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| **Brueckner Lab-Specific Standard Operating Procedure (LSOP): Methylating Agents:  Dimethyl Sulfate ((MeO)2SO2) and Methyl Iodide (CH3I)**  **(see for separate LSOP for diazomethane)** | | | | | |
| **Principal Investigator(PI):** Christian Brueckner | | | | | |
| **Building:** Chemistry | | | | | **Lab(s) Covered by LSOP:** R413/R415 |
| **Department:** Chemistry | | | | | **Lab Phone Number(s):** 6-6596/6-6598 |
| **Chemical** | | **GHS Pictograms** | | **Definitions** | | |
| **Dimethyl Sulfate and Methyl Iodide** | |  | | **Acute Toxicity**. Severe toxicity (oral, dermal, inhalation) immediately after exposure.  **Respiratory.** Refers to aspiration hazards. Carcinogenicity, cell mutagenicity, reproductive toxicity, and organ targeting.  ***Corrosive.*** Skin corrosion/burns. May cause ocular damage. | | |
| **SECTION 1 – CHEMICAL(S) and HAZARDS** | | | | | | |
| Dimethyl Sulfate is a low volatility, combustible liquid that is toxic if ingested and can be fatal if inhaled or absorbed through skin. Can cause severe burns to digestive tract, respiratory tract, eyes, and skin. Previously used as a war gas. Carcinogen. Suspected mutagen. Suspected of causing genetic defects.  Methyl iodide is a very volatile skin and eye irritant. It is hazardous when ingested or inhaled. Severe over exposure may result in death. Classified as A2 carcinogen (suspected for human). Mutagenic for mammalian somatic cells. Mutagenic for bacteria and/or yeast. Teratogenic and developmental toxicity: N/A. | | | | | | |
| **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) * Lab-specific safety training must be provided by the principal investigator (PI) or other qualified personnel to all researchers working with dimethyl sulfate or methyl iodide. Documentation of training is required. * Read the safety data sheet (SDS) for dimethyl sulfate or methyl iodide prior to use: <http://www.msds.com> * Whenever possible, find safer substitutes or reduce the quantity of dimethyl sulfate/methyl iodide being used. * [Working Alone](http://policy.uconn.edu/2012/07/30/working-alone-policy/) is not permitted when using chemicals or processes described in this LSOP. * Experiments should be performed during normal business hours (i.e., 9:00 am-5:00 pm Mon-Fri), if possible. * Label reaction flasks containing either of the methylating agents clearly as such. * An eyewash and safety shower must be in the immediate work area where dimethyl sulfate is used. | | | | | | |
| **SECTION 3 – ENGINEERING CONTROLS** | | | | | | |
| * All research with dimethyl sulfate/methyl iodide must be conducted in a chemical fume hood with the sash at the lowest working height/with sliding sash panels to form a barrier between researcher and 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 EHS to retest (486-3613). * Use of dimethyl sulfate/methyl iodide outside of the fume hood is not permitted. | | | | | | |
| **SECTION 4 – WORK PRACTICES** | | | | | | |
| * Dimethyl sulfate/methyl iodide must be handled under the fume hood. * Keep away from incompatible materials and conditions. * Keep cool and protect from sunlight. * All containers of dimethyl sulfate/methyl iodide must be clearly labeled with the chemical name and hazard classes and kept tightly-sealed. * Empty containers of dimethyl sulfate/methyl iodide must be handled carefully since product residues (vapors + liquid) are still harmful. * The rotary evaporator used to evaporate solvents used in methylation reactions may be contaminated with the methylating agents – rinse carefully right after use. * The evaporated solvents may also still contain dimethyl sulfate/methyl iodide – dispose of all solvents, do not recycle! * The methylating agents are not to be distilled! If you think the chemical is old, dispose of the old bottle and order a new one. | | | | | | |
| **SECTION 5 – PERSONAL PROTECTIVE EQUIPMENT** | | | | | | |
| * At a minimum, a lab coat, long pants as well as closed-toed footwear and chemical safety glasses that meet American National Standards Institute (ANSI) standard Z-87.1 must be worn when handling sulfate/methyl iodide. * Nitrile gloves must be worn while handling small (up to 5 mL) quantities of dimethyl sulfate/methyl iodide; larger quantities necessitate heavy-duty butyl gloves. | | | | | | |
| **SECTION 6 – STORAGE** | | | | | | |
| * Ensure labels on original bottles remain legible and prominently displayed to identify contents. * Ensure both original and secondary containers remain intact and are stored with tight-fitting caps or lids. * Store dimethyl sulfate/methyl iodide away from heat/sources of ignition in a cool and well-ventilated place (under the fume cupboards or the ventilated organic chemicals cabinet in R413). | | | | | | |
| **SECTION 7 – SPILLS AND ACCIDENTS PROCEDURES (LARGE SPILLS)** | | | | | | |
| * Evacuate the laboratory immediately if any spill of the methylating agents has occurred outside the fume hood. * Close door(s) to lab and post a “NO ENTRY” sign spelling out the origin of the danger. * In case of a spill of 50+ mL of any of the methylating agents, activate the fire alarm and call **911** and inform them of the nature of the chemical spill. * Do not re-enter area until instructed to do so by UCFD or other emergency personnel.   **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** | | | | | | |
| First Aid - Eyes | | | 1. Immediately move to the eyewash station, hold eyelids open and flush with water. Remove contact lenses while flushing (if applicable). 2. Have another person from the lab dial **911** and specifically mention methylating agent exposure. 3. Continue flushing the eyes until emergency personnel arrive. | | | |
| First Aid - Skin | | | 1. Immediately move to safety shower or other water source and begin rinsing affected area(s). Remove contaminated clothing (if applicable) while flushing. 2. Have another person from the lab dial **911** and specifically mention specific methylating agent exposure. 3. Flush affected area(s) under safety shower for 15 minutes. 4. Keep rinsing affected area(s) until emergency personnel arrive. | | | |
| First Aid - Ingestion | | | 1. Immediately rinse the mouth with cold water. Do NOT induce vomiting. Do NOT give emetics or baking soda. 2. Have another person from the lab dial **911** and specifically mention the exposure to a specific methylating agent. | | | |
| First Aid - Inhalation | | | 1. Move to fresh air 2. Dial **911** 3. Inform emergency responders which methylating agent was involved in the accident | | | |
| **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 – HAZARDOUS WASTE MANAGEMENT** | | | | | | |
| * 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. | | | | | | |
| **SECTION 10 – DECONTAMINATION PROCEDURES** | | | | | | |
| Work Area | Equipment can be decontaminated through a rinse with copious amounts of cold water or a base bath; use surfactants. Make sure not to volatilize possible residues; use cold (!) water. | | | | | |
| Personal Hygiene | Use standard chemical hygiene practices regarding PPE.  Wash your hands after having worked with the methylating agents. | | | | | |
| **SECTION 11 – SPECIFIC PROCEDURE** | | | | | | |
| A typical use of a dimethyl sulfate/methyl iodide agent in our laboratories is described in:  Samankumara, L. P.; Zeller, M.; Krause Bauer, J. A.; Brückner, C., ‘Syntheses, Structures, Modification, and Optical Properties of *meso*-Tetraphenyl-2,3-dimethoxychlorin and Two Isomeric *meso*-Tetraaryl-2,3,12,13-tetrahydroxybacteriochlorins’ *Org. Biomol. Chem.***2010**, *8*, 1951–1965.  *meso-Tetraaryl-2,3-cis-dimethoxychlorins (****5****) and meso-tetraphenyl-2,3-cis-hydroxymethoxychlorin (****6a****). General procedure for the methylation of diolchlorins and tetraolbacteriochlorins.*  *meso*-Tetraphenyl-2,3-cis-dihydroxychlorin (**3a**) (200 mg, 3.08 × 10-1 mmol) was, under N2, dissolved in THF in a 250 ml round bottom flask equipped with a magnetic stir bar (500.0 ml) and excess (~125 mg) NaH (60% emulsion in oil) was added in portions. After stirring 30-45 min at ambient temperature, the reaction mixture turned from purple to dark green (time and colour change depend on the amount of NaH added). After this time, CH3I (0.25 mL, 12-fold molar excess per OH group to make up for evaporative losses) was added by syringe and the reaction mixture was allowed to stir for ~2 hours at ambient temperature (Caution: gloves and fume hood!). The completion of the reaction was monitored by TLC. After all the starting material was consumed, the reaction was quenched by the slow addition of water and the product was extracted into CHCl3. The organic phase was evaporated to dryness and the residue was purified by column chromatography (silica-CH2Cl2) to provide **5a**, after recrystallization by slow solvent exchange of CHCl3 to EtOH on the rotary evaporator, as purple, crystalline material in 60% yield (120 mg, 1.8 × 10-1 mmol). A minor, higher polarity fraction formed, depending on the amount of MeI added and the reaction time, in variable amounts, and was identified as the monohydroxy­monomethoxychlorin **6a**. | | | | | | |

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| **SECTION 12A. APPROVAL** | | |
| I have reviewed, understand and agree to follow this lab-specific standard operating procedure (LSOP) for working with dimethyl sulfate/methyl iodide agents*.* 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/Supervisor 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 temp, 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.) | | |
| **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.** | | |