

7.4. Extraction and Washing Guide

Overview:

This handout describes standard extraction and washing protocols that can be applied to virtually any crude reaction mixture. Aqueous washings are done to remove water soluble impurities from organic products since normally the compound that you desire will be dissolved in the organic layer.

Reference:

For an excellent discussion, read Zubrick pages 127–138.

Standard Aqueous Workup Protocol:

1) Pick an organic solvent. Ether is the most popular because it can be removed easily on the rotary evaporator, ethyl acetate also works well but is harder to remove, dichloromethane is a poor choice and should be avoided, if possible, since it often forms nasty emulsions and complicates matters because it is heavier than water.

2) Pick the size of your separatory (sep.) funnel. You will usually use 125 or 250-mL, large scale reactions (1–10 g) can require 500-mL or 1-L sizes. Remember that your sep. funnel will contain the solvent and wash liquid which must be thoroughly mixed.

3) Dilute the crude reaction mixture with your solvent of choice and transfer to your chosen sep. funnel. Large amounts of material require large amounts of solvent. Normal reactions (50–500 mg of product) can be diluted with between 25–100 mL of solvent.

4) Wash the organic layer to remove impurities. The volume of a wash phase is typically one tenth to one half the volume of the organic phase. It is sometimes best to repeat a wash two or three times. An acid wash (usually 10% HCl) is used to remove amines, while a basic wash (usually sat. NaHCO₃ or 10% NaOH) is used to remove unwanted acids. In most cases, when neither acidic nor basic impurities are an issue, the solution is washed with distilled water to remove any non-organic compounds. (*Note: When shaking mixtures in a sep. funnel be sure to vent it regularly by holding it upside-*

down, pointing it up and to the back of your hood, then opening the stopcock. This will release any pressure that has built up during mixing. Additionally, when draining liquids out of the sep. funnel, be sure to first remove the stopper.)

5) Back-extract to recover lost product. If your compound is somewhat water soluble (has several polar functional groups), you may need to back-extract the water layers with ether or ethyl acetate to avoid significant loss of compound in the aqueous phase. TLC can be used to determine when all of your compound has been removed from the water.

6) Finish with a brine (saturated NaCl solution) wash. This helps disrupt any emulsions and will "dry" the organic layer by extracting water that may have dissolved in the organic phase.

7) Dry the organic layer. After removing your solution from the aqueous phase, a drying agent is added to remove all traces of water. This is usually MgSO_4 , more effective and faster, but slightly acidic; or Na_2SO_4 , less effective and slower, but neutral. These compounds bind to any water remaining in the organic solution, forming clumps when they react. A decent amount of drying agent should be added, but as long as some solid is not clumped, no more needs to be added. (This will make sense once you've done this a couple of times.)

8) While the compound is drying, it is time to flute the filter paper. Refer to Zubrick page 136-138 for directions. Some chemists prefer to use a Büchner funnel and unfluted filter paper (or a fritted funnel) under mild vacuum as their standard filtration method. Their motive is a slightly higher yield of product.

9) Filter the solution into a large round bottom flask using your expertly fluted filter paper and a large funnel (or the Büchner method). To guard against bumping on the rotavap, do not fill the flask more than half full.

10) Concentrate the solution on the rotavap, then dissolve the compound in a small amount of solvent and transfer to a small pre-weighed (tared) flask.

11) Concentrate the solution on the rotavap again. Higher boiling solvents are more effectively removed by concentrating, adding dichloromethane then repeating once more.

12) Use the vacuum pump to remove residual solvent. For non-volatile compounds, residual solvent is most effectively removed by using the vacuum pump. One useful trick to speed up this process is the following: evacuate the flask and vent to N₂, repeat this again, then pump on the flask for 30 minutes. If your compound is volatile—low molecular weight and/or low boiling point—obtain a constant weight using the rotavap, not the vacuum pump.

13) Obtain a constant weight. Weigh the flask after leaving it on the vacuum pump (or rotavap), then return to the pump (or rotavap) for 15 to 30 minutes and weigh again. Once two weights in a row are the same, you're ready to take an NMR.