From Laboratory Inspections to SOP Development to Enhancing Safety Culture

Tilak Chandra, Ph.D.
Environment, Health & Safety
University of Wisconsin-Madison

250th American Chemical Society National Meeting & Exposition
Boston, MA Aug. 16-20, 2015
Learning from Chemical Incidents

\[
\text{Pd/C-Catalyst fire} \quad \text{Over pressurization of pressure vessel}
\]

Ref. Z. Naturforschg. 21 b, 920-923, 1966.
Need for Technically Instructive SOPs for Chemical Manipulations

- Includes technical information and literature findings about analogous reactions & substrates
- Incorporates safety protocols into the regular steps of an experiment
- Eliminates guesswork for researchers for safety decisions such as PPE selection, use of fume hood, waste determination, etc.

Inadequate disposal of hydrogenation catalyst

Raney nickel fire
Chemistry: Inspection Process

Chemical fume hoods = 3000
Biological Safety Cabinets = 1500
Inspection and SOP Review

University of Wisconsin–Madison

Five Largest Majors by Degrees Conferred

<table>
<thead>
<tr>
<th>Major</th>
<th>2008-09</th>
<th>2009-10</th>
<th>2010-11</th>
<th>2011-12</th>
<th>2012-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Doctorate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemistry</td>
<td>40</td>
<td>39</td>
<td>47</td>
<td>Curriculum and Instruction 35</td>
<td>43</td>
</tr>
<tr>
<td>Electrical Engineering</td>
<td>29</td>
<td>Biochemistry</td>
<td>31</td>
<td>Physics</td>
<td>30</td>
</tr>
</tbody>
</table>

2013 – 2014 Data Digest | Students
Chemical Safety Inspections: Areas of Review

Areas of Review:

- **Documentation** (training records, Standard Operating Procedures, Chemical Hygiene Plan)
- Egress and Housekeeping
- Emergency Equipment
- **General Safety** (machine guards, refrigerators, electrical safety)
- **Chemical Safety** (storage, usage, labeling)
- Compressed Gases
- Chemical Waste and Unwanted Chemicals
- Personal Protective Equipment (PPE)
- Ventilation and Engineering Controls
- **Regulatory codes and other requirements** (OSHA, EPA, Building university requirements)
Lab Safety Inspections: What We Can Accomplish During 1-2 Hrs. of Lab Visits/Inspections?

UNSTABLE H₂ TORCH

Loose chains

Broken Vacuum Tube

 tert-BuLi inside a refrigerator
Laboratory Inspections: Larger Vs Smaller Safety Issues

Ammonia: HIGHLY CORRODED

Damaged cord
Laboratory Inspections: Larger Vs Smaller Safety Issues
## SOP: Pyrophoric Chemical Manipulations

---

**Section 4: Laboratory SOPs – Procedure Form**

<table>
<thead>
<tr>
<th>Title: tert-BuLi manipulation</th>
<th>Rev. Date: 06/04/15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prepared By: XXXXX</td>
<td>P.I.: Prof. XXXXXX</td>
</tr>
</tbody>
</table>

**Prior Approval:** This procedure is considered hazardous enough that prior approval is needed from the Principal Investigator:  
- [ ] Y  
- [x] N

**Involves Use of Particularly Hazardous Substance (PHS)?**  
- [ ] Y  
- [ ] N

- [ ] Carcinogen  
- [ ] Reproductive Toxin  
- [x] Flammable

**Does this procedure require medical surveillance?**  
- [ ] Y  
- [x] N

**Does this require use of a fit-tested respirator?**  
- [ ] Y  
- [x] N

**Brief Description of Procedure (100 words or less):**

Transfer of tert-BuLi via syringe: (should not be used for more than 10 mL). At first secure the tert-BuLi containing bottle with proper clamp and do not over-tight the bottle (use cotton or other compatible material for the extra safety; also use a secondary containment for reagent bottle).

I. Insert a fine needle from an inert gas source with a bubbler outlet into the bottle keeping the needle tip above the liquid level. Do not over-pressurize the bottle containing pyrophoric chemical. The goal of this technique is to equalize the pressure in the reagent bottle. (A different technique is to use inert gas pressure to compel reagent into the syringe, but that has the danger of blowing the plunger out of the syringe body and spilling out pyrophoric reagent.) Flush dry syringe with inert gas, depress the plunger and insert the needle into the Sure-Seal bottle (Fig. 4a).

II. Insert a fine needle from an inert gas source with a bubbler outlet into the bottle keeping the needle tip above the liquid level. Do not over-pressurize the bottle containing pyrophoric chemical. The goal of this technique is to equalize the pressure in the reagent bottle. (A different technique is to use inert gas pressure to compel reagent into the syringe, but that has the danger of blowing the plunger out of the syringe body and spilling out pyrophoric reagent.) Flush dry syringe with inert gas, depress the plunger and insert the needle into the Sure-Seal bottle (Fig. 4a).
Collecting Technical Information from Researchers

Manipulations of interest:
• Hydrogenations/high pressure reactions
• Grignard reaction
• Lithiation
• Azide formation
• Schlenk line use
Gathering Technical Information for SOP Generation

Heat control

Laboratory jack
Preparing Inspection Reports

Date of Inspection: February 17, 2015
Research Group: Prof. XXX XX (Chemistry); CHO: XXX XX
Inspectors: Dr. Rob McClain & Tilak Chandra

A laboratory safety inspection was conducted in Prof. XXX XX’s laboratories by Dr. Rob McClain & Tilak Chandra on February 17, 2015. Chemical safety inspections were carried out in XXX hall for rooms XX, XX, XX, XX (electronic lab). These inspections covered documentation, chemical storage and compatibility, compressed gas safety, waste/unwanted material management, PPE, ventilation, regulatory requirements and egress. XX XX (CHO) was present during the inspection process. Dyes are used in laboratories for research purpose. XXX XX’s lab is heavily involved in spectroscopy using a variety of lasers. Several corrosive and toxic compressed gas cylinders and lecture bottles such as HBr, Cl₂, H₂S, NO₂, NH₃, H₂ etc. are present in the labs.

Specific comments and recommendations:

Laboratory Safety Visit Checklist Form

<table>
<thead>
<tr>
<th>Principal Investigator: Prof. XXXX XX</th>
<th>CHO: XXXX XX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Building: XXX Hall XXX</td>
<td>Room #: X, XX, XXX, XXX (electronic lab)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>NA</th>
<th>Documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>☒</td>
<td></td>
<td></td>
<td>Is the emergency door card present and up to date?</td>
</tr>
<tr>
<td></td>
<td>☐</td>
<td></td>
<td>Is a Chemical Hygiene Plan available?</td>
</tr>
<tr>
<td>☒</td>
<td>☒</td>
<td></td>
<td>Are laboratory Standard Operating Procedures available?</td>
</tr>
<tr>
<td>☒</td>
<td>☐</td>
<td></td>
<td>Are Safety Data Sheets (SDS) readily available?</td>
</tr>
<tr>
<td>☒</td>
<td>☐</td>
<td></td>
<td>Is the laboratory’s chemical inventory available?</td>
</tr>
<tr>
<td>☒</td>
<td>☐</td>
<td></td>
<td>Have employees been trained in the OSHA Laboratory Safety Standard and lab specific hazards associated with the lab?</td>
</tr>
<tr>
<td>☒</td>
<td>☒</td>
<td></td>
<td>Are training records available?</td>
</tr>
</tbody>
</table>
Preparing Inspection Reports

Anhydrous hydrogen fluoride or hydrogen bromide in carbon steel cylinders may react slowly over years with the iron in the steel to form iron fluoride and hydrogen. The hydrogen pressure can ultimately build to the point where it ruptures the cylinder. All corrosive gases should be used up or returned within two years of purchase.

- HBr
- Incorrect storage

Request for a disposal container in shrinking due to chemicals

Inspection report

- PI/Lab manager, CHO
- Department safety chair, Building manager
Benefits from Chemical Safety Inspection

- Improves laboratory housekeeping
- Reduces overall chemical loads within the building
- Improves LSCHP & record keepings
- Waste management/unwanted materials.
SOP Generations for Hazardous Chemical Manipulations

Elements of SOPs for Chemical Manipulations:

• **Introduction** (brief description about the rexn.)
• **Reaction set-up** (glassware, reactor, transfer system)
• **Best practices** (moisture/temperature sensitivity)
• **Safety considerations**

• **Hazards & controls**
  
  *Hazard identification*
  
  • **Literature search** (substrate reactivity, intermediate stability etc.)
  • **Heat control during halide addition/pressure control**

• **Hazards control**

• **Emergency response**
  
  *Spills and exposures*
Hazard identification: Literature Search

Mg, 20 volumes THF
1 mol% DIBAH
5% aryl bromide, 5 °C

1
  \(\text{CF}_3\)
  \(\text{MeO}\)
  \(\text{MeO}\)
  \(\text{Br}\)

2
  \(\text{MgBr}\)
  \(\text{F}_3\text{C}\)

3
  \(\text{MgBr}\)
  \(\text{F}_3\text{C}\)

4
  \(\text{MgBr}\)
  \(\text{CF}_3\)

\(\text{NO}_2\)
\(\text{H}_2\)
\(\text{R}\)
\(\text{R}\)
\(\text{NO}\)
\(\text{NHOH}\)
\(\text{NH}_2\)

Unstable intermediates
Hazard identification for Chemical Manipulations

- **H₂ related hazards**: Fire/explosion
- **Catalyst manipulation hazards**: Pyrophoric when mixed with hydrogen
- **Use of flammable solvents**: Fire/explosion
- **Generation of unstable intermediates**: Explosion
- **Implosion from Glassware fatigue or vacuum**
- **Frostbite from liquid Nitrogen**
- **Explosion from liquid oxygen condensation**
- **Explosion due to inert gas over pressurization**
- **Explosion due to heating closed diffusion pump**

Schlenk Line
Example: Common SOP (Hydrogenation)

1. **Introduction**

Hydrogenation/hydrogenolysis reactions are generally carried out using appropriate transition metal catalysts such as Pd, Pt, Rh, Ni, and Ru. Various functional groups can be reduced with hydrogen using a suitable catalyst and appropriate solvents. However, because of the inconvenience of using a hydrogenation apparatus or pressure bottle for small scale laboratory use, hydrogenations are usually only when other more convenient reagents are not up to the task (for example, carbonyl reductions are usually done using boron or aluminum hydride reagents).

![Hydrogenation Reaction](image1.png)

2. **Setup (ambient pressure hydrogenation)**

- Assemble Glassware (Figure 2; a detailed process is described in appendix 1).

![Setup Diagram](image2.png)

3. **General use procedure (Ambient pressure hydrogenation)**

- Remove stopper and add catalyst (wet catalyst is preferred) to the reaction vessel under inert atmosphere (slight nitrogen pressure may apply from the Schlenk line, higher flow of nitrogen will blow the catalyst powder) replacing the stopper once addition is complete.
- Add desired solvent to reaction vessel with precaution. **Best Practice: All of the catalyst must be submerged into the solvent inside the flask.** Never leave the dry catalyst on the wall of the flask. Add substrate to the reaction flask using solvent followed by nitrogen purging.
- Replace nitrogen with hydrogen supply and slowly start bubbling hydrogen into the reaction mixture.
- Monitor the reaction prudently and if possible do not leave the reaction unattended overnight.
- Check the completion of reaction using suitable chromatography.
- Once the reaction is complete, replace hydrogen with nitrogen in order to remove remaining hydrogen from the reaction mixture.
- After complete conversion of the substrate into the product, filter the reaction mixture carefully using a Celite® pad and filter paper for the recovery of the catalyst (detailed filtration process is explained in appendix B).
- Wash the Celite® pad with a mixture of methanol and water (50 mL).

4. **Safety considerations**

The major safety concern for hydrogenation reactions is fire and explosion due to the pyrophoric nature of the catalyst and pressure. Also, hydrogen and flammable solvents are involved in the process. The catalytic hydrogenation of aromatic nitro compounds is a well-defined class with a high hazard potential. Thus applying a systemic approach of risk analysis is crucial. Perform a thorough literature search about substrate/intermediate reactivity and catalyst before starting the reaction.

- All catalysts must be handled prudently because of their high reactivity before or after use.
- Never use gas burners and open flames near to hydrogenation set-up.
- Some hydrogenation reactions are exothermic and may lead to an increase in pressure inside the vessel. **Best Practice:** select a vessel appropriate for the experiment such as a steel bomb, pressure vessel and Parr apparatus (http://www.parrinstruments.com).
- Reduction of nitro compounds requires higher temperature and alcoholic solvents. In case of a leak, a flammable vapor cloud will arise and most likely will ignite.
- Review the operating procedures for the apparatus and inspect the vessel before each experiment. Glass vessels with a crack are at risk to break under pressure (**Appendix 1**).
- Remove all oxygen from the vessels/solutions before adding hydrogen.
- Stay well below the rated safe-pressure limit of the vessel or steel bomb due to exothermicity or intermediate unpredictability.
- Monitor reaction prudently and do not leave reaction unattended.

5. **Hazards and Control**

5a. **Hazard identification**

Hydrogenation catalysts are pyrophoric when hydrogen is absorbed on the catalyst surface. Hydrogen gas is flammable and difficult to detect the leaks. The primary hazard associated with any form of hydrogen is unintentionally producing a flammable or detonable mixture leading to a fire or explosion.

5b. **Hazard control**

PPE: Safety glasses/goggles, gloves (nitriles/Nonex) and cotton blend lab coat. Nitrile gloves are good for dexterity purpose but are combustible.
Common chemicals used for Biochemical Manipulations:

- BrDu; Ethidium bromide
- Sodium azide
- Phenol:chloroform
Conclusions

- Laboratory safety inspections enhance overall laboratory safety and awareness
- Improves connectivity and relations between safety and labs/department
- Reduces communication gaps between safety and researchers
- Aids to know about the chemical process and safety mechanism
- Provides mechanism to improve the LSCHPs and SOPs for chemical manipulations.
Acknowledgement

Dr. Jeff Zebrowski, CHO
Dr. Paul Umbeck, Director EH&S
Dr. Rob McClain (Chair campus chemical safety committee)
Chemistry faculty & staff
EH & S Staff