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| **Brueckner Lab-Specific Standard Operating Procedure (LSOP)****Diazald and Diazomethane Generators** |
| **Principal Investigator(PI):** Christian Brueckner |
| **Building:** Chemistry | **Lab(s) Covered by LSOP:** R413/R415 |
| **Department:** Chemistry | **Lab Phone Number(s):** 6-6596/6-6598 |
| **SECTION 1 – HAZARDOUS CHEMICAL(S) or PROCESS(ES) and HAZARDS INVOLVED** |
| Although diazomethane can be handled safely as a dilute solution in an inert solvent, it presents several safety hazards: it is extremely toxic and highly irritating:Diazomethane is a yellowish, explosive, and highly toxic gas with a boiling point of -23oC and a melting point of -145oC. It can be explosive in its pure and undiluted form but has also been known to detonate unexpectedly in the diluted form. Bright light, sharp/rough edges, and scratched glassware all have been known to trigger diazomethane explosions, as have certain metal ions in drying agents (e.g., CaCl2, MgSO4, CaSO4, Na2SO4).Diazomethane is an irritant and highly toxic (more toxic than hydrogen cyanide) by inhalation or contact with skin or eyes. Diazomethane may cause pulmonary edema when inhaled in high concentrations. Diazomethane is also a sensitizer, and long-term exposures can lead to asthma-like symptoms, including chest discomfort, headache, weakness, and/or collapse. The time-weighted average maximum allowable concentration for diazomethane is lower than that of hydrogen cyanide illustrating its extremely hazardous nature.Diazomethane is useful as a powerful and fast acting alkylating agent and carbene source for laboratory-work; however, these same characteristics make it an equally powerful genotoxic compound. Diazomethane has been cited as a carcinogen. Inexperienced laboratory workers should not attempt to create or manipulate diazomethane reactions without first getting guidance from senior laboratory personnel. Whenever possible, trimethylsilyldiazomethane (also known as TMS-diazomethane, CAS# 18107-18-1) should be used in place of diazomethane because it is less likely to explode |
| **SECTION 2 – ADMINISTRATIVE CONTROLS** |
| * Anyone using the chemicals and procedures described herein needs to have undergone the annual EH&S [Chemical Hygiene Training](http://www.ehs.uconn.edu/Chemical/?p=training)
* Be aware of the applicable safety data sheets (SDS): <http://www.msds.com>
* [Working Alone](http://policy.uconn.edu/2012/07/30/working-alone-policy/) is not permitted when using chemicals or processes described in this LSOP.
* Any reaction flask containing diazald/diazomethane need to be clearly labelled as such.
* Diazomethane should be generated only during normal business hours (i.e., 8:00 am-5:00 pm Mon-Fri).
* An eyewash and safety shower must be in the immediate work area where diazald is used.
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| **SECTION 3- ENGINEERING CONTROLS** |
| * Diazomethane must only be generated from Diazald® in the dedicated flame-polished glassware.
* All research with diazomethane must be conducted in a chemical fume hood, under dry conditions, with the sash at the lowest working height and with sliding sash panels (if applicable) aligned to form a barrier between the researcher and the experiment.
* Chemical fume hoods must have been tested by EHS within the last year. If the hood is not working properly, contact Facilities (486-3113) to repair the hood or EH&S to retest (486-3613).
* All reactions using this material must be performed in a properly operating fume hood.
* Avoid contact with skin, eyes and clothing. Wash hands before breaks and immediately after handling the product.
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| **SECTION 4 – WORK PRACTICES** |
| * Diazomethane should not be generated or handled when working alone.
* Diazomethane must only be generated from Diazald® in the dedicated flame-polished glassware.
* You must have read the Aldrich procedure before commencing with the diazomethane generation
* All containers must be clearly labeled with the chemical name and hazard classes and kept tightly-sealed.
* Used equipment used to generate diazomethane must be handled carefully since product residues may still be harmful: Leave all contaminated glassware in the fume hood for at least a day.
* Be aware that the rotary evaporator used to evaporate solvent used to work up diazomethane reactions may still contain diazomethane – rinse carefully right after use.
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| **SECTION 5 – PERSONAL PROTECTIVE EQUIPMENT (PPE)** |
| * At a minimum, a lab coat, long pants as well as closed-toed footwear and chemical safety glasses that meet ANSI standard Z-87.1 must be worn when handling diazald/diazomethane
* Work involving diazomethane should be carried out only within a properly functioning chemical fume hood with some form of shielding being used.
* Diazomethane distillations must use a blast shield that protects the researcher from the apparatus without hindering his/her ability to manipulate the experiment.
* Standard laboratory personal protective equipment (PPE) (laboratory coat, safety eye wear, and gloves) should be used when working with diazomethane.
* Due to the chemical’s explosive and highly toxic nature, a face shield and double gloving are recommended.
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| **SECTION 6 – STORAGE** |
| Storage of diazomethane solutions is not permitted! Prepare the smallest amounts of diazomethane needed each time you need it. |
| **SECTION 7 – SPILL AND ACCIDENT PROCEDURES** |
| * Spills of diazomethane should not be handled.
* Activate the fire alarm and call **911** in case of a large diazomethane solution (>500 mL) spill outside the fume hood.
* Close door(s) to lab and post a “**NO ENTRY**” sign(s) explicitly mentioning the type of hazard
* Do not re-enter area until instructed to do so by an emergency personnel and/or all solvents have evaporated.
* If a small spill happens inside a chemical fume hood, immediately close the sashes and let it evaporate; activate the emergency exhaust.

**Report any incident to the PI and fill out the** [**accident form**](https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0ahUKEwiF3bPe1dPXAhVRRN8KHX4wDf4QFggmMAA&url=https%3A%2F%2Fchemistry.uconn.edu%2Fwp-content%2Fuploads%2Fsites%2F1259%2F2015%2F09%2FIncident-Report-Form.doc&usg=AOvVaw3Uov8IQ2Z-Kan) |
| **SECTION 8 – FIRST AID PROCEDURES** |
| *Eyes** Eyewash station that can provide quick drenching or flushing of the eyes must be immediately available within 10 seconds travel time for emergency use. Ensure the locations of the eyewashes and safety showers, and how to activate them, are known prior to an emergency.
* Should be treated by flushing with large quantities of water for 15 minutes. Adding soap for skin exposures can help neutralize diazomethane.
* Have another person from the lab dial **911** and specifically mention diazomethane exposure.
* Continue flushing the eyes until emergency personnel arrive.

*Skin** Safety drench shower must also be available within 10 seconds travel time from where diazomethane is used. Ensure the locations of the eyewashes and safety showers, and how to activate them, are known prior to an emergency.
* Should be treated by flushing with large quantities of water for 15 minutes. Adding soap for skin exposures can help neutralize diazomethane.
* Have another person from the lab dial **911** if intense skin irritation is observed and specifically mention diazomethane
* Keep applying water to rinse the affected area(s) until emergency personnel arrive

*Ingestion** Have another person from the lab dial **911** and specifically mention diazomethaneexposure

*Inhalation** Immediately exposure to fresh air followed by prompt care at an emergency room. Because a Safety Data Sheet (SDS) of diazomethane is not available (it is too short-lived and dangerous to transport), take the SDS for TMS-diazomethane to inform emergency health care workers of diazomethane’s hazards
* Dial **911** and inform emergency responders that the accident involved diazomethane

**Report any incident to the PI and fill out the** [**accident form**](https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0ahUKEwiF3bPe1dPXAhVRRN8KHX4wDf4QFggmMAA&url=https%3A%2F%2Fchemistry.uconn.edu%2Fwp-content%2Fuploads%2Fsites%2F1259%2F2015%2F09%2FIncident-Report-Form.doc&usg=AOvVaw3Uov8IQ2Z-Kan) |
| **SECTION 9 – WASTE MANAGEMENT** |
| * Do not dispose of diazomethane solutions via normal waste streams due to its explosive and highly toxic nature. Quench diazomethane first and then dispose of it through normal waste streams.
* To quench excess diazomethane, add a few drops of acetic acid into the reaction mixture. Add drops of acetic acid until the yellow color of the diazomethane disappears and it stops producing nitrogen gas bubbles. This also applies to the residual KOH solution left over from the diazomethane generation procedure. Add acetic acid until the yellow color disappears. The excess diazomethane will react with the acetic acid to produce methyl acetate. You can add the decolorized solution to the regular waste stream.
* All waste must be labeled with “Hazardous Waste” stickers or tags, use full chemical names to describe the waste (i.e., no chemical abbreviations or symbols), be stored in sturdy containers with tight-fitting caps or lids, and be stored alone or with other compatible chemicals.
* Hazardous wastes must be stored at or near a green “Satellite Accumulation Area” sign prior to disposal by EHS. Once the containers are 80% filled, fill our EH&S chemical [waste pickup form](http://ehs.uconn.edu/Regulated%20Waste%20Management/index.php)
* The [Chemical Waste Disposal Manual](http://ehs.uconn.edu/Chemical/ChemWasteDisp.pdf) must be used as a reference.
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| **SECTION 10 – DECONTAMINATION PROCEDURES** |
| Work Area | * Equipment and bench tops using soap and water and properly dispose of all chemical and contaminated disposables as hazardous waste
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| Personal Hygiene | * Use standard chemical hygiene practices regarding PPE (see above).
* Wash hand thoroughly after handling diazald/diazomethane
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| **SECTION 11 – SPECIFIC PROCEDURE** |
| Use of Aldrich Mini Diazald® apparatus setup (procedure from Aldrich); consult the documents that are part of the apparatus.**Description*** This unit is designed for the preparation of 1 to 50 mmol of diazomethane from Diazald® or a 25 wt. % solution of Diazald® in 2-methoxyethyl ether (diglyme), and consists of a reaction vessel and condenser in one compact piece (with 19/22 Clear-Seal® joints).
* The only additional equipment needed consists of an addition funnel and receiver (both of which must have Clear-Seal® joints).
* The major feature of this apparatus is the “cold-finger” in place of a water-jacketed condenser. When filled with dry ice/isopropanol slush, the condenser very efficiently prevents diazomethane/ether vapor from escaping into the atmosphere. A typical experimental procedure employing this apparatus follows.

**Procedure for an alcohol-containing ethereal solution** * Fill the condenser with dry ice, then add isopropanol slowly until the cold-finger is about one-third full. Add ethanol (95%, 10 mL) to a solution of potassium hydroxide (5 g) in water (8 mL) in the reaction vessel.
* Attach a 100 mL receiving flask (with Clear-Seal® joint) to the condenser and cool the receiver in dry ice/isopropanol bath. Provide an ether trap at the side-arm (the glass tube must have firepolished ends). The trap should be cooled in a dry ice/isopropanol bath.
* Place a separatory funnel (with Clear-Seal® joint) over the reaction vessel and charge the funnel with a solution of Diazald® (5.0 g, 23 mmol) in ether (45 mL) or 20 mL of 25 wt. % Diazald® in diglyme (5 g, 23.3 mmol) and 30 mL of ether.
* Warm the reaction vessel to 65 °C with a water bath and add the Diazald® solution over a period of 20 minutes. The rate of distillation should be approximately the rate of addition. Replenish the cold-finger with dry ice as necessary.
* When all the Diazald® has been used up, slowly add 10 mL of ether and continue the distillation until the distillate is colorless.
* If the distillate is still yellow, add another 10 mL of ether and continue the distillation. The ether will contain 700 mg to 900 mg (16.6 mmol to 21.4 mmol) of diazomethane depending on whether Diazald® or Diazald® in diglyme is used respectively.

**Procedure for an alcohol-free ethereal solution*** If an alcohol-free ethereal solution of diazomethane is required, add 2-(2-ethoxyethoxy)ethanol (14 mL) and ether (8 mL) to a solution of potassium hydroxide (2.5 g) in water (4 mL) in the reaction vessel. Distill diazomethane as above.

**Quenching*** To quench excess diazomethane (in the waste solvents), add a few drops of acetic acid into the reaction mixture. Add drops of acetic acid until the yellow color of the diazomethane disappears and it stops producing nitrogen gas bubbles. This also applies to the residual KOH solution left over from the diazomethane generation procedure. Add acetic acid until the yellow color disappears. The excess diazomethane will react with the acetic acid to produce methyl acetate.
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| **SECTION 12A. APPROVAL** |
| I have reviewed, understand and agree to follow this lab-specific standard operating procedure (LSOP) for the use of Diazald/diazomethane*.* Failure to follow this LSOP or lab-specific training guidelines is a violation of the [*University Health & Safety Policy*](http://policy.uconn.edu/2011/05/19/health-and-safety-policy/) and [*University Code of Conduct*](http://policy.uconn.edu/2011/05/17/employee-code-of-conduct/).Further approval and/or review of this LSOP by the PI is required if any of the following events occur:* A significant change in amount (i.e., doubling of the scale of reaction) or substitution of the chemicals in the procedure is planned
* A major change in the agreed-upon experimental set-up is planned (heating instead of room T, etc.)
* Any signs of a failure in safety design or equipment are observed
* Any signs or symptoms of a chemical exposure to any personnel are observed
* Unexpected and/or potentially dangerous experimental results occur (e.g., fire, uncontrolled buildup of heat and/or pressure, etc.)
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| **Researcher Name/Signature** | **Trainer Name/Signature** | **Training Date** |
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| **SECTION 12B. PRINCIPAL INVESTIGATOR CERTIFICATION** |
| I approve the contents of the lab-specific standard operating procedure listed above. |
| **PI Signature:** | **Date:** |
| **A HARD OR ELECTRONIC COPY (https://bruckner.research.uconn.edu/safety-resources/) OF EACH LAB-SPECIFIC STANDARD OPERATING PROCEDURE MUST BE READILY AVAILBALE IN THE LAB.** |