## Standard Operating Procedure (SOP)

Author:	David Shultz	Date:	02/13/2025		
User(s)					
PI/Advisor:	David A. Shultz				
Process Name:	Azeotropic Removal of Water from a Reaction Mixture				
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This SOP details the procedure for lithium-halogen exchange using *tert*-butyl lithium. <u>This reaction should only be conducted after (1) observing an experienced</u> <u>graduate student or postdoc perform the procedure at least once, and (2) under</u> <u>direct supervision of an experienced graduate student or postdoctoral researcher</u>.

I. Purpose
This SOP details the step-by-step procedure to perform azeotropic removal of water from a heated reaction solution. It is the responsibility of the user to read and acknowledge their understanding of this SOP.
<ul> <li><u>Prior to</u> using the equipment, the users must:</li> <li>1- Read this SOP.</li> <li>2- Be a registered worker or formally allowed to enter the lab with the corresponding safety trainings.</li> </ul>
II. Outline of Method
<ol> <li>Use of correct PPE (disposable gloves, protective eyewear, and lab coat)</li> <li>Since water is generated in the reaction (<i>e.g.</i>, Knoevenagel condensation or Fischer esterification), there is no need to oven dry the glassware.</li> <li>Assemble pictured below. The components include a 1-, 2-, or 2-neck round bottom flask containing a stir bar, solvent, substrate, and reagents. A Dean- Stark (stopcock) or Barrett (no stopcock) trap is attached to the center neck, and a water-cooled condenser (caution! Use wire or Teflon clamps to secure water lines to condenser to insure they do not detach when pressure changes. Use of a circulating water pump is STRONGLY recommended) is attached to the top of the trap. The condenser can be fitted with a duck head leading to an inert gas line, but in most cases, a 180° CaCl<sub>2</sub> drying tube will suffice. (Such reactions are not typically under inert gas, so one does not want to expel oxygen into the gas line.)</li> </ol>
<ol> <li>Most condensation reactions require heat, but consult the published procedure you're following. For applying heat, use an electric heating mantle</li> </ol>



	attached to a variable transformer. Slowly heat the reaction mixture to			
	reflux. You can add a thermometer and appropriate adapter to one of the			
_	necks of the reaction flask.			
5.	Common solvents used to azeotropically remove water include benzene and			
	toluene. The latter is less toxic, but bolis higher (TTU C VS. 80 Tor			
6	When the reaction flask reaches sufficient temperature to boil the solvent			
0.	the azeotropic mixture of solvent and water by-product will condense in the			
	water-cooled condenser and collect in the trap (a Dean-Stark trap is			
	preferable since the denser water can be drained from the trap using the			
	stopcock).			
7.	When no more water collects in the trap, the reaction is complete.			
8.	Turn the variac off and allow the reaction to cool to room temperature.			
9.	Ensure complete reaction by performing TLC analysis.			
10	. Some procedures call for adding a denydrating agent such as acetic			
11	Complete procedure as per published instructions			
	Hazaros			
	Fume hazard (benzene is toxic)			
	<ul> <li>Actu catalysis call cause builts</li> <li>Fire Hazard (toluene, benzene, and alcohols are flammable)</li> </ul>			
IV	Laboratory Equipment Materials & Personal Protective Equipment			
(P	PE)			
•	• Materials: Alcohols, toluene or benzene solvent, substrates (aldehydes			
	or carboxylic acids or their derivatives)			
	PPE: safety goggles, lab coat, and gloves.			
۷.	Emergency Procedures			
In	case of emergency, dial 911 or 919-515-3000. In case of mercury spill,			
CC	ontact 919-515-7915 (EHSA).			
Contact Emergency: David A. Shultz (919) 656-9774				
VI	Relevant Photos of Glassware Setups			
٠	Below is a photo of a 1-neck flask with a Dean-Stark trap attached. The glass			
	wool and foil act as insulation to prevent condensation of azeotrope/solvent			
	vapor prior to reaching the condenser. Only the bottom of the condenser is			









## VII. Authorized Personnel

Record acknowledgements that the SOP has been read and understood. Authorized Users:

I have read this Standard Operating Procedure, understand the contents, have been trained on implementing the contents, and will utilize this procedure without exception.

NAME (print)	Signature	Date	PI Initial

