

Laboratory Safe Operating Procedure

Process: Preparation and use of diazomethane

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Location: CHEM W5-54AA

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Hazard Identification:

- Diazomethane is toxic
 - Causes pulmonary edema if breathed in; also cited as a carcinogen
- Diazomethane is explosive
 - Do not use ground glass joints; avoid using scratched glassware as sharp surfaces can cause crystallization and explosion
 - A Teflon-coated stir bar should be used to stir the reaction; do not swirl by hand
 - Do not expose the apparatus to direct sunlight or strong artificial light, as this may cause an explosion
 - Use ether to prepare and use diazomethane as higher boiling solvents have lower vapour pressure, leading to a greater concentration of diazomethane in the vapour and an increased risk of explosion

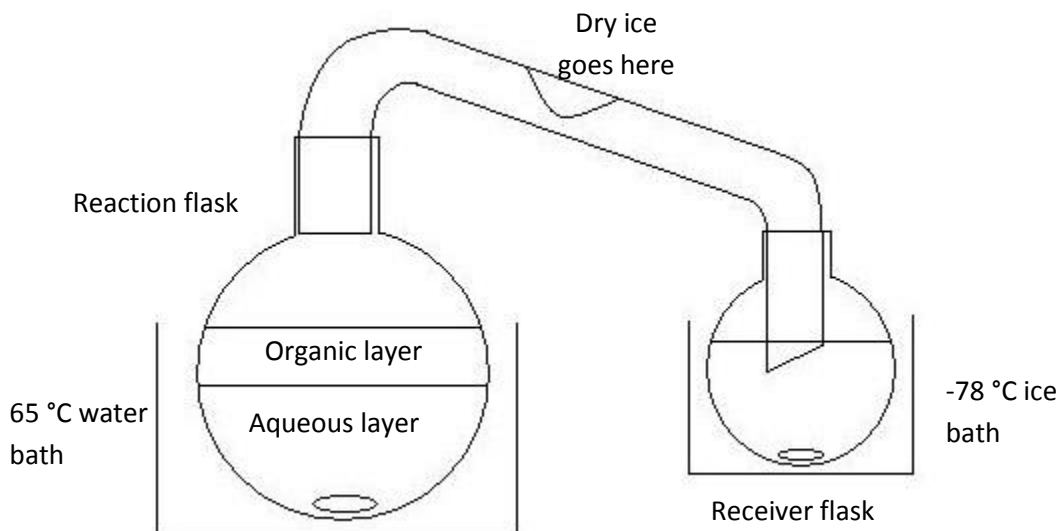
Procedure:

Reagents to make 2.1 mmol of diazomethane (adjust as necessary):

Reagent	Molecular Weight	Weight/Vol Used	Moles Used	Equiv. Used	Properties
Diazald (N-methyl-N-nitroso-p-toluenesulfonamide)	214.24	0.50 g	0.0023	1.0	mp 61-62 °C reactive, irritant
potassium hydroxide	56.11	0.50 g	0.0089	3.8	
ethanol	46.07	1.0 mL	0.017	7.3	d 0.789; bp 78 °C
water	18.02	0.8 mL	0.044	19	
diethyl ether	74.12	4.5 mL	0.043	18	d 0.706; bp 34.6 °C

Note: special glassware for the preparation of diazomethane can be found in W5-54AA; Diazald is kept in the fridge

<2 mmol: (Glassware designed by Dr. Graham Murphy)



Add ethanol, water, and potassium hydroxide to reaction flask. Stir and heat the reaction flask to 65 °C using a water bath to dissolve the KOH.

Set up distillation arm with dry ice, receiver flask containing your acid chloride in ether, -78 °C ice bath under receiver, and water bath under reaction flask.

Add solution of Diazald in ether to the reaction flask in one portion, replacing the distillation arm quickly. Note that the end of the distillation arm should be below the level of the solvent in the receiver flask.

Once diazomethane has stopped distilling over (no more bubbles in reaction flask) and the yellow colour has disappeared, this assembly can be removed from the receiver flask and cleaned. Note that more ether may have to be added to complete transfer of the diazomethane from the reaction flask to the receiver (if the yellow colour remains).

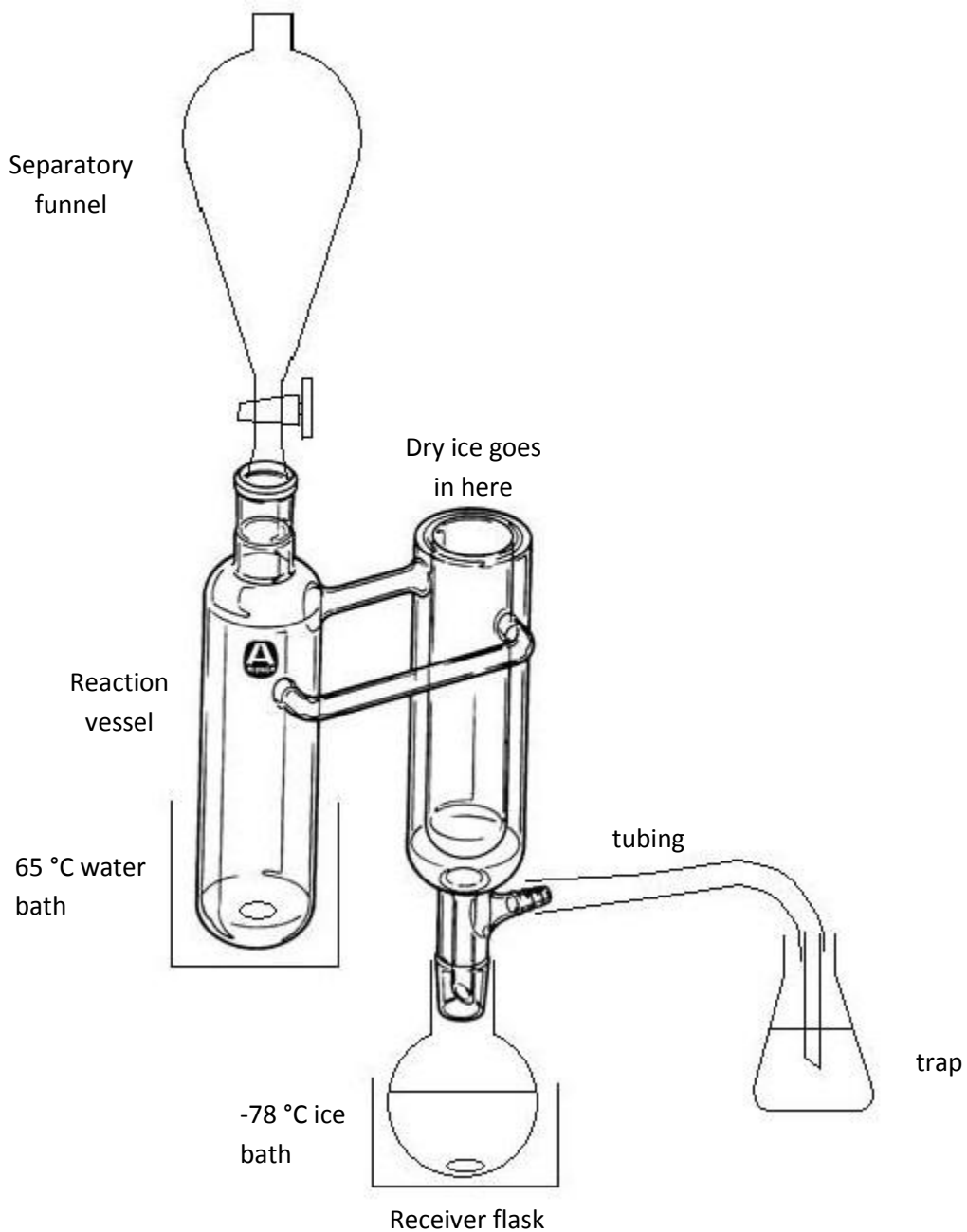
1 – 50 mmol:

Set up apparatus as shown (next page).

Add ethanol, water, potassium hydroxide to reaction vessel. Add dry ice and acetone to condenser. Add ether to the trap (Erlenmeyer flask), making sure the end of the glass tube is below the level of the ether. Have receiver flask in -78 °C ice bath, and the reaction vessel in a 65 °C water bath.

Add the ether and Diazald to the separatory funnel. Begin adding this mixture dropwise to the reaction vessel. The addition should take 20 to 30 min.

Once the addition is finished, add more ether to the separatory funnel and add this until the reaction mixture is colourless. Once there is no more bubbling from the reaction vessel, this assembly can be removed from the receiver flask and any excess diazomethane in the reaction vessel and in the trap can be quenched with acetic acid.



Notes:

- The temperature of the water bath should never exceed 70 °C
- The reaction should always be carried out in the fume hood; a blast shield should be used for large scale preparations
- The specialized glassware should be rinsed with water and acetone; it should never be scrubbed with a brush, as this may scratch it and increase the risk of explosion
- Never store diazomethane; make it only as needed

Engineering Controls:

- Fume hood should be on and functioning

Administrative Controls:

- Any person attempting this procedure should review and sign this document, as well as watch someone perform the procedure who has done it before (Nargess, Venkata)
- Never attempt this procedure when alone in the lab

Personal Protective Equipment:

- Safety glasses
- Gloves
- Lab coat
- Blast shield

Emergency Response Procedures:

- Any person attempting this procedure should be aware of the location of the fire extinguisher, eye wash station, and safety shower. Additionally, this person should be trained in the use of the fire extinguisher or have someone nearby who is.

References:

1. "Aldrich Technical Bulletin AL180: Diazald® and Diazomethane Generators"
http://www.sigmaaldrich.com/etc/medialib/docs/Aldrich/Bulletin/al_techbull_al180.Par.0001.File.tmp/al_techbull_al180.pdf (Accessed Jan 12, 2012)
2. Moore, J. A.; Reed, D. E. *Org. Synth.* **1961**, *41*, 16 (and references therein).

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Approved by: Professor Frederick G. West

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