

Safety Module

Safety Topic: Titration of Butyl Lithium Solutions

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- **Purpose** – To determine the exact concentration of active base in a bottle of commercial butyl lithium (BuLi) reagent. The concentration of active base often decreases over time as the reagents is quenched by water, oxygen, or otherwise decomposes.
- **Equipment** – Bottle of BuLi, medium cork ring, *N*-benzyl benzamide, anhydrous THF, small round bottom with stir bar and septa, nitrogen balloon, 1 mL syringe, cold bath, aq ammonium chloride, 50:1 hexanes:methanol solution.
- **Process** – To a flame dried 10 mL round bottom with a stir bar was added ~100 mg of *N*-benzylbenzamide (record the exact mass). The flask was evacuated and back filled with nitrogen and ~5 mL of THF was added. The *N*-benzylbenzamide was stirred to fully dissolve. The flask was cooled to -40 °C for *n*-BuLi and -78 °C for *t*-BuLi or *s*-BuLi. The bottle of BuLi is place into a cork ring to avoid being knocked over. A nitrogen balloon was placed into the bottle. The BuLi is added to the flask by syringe drop-wise until a blue color just persists. The concentration of butyl lithium was back calculated from the exact mmols of *N*-benzylbenzamide used and the volume of butyl lithium solution added. This is typically repeated 3x and averaged for an accurate result.
- **Specific considerations** – Be sure to hold the syringe and needle to prevent disconnection at the joint especially as you empty the syringe. Only use a nitrogen balloon on bottles of pyrophoric reagents not “spaghetti lines” or nitrogen lines connected directly to a manifold. (This can result in over pressurization of the bottle, disconnection of the needle from the syringe, and/or a stream of pyrophoric reagent from the bottle.)
- **Waste handling** – The resultant amide solutions in the flask are quenched with sat. aq. ammonium chloride and transferred to an organic waste container. Quench remaining BuLi in the syringe by adding it slowly to a 50:1 solution of hexanes:methanol. Empty or “bad” organometallic reagents in sealed “Sure-Seal” bottles can be removed by EHS without further treatment. Only an individual waste label sticker on the bottle with the contents spelled out is necessary.
- **For more information see** –
 - Handling pyrophorics https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Aldrich/Bulletin/al_techbull_al164.pdf
 - Titration of organometallic reagents www.chemistry.mcmaster.ca/emslic/Assets/Titrating%20RLi.pdf
 - Pyrophoric and water-reactive substrates <https://ehs.yale.edu/restricted-particularly-hazardous-substances>

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