

Safety Seminar: Handling of Dangerous Chemicals

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The University of Tokyo, Department of Chemistry
Environmental Safety Committee

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Handling of highly reactive compounds

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Lithium aluminum hydride (LiAlH_4 , LAH)

LiAlH_4 Gray-white powder. Strong reductant, often used for the reduction of esters and amides.



Reacts violently with water, even with moisture in the air. For synthetic purposes, **anhydrous organic solvents** must be used. Pure reagent is very reactive, it may ignite from **static electricity**, and it is especially dangerous in combination with volatile solvents (ether, etc.). In case of fire, **sand or powder extinguisher** must be used.

LAH: Caution Points (1)

- ❑ Weight LAH just before use. Use **well dried glassware and anhydrous solvents**. Add LAH **TO** the solvent, the opposite may start a fire if the solvent is not dry. Quite often dangerous procedures are reported in the literature → evaluate the hazards of YOUR reaction and procedure!
- ❑ Don't use paper to weight LAH, **use glassware such as a beaker**.
- ❑ If you spill LAH, don't wipe it with **paper**, it will ignite. Use a small broom and carefully clean it.

LAH: Caution Points (2)

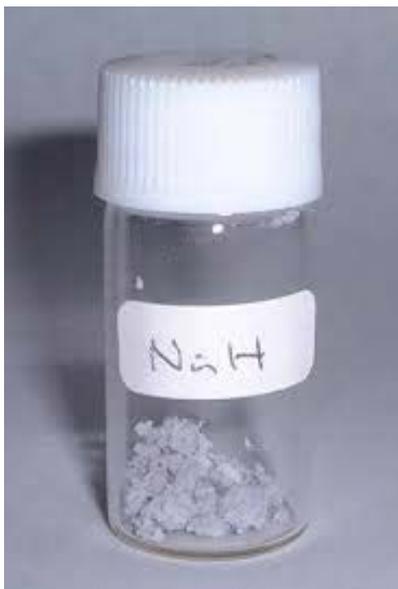
- ❑ To dispose of a large amount of LAH: under inert atmosphere disperse it in anhydrous ether, then slowly add ethyl acetate with cooling, and after that add diluted HCl with stirring. For a small amount (less than 50 mg), you may also slowly add it to lots of iced water. These operations **must be done in a fume hood**.
- ❑ In case of fire, **use sand or powder extinguisher**. Never use carbon dioxide extinguisher, it spreads the fire and reacts with LAH.

Recent Examples of Accidents

- When adding 10 g of LAH to a solution of a substrate, instead of slowly adding it over 1 hour, by mistake a large amount of LAH was dumped in. A violent reaction occurred, the reaction mixture started spewing out from the flask, and the ether vapours instantly caught fire.
- To a 500 mL flask containing 2 g of LAH, 100 mL of THF was added at once. The solvent (probably not dry) caught fire, and in panic the flask was dropped on the floor, spreading the fire.

Sodium Hydride (NaH)

NaH Gray to white powder. Highly flammable and corrosive, strong base often used in organic synthesis. It is insoluble in most organic solvents, and reactions take place at the surface.



NaH reacts violently with water, generating H₂ and NaOH. It is typically available as a 60% oil dispersion, which is safer to handle. The oil can be washed away with hexane or pentane. Oil-free, >90% reagent is also commercially available, but it is highly reactive and should be handled under an inert atmosphere such as in a glove box.

Caution Points in Handling NaH

- ❑ Don't use paper to weight the NaH dispersion, **use a beaker or other glassware**
- ❑ If you spill LAH, don't wipe it with **paper**, it will ignite. Use a small broom and carefully clean it.
- ❑ To dispose a large amount of NaH, suspend it in toluene or hexane under an inert atmosphere, and slowly add alcohol, and then water. Cooling is recommended. For a small amount (less than 50 mg), you may also slowly add it to lots of iced water. These operations **must be done in a fume hood**.
- ❑ In case of fire, **use sand or powder extinguisher** .

Recent Example of an Accident

- While weighting NaH using weighting paper, when about 0.3 g of reagent were added , it ignited. The burning paper was placed on a rubber mat, and after the fire died out (about 30 s), the remaining reagent was wiped with a cloth wetted with acetone and water. A 1 cm hole was left on the rubber mat.

Metallic Sodium (Na)

Na Silver color, soft metal, strong single-electron transfer reagent. Reacts with protic solvents with generation of H₂.



Highly reactive metal, **reacts violently with water**. Touched with bare hands, it reacts with skin moisture to generate alkali base and burn the skin. Readily oxidized in air, covers with a layer of oxide. It reacts with protic solvents such as alcohol, but it doesn't react with ether or hydrocarbons. It is typically stored under paraffin oil.

Caution Points in Handling Na

- ❑ **Reacts violently with water**, so remove all water sources when handling Na; for reactions, use anhydrous solvents.
- ❑ For weighting, place a beaker containing hydrocarbon on the scale, tare it, then rapidly cut small pieces of Na and add them to the beaker.
- ❑ The Na leftovers should be destroyed by adding them slowly to isopropanol **in a fume hood**.
- ❑ In case of fire, **use sand or powder extinguisher**.

Recent Example of an Accident

A mixture of benzophenone / Na left over after distillation was placed under alcohol in a fume hood, in order to destroy Na. The alcohol slowly evaporated, and the vapors caught fire, which destroyed the fume hood.



Disposal of benzophenone / Na (1)

Use a metallic bucket in a fume hood, far away from flammable compounds. Use an appropriate amount of alcohol (isopropanol best, ethanol also ok). Have sand and/or a fire extinguisher (powder or CO₂) handy. Also, it is recommended to have a lid for the bucket.

(1) Slowly add the benzophenone / Na contents from the flask to the bucket with alcohol. Use a spatula and hexane if necessary.



Disposal of benzophenone / Na (2)

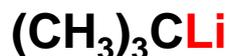
(2) If solids are left, carefully cut them under alcohol and allow Na to react. Filter them off, and further crush/cut them and treat Na with alcohol. When all the sodium seems reacted, you can carefully treat the solids with water. The alcohol used for destroying Na should be slowly added to water. Don't leave the solution overnight.

Caution: sodium covers with oxide, which is not soluble in alcohol, but dissolves in water. Upon adding water, sudden reaction may occur.

An alternative to benzophenone/Na distillation is the solvent purification system, or drying the solvent over molecular sieves.



Alkylolithiums (*n*- / *s*- / *t*-BuLi)



n-, *s*-, *t*-butyllithium

Typically available as a solution in hydrocarbon or ether. Often used in synthesis as a strong base. Reactivity order (and danger order): *n*- < *s*- < *t*-.



Extremely sensitive to water and air. *t*-BuLi ignites at the top of the needle! Must be used under an inert atmosphere, use well dried solvents, avoid anything protic. Typically used to generate organolithium intermediates *in situ* by deprotonation or halide exchange.

Caution Points in Handling Alkylolithiums (1)

- When taking alkylolithium with a syringe, make sure to dry and flush the syringe with argon, and also flow an argon stream through the reagent bottle. **The bottle must be firmly fixed with a clamp.** When handling *t*-BuLi, **a gas-tight syringe (or a plastic syringe) fitted with a Luer lock** must be used. Sealing the lock with tape, and use of a “bus module” are recommended.



Caution Points in Handling Alkylolithiums (2)

- ❑ Use a large enough syringe. It reduces the danger of pulling the plunger out.
- ❑ After use, rinse the syringe and needle with dry hexane or toluene, then treat the residue with alcohol, water, then diluted HCl.
- ❑ For a large amount of alkylolithium (> 50 mL), transfer by cannulating is preferred.
- ❑ In case of fire, use sand or powder extinguisher.

Recent Example of an Accident

- When taking a *t*-BuLi with a syringe, the needle broke, and the spilled reagent ignited. It seems that the needle was old, or not properly locked; make sure to double check before use.

There are many examples of accidents that occurred because the needle was not properly locked and came out from the syringe!



Sangji case (UCLA, 2009):

<https://cen.acs.org/articles/87/i31/Learning-UCLA.html>

General Caution Points (1)

1. Keep the lab **clean**.
2. Don't keep many reagents and flammable materials (including paper) on your bench. It is forbidden to keep reagent bottles on the floor.
3. Protect yourself! **Goggles, lab coat, gloves**, etc.
4. **Don't do experiments late at night or on weekends**, especially dangerous ones. Never do experiments alone. Let others know when you handle dangerous stuff.

Safety manual:

http://jimubu.adm.s.u-tokyo.ac.jp/inside/images/0/07/2017Safety_Manual.pdf

General Caution Points (2)

6. Familiarize yourself with the place of the **emergency door** and of **extinguishers**, and educate yourself on their types, use, etc.
7. When performing experiments overnight, including keeping instruments on for a long time, make sure to check safety, and that emergency contact is visible placed.
8. In rooms where volatile organic compounds are used, **open fire is forbidden**.

Electric Instruments (1)

If handling of electric instrument or appliances (power tap, etc.) is not appropriate, there is danger of electric shock or fire initiated by overheating or electric spark.

Please follow the safety points below.

- ❑ **If you feel an electric sting when you touch an instrument of appliance**, make sure to immediately turn it off and call a specialist. There is a high probability of an electric leak.
- ❑ **Check the electric cords for any fatigue or cuts**
Immediately replace old or damaged cords, they are a high hazard.
- ❑ **If the screws or connectors, etc. are loose**, use an insulated screwdriver to tighten them

Electric Instruments (2)

- ❑ If the color of the cords changes, or if they are hot, there may be an overcurrent, immediately turn off
- ❑ If there is an odd smell or sound, immediately turn off
- ❑ Make sure that the earthing is properly connected
- ❑ Make sure that there are not too many plugs in one outlet: dust, etc. may easily cause a fire
- ❑ Make sure that the instruments connected to one outlet do not exceed the maximum current capacity

If you use an outlet at overcapacity for a long time, there is a high hazard of fire.

Electric Instruments (3)

- ❑ Check the resistance of the earth connection at least once a year.
- ❑ **Prevent electric leaks and short-circuits**
Use an earth leakage circuit breaker (ELCB) or a circuit breaker
- ❑ **Check instruments for water leakage and if electric cords are not strangled under heavy objects**
- ❑ **Use an appropriate cord and plug for the current used**
If not, overheating and fire may occur.
- ❑ Check insulating equipment every 6 months