

Work up tips:

Reactions with Triphenylphosphine oxide:

If your product is stable and relatively-non polar, a good way of removing triphenylphosphine oxide (produced in Wittig, Mitsunobu, bromination, and other reactions) is to concentrate the reaction mixture to a lower flow, suspend the residue in pentane (or hexane)/ether and filter over a silica plug. The compound can then be eluted with ether, leaving most of the phosphine oxide at the top of the column. Sometimes it is necessary to repeat this procedure 2-3 to remove most of the phosphine oxide.

Copper Salts:

1. Quench rxn w/ sat NH_4Cl aq solution. stir up to a few hours at r.t. or until the solution becomes a dark blue (indicates complexation).
2. Remove aq layer and wash organic a few times with sat. NH_4Cl aq.
3. Isolate crude material as in step 4 above.

Boron Compounds:

A number of boron compounds and residues (for example from hydroboration, allylation, reduction, Suzuki coupling, etc) can be removed by concentrating the reaction mixture repeatedly from MeOH . This process forms $(\text{MeO})_3\text{B}$, which is volatile.

$\text{R}_3\text{Sn-X}$ Byproducts:

1. Byproducts of tin based reactions such as Bu_3SnBr can be removed by treatment with AlMe_3 to create the nonpolar Bu_3SnMe or NaOH to create the polar Bu_3SnOH . (See: P. Renaud, E. Lacote, L. Quaranta *Tetrahedron Lett.* **1998**, 39, 2123.)
2. Filter through a mixture of KF/Celite
3. a) Dilute rxn with suitable organic solvent
b) Add aqueous phase (water, sat. NH_4Cl , etc.)
c) Remove aq layer and wash organic phase 2-3 times with 1M KF aq solution. Shake in sep funnel for up to 1 minute for each wash. Solid Bu_3SnF precip may form at organic/aqueous interface. If a problem, filter through celite.
d) Wash aq 1 X brine, dry organic phase and remove solvent.
4. In many Stille reactions, the Bu_3SnX junk can be almost entirely removed by filtering through (or columning directly) on silica made up with ~2-5% triethylamine in the eluent. Run in the same solvent. Quicker than stirring with aq, KF, and more fun than grinding a big bowl of toxic KF with silica or celite for a good dispersion.
5. For Bu_3SnH : add I_2 to convert $\text{Bu}_3\text{SnSnBu}_3$ and unreacted Bu_3SnH to Bu_3SnI , KF treatment (see above) then converts this to Bu_3SnF , which is more easily removed.

Metal Salts

Many transition metals can be removed by precipitation of the sulfides. Wash with aqueous sodium sulfide. If necessary, adjust pH to create H_2S . Some transition metals can be removed by aqueous extraction with tris(hydroxymethyl)phosphine.

(See: R. H. Grubs *Tetrahedron Lett.* **1999**, 40, 4137.)

Aluminum based Reductions:

A. To workup a reaction containing x g lithium aluminum hydride:

1. Dilute with ether and cool to 0°C
2. Slowly add x mL water
3. Add x mL 15 % aqueous sodium hydroxide
4. Add 3x mL water
5. Warm to RT and stir 15 min
6. Add some anhydrous magnesium sulfate
7. Stir 15 min and filter to remove salts

B. To workup a reaction containing x mmol of an agent such as Diisobutyl aluminum hydride (Dibal):

1. Dilute with ether and cool to 0°C
2. Slowly add 0.04x mL water
3. Add 0.04x mL 15 % aqueous sodium hydroxide
4. Add 0.1x mL water
5. Warm to RT and stir 15 min
6. Add some anhydrous magnesium sulfate
7. Stir 15 min and filter to remove salts

Titanium:

Quench with Aqueous ammonium chloride, the titanium byproduct will partition into the aqueous layer during workup.

Chromium Oxidations:

1. PCC/PDC: Filter the reaction mixture through a pad of florisil.
2. Jones: Add isopropanol until the reaction turns from orange/red to green: this indicates that the oxidant has been consumed.

m-CPBA:

If reaction is done in refluxing DCE (for example), cool reaction mixture to 0 °C to precipitate out all m-CPBA. Then add 10% aqueous solution of Na₂SO₄. Two layers form. Separate and extract with DCM. Repeat the addition of Na₂SO₄ several times then combine all organic layers, wash with saturated solution of NaHCO₃, then saturated aqueous solution of NaCl, then dry (MgSO₄) and evaporate under reduced pressure. If purifying product by FCC, any m-CPBA still present is easily separated as it is UV active, extremely polar and it tends to deposit on column tip during purification. This is easily taken care of as m-CPBA is soluble in EtOAc.

DCC:

Filter the reaction mixture through a medium frit, rinsing with a minimal amount of reaction solvent, then work up. Depending one runs reaction in dioxane, THF, DMF, dichloromethane, etc., but urea is mostly insoluble in most solvents and this is a good way to get rid of it (the rest can be flashed away pretty straightforwardly). If it is too soluble, one can concentrate the reaction mixture first and take it up in ether, then filter and rinse.

Source: <http://chem.chem.rochester.edu/~nvd/workupformulas.html>

If no procedure is given to quench a reaction, follow these general guidelines:

- Strongly basic non-aqueous reactions
 - o Typical examples: alkylation using strong bases (BuLi), many organometallic reagents (MeLi, Gringnards), hydride reducing agents (LAH, DIBAL-H), and cuprate reactions.
 - o Slowly add excess aqueous ammonium chloride to protonate anions present and to destroy unreacted reagent at low temperature. If you are concerned with aqueous solution freezing out, you can substitute with acetic acid. Adding too much ammonium chloride might make extraction difficult.
 - o For aluminum reactions, use Rochelle's salt (add a saturated solution of Rochelle's salt and stir rapidly for at least an hour) or sodium sulfate (add a saturated aqueous solution of sodium sulfate dropwise while stirring & cooling until a very heavy precipitate is formed. Decant the supernatant and extract the solid a few times).
- 'Neutral' non-aqueous reactions
 - o All reactions that does not involve strong base or strong acid. Can be slightly acidic/basic. (ie. Acid-catalyzed ketalization or tosylation of alcohol with pyridine/triethylamine as base)
 - o Quench with ammonium chloride or water for mildly basic reactions. Dilute with sodium bicarbonate for mildly acidic reaction.
- Strongly acidic non-aqueous reactions
 - o Examples: reaction involving the use of a strong Lewis acid (i.e. TiCl₄ or BF₃.OEt₂)
 - o If the product is likely to be unaffected strong protic acid, quench with water while cooling.
 - o If the product is unstable with acid, add aqueous sodium bicarbonate while cooling.
 - o If a non-aqueous quench is needed, use a solution of gaseous ammonia in the reaction solvent while cooling.
- Acidic or basic aqueous reaction
 - o Dilute the reaction and neutralize the diluted acid or base.
- Liquid ammonia reactions
 - o Add an excess of solid ammonium chloride, then allow the ammonia to evaporate.

If you are ever unsure about a work up, test it on small scale first.

Source: Lenodard, J. *et al.* Advanced Practical Organic Chemistry. 2nd ed. 1998: CRC Press.