# Standard Operating Procedure

**Task:** Unknown inorganic reaction workup
**Date:** 1/31/2014 (revised 3/19/2021)

**Background:**

- The "inorganic workup" is meant to provide a good standard procedure for assessing the success of exploratory reactions involving inorganic or organometallic complexes. This SOP details a great first step for purification: solvent washes and extraction. The detailed work-up procedure can provide valuable solubility information that can help guide large scale separation, purification, and crystallization strategies. The treatments below are meant as general guidelines, and not all reactions need to be treated in the same way. Note: the terms "wash" and "extract" are *different than the usage in organic chemistry!* There is no aqueous layer, so "wash" refers to adding a solvent to a solid sample and dissolving unwanted impurities. The desired product is left behind while the impurities are washed away. The terms "extract" refers to the process of dissolving the desired product away from insoluble solids with an appropriate solvent.
- In most cases, a crude NMR should be taken before workup is attempted.
- It is important to keep in mind the polarity of common organic solvents. Not all of these will be available in all gloveboxes, so please check with the czar to see which are OK to use. Polarity is often equated with dielectric constant, $\varepsilon$. A table is provided below. The list of solvents provided below is based upon the suggested order of addition.
- Read the entire document before proceeding. This document contains solvent information, training requirements, hazards, materials, and a general procedure. This is followed by tips and tricks from the group and a table of the solubility of common salts in various solvents.

| **Solvent** (protic in blue) | **Dielectric Constant** | **Dipole Moment** | **Notes** |
|---|---|---|---|
| Pentane (hexanes) | 1.8 | 0.0 | bp 36 ºC |
| Benzene | 2.3 | 0.0 | |
| Toluene (xylenes) | 2.4 | 0.36 | |
| Dioxane | 2.3 | 0.45 | $Mg^{2+}$ chelate |
| Diethyl ether | 4.3 | 1.15 | |
| Chloroform | 4.8 | 1.04 | Possible $H^+$ source |
| Tetrahydrofuran | 7.5 | 1.75 | Polymerizable |
| DCM (DCE) | 9.1 | 1.60 | |
| Ethyl acetate | 6.0 | 1.78 | |
| Acetone | 21 | 2.88 | |
| Ethanol | 25 | 1.69 | |
| Methanol | 33 | 1.70 | |
| Acetonitrile | 38 | 3.92 | |
| DMF | 38 | 3.82 | bp 153 ºC |
| DMSO | 47 | 3.96 | bp 189 ºC |
| $H_2O$ | 80 | 1.85 | |

**Training Requirements:**

- Lab safety training
- Glovebox training required (if workup performed in box).

**Potential Hazards:**

- Case dependent — assess risks of all new reactions. Look at SDS for solvents and starting materials used in the reaction.

**Special PPE requirements:**

- Case dependent

**Materials Needed:**

- An exploratory reaction involving transition metals.
- Organic solvents.

**Procedure:**

- Run a reaction. Let the reaction equilibrate to room temperature if it was heated or chilled.
- Filter the reaction mixture to remove any insoluble materials. This is often done using a "pipet filter" consisting of a glass pipet and a piece of microporous glass filter "paper". If you expected your product to precipitate, collect the solids manually or by extraction.
- Evaporate the filtrate to dryness under vacuum. The workup procedure is amenable to solids or oily residues. If the reaction was performed outside of the glovebox, concentrate it on the Schlenk line before bringing it into the glovebox.
- Take an NMR spectrum of the crude reaction mixture. The solvent choice will rely on your intuition on the solubility and stability of the products. Benzene, dichloromethane, and acetonitrile are good starting points to provide a range of polarity.
- Make sure the purifier on the glovebox is turned off when you use halogenated solvents and purge after use. Before opening deuterated solvents in the glovebox, run a purge to protect the deuterated solvents from contamination.
- If the NMR spectrum is clean, congratulate yourself on running a successful reaction and turn to other spectroscopic tools to ensure purity.
- If the NMR spectrum is not clean, continue with the inorganic workup.
- The inorganic workup is designed to separate the desired product from impurities. An impurity can be washed away using a solvent, leaving behind pure solid product. Or the product can be extracted from the mixture to give the product in the filtrate.
- Start by treating your crude reaction mixture with a **non-polar solvent**. The precise choice will depend on your system and your instincts on solubility. Pentane is recommended as a common starting point. Organic byproducts and neutral metal complexes are sometimes soluble in alkane solvents.
    - Add the non-polar solvent to the vial, scrape or stir to try and dissolve anything. Then filter the solvent through a pipet filter into a **tared vial**.
    - Repeat 2 more times (suggest 1-2 mL per wash on a small scale), or until the filtrate is not colored. Color can be a great way to tell if anything is being extracted.
    - After the procedure, you should have a vial containing the filtrate in a non-polar solvent. Cap and retain this vial. In your reaction vial there should be any residual materials (but no bulk solvent).

- Treat the residual materials in the reaction vial with a second solvent. This solvent should be slightly more polar than the first (common choices: toluene, diethyl ether). Scrape or stir to mix, washing 3 times as before. Filter each aliquot of solvent through the **same pipet filter** into a **new tared** vial. Cap and retain the second solvent vial.
- Treat the residual materials in the original reaction vial with a third solvent. This solvent should be more polar again (common choices: tetrahydrofuran, dichloromethane). Repeat extraction procedure as before, filtering each wash through the **same pipet filter** into another **new** vial.
- Continue washing with increasingly polar solvents until the bulk of the material has dissolved. The next tier of solvents are MeCN and alcohols. The most effective solvents for dissolving the last of the material are DMF, DMSO, and $H_2O$, but these are hard to remove and may decompose your material.
- Now you will have anywhere from 2 to 6 vials of solvent from your extractions/filtrations. Based on color or how much material dissolved in each one, select the 2 or 3 vials that are the most likely to contain your product. Remove the solvents under vacuum, add an appropriate deuterated solvent to dissolve the residues, and take an NMR spectrum. If your reaction mixture had species with different solubility traits, the workup procedure should lead to good separation.
- If no separation was achieved, it's time to start thinking about crystallization, a column, or a distillation. An inorganic workup is sometimes a good first step, for example if you separate one impurity to leave a more tractable mixture. Washes are easy to implement, so it is often beneficial to perform this on the bulk of the material so that you are running a column on a mixture containing fewer species. Remember to keep what you learned about solubility in mind as you move forward. For example, if none of the materials dissolved in diethyl ether, but everything dissolved in acetonitrile, you could try an ether/acetonitrile vapor diffusion crystallization.

**Tips and Tricks:**

- A simple filtration device is great for performing an inorganic workup on small scale reactions. Add some glass microfiber "paper" to a small glass pipet, pushing it to the point where the pipet narrows. A plastic syringe fitted with rubber tubing can provide positive pressure to push the filtrate through the filter.

- Consider the solubility of your expected product and any possible impurities. Neutral metal complexes are typically soluble in nonpolar solvents (e.g. pentane, benzene, toluene, diethyl ether), while cationic complexes often require more polar solvents (e.g. tetrahydrofuran, dichloromethane, acetonitrile).
- Consider the solubility of salt byproducts that must be separated from the desired product. Alkali and alkaline earth metal salts are typically highly insoluble in hydrocarbons and chloroalkanes, with the exception of fluoroarylborate salts.
- Precipitation can be a valuable strategy to incorporate into a workup. For example, addition of excess diethyl ether can precipitate metal complex salts of $BF_4$ or $PF_6$. Precipitation can be performed either by adding an antisolvent to a concentrated solution of the complex, or by adding a concentrated solution dropwise to a large volume of antisolvent. The precipitation process will hopefully improve purity, and if needed the inorganic workup can proceed as described above to further purify.
- Benzene solutions can be frozen before exposure to vacuum to enable sublimation of the benzene, often leaving a fluffy powder of the desired species.
- Adding pentane and then removing it under vacuum a few times can help to remove residual polar solvents preventing “false” solubility observations.
- Oily materials can often be converted to solids by trituration, in which an antisolvent (e.g. pentane, diethyl ether) is added to the oil and stirred vigorously for several minutes or hours.

**Related SOPs:**

- Waste SOP
- Recrystallization SOP