing the drying agent. To remove the drying agent, perform a gravity filtration with fluted filter paper. Once you have filtered the entire solution, be sure to rinse the drying agent very well so that you don't leave any product stuck to the surface. It is a good idea to rinse the drying agent three times with clean, dry solvent, adding each of these rinses to the flask.

Once you are confident that you have transferred all of the desired material to the round-bottom flask, you are ready to proceed to the rotavap, and concentrate the solution in vacuo. For detailed information on proper use of the rotavap, you can watch the second reaction work-up video.

[CHIMING]

Remember, this video is intended to help you prepare for lab by providing a demonstration of the proper experimental technique. It is not intended as a replacement for reading your lab manual or the supplementary material. In order to become a great experimentalist, it is important that you understand both theory and technique. Now it's your turn. Good luck.

[MUSIC - CLAUDE DEBUSSY, "CLAIR DE LUNE"]