ORGANIC SYNTHESES

Collective Volume 8

A REVISED EDITION OF ANNUAL VOLUMES 65–69

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The procedures in this text are intended for use only by persons with prior training in the field of organic chemistry. In the checking and editing of these procedures, every effort has been made to identify potentially hazardous steps and to eliminate as much as possible the handling of potentially dangerous materials; safety precautions have been inserted where appropriate. If performed with the materials and equipment specified, in careful accordance with the instructions and methods in this text, the Editors believe the procedures to be very useful tools. However, these procedures must be conducted at one's own risk. Organic Syntheses, Inc., its Editors, who act as checkers, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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HANDLING HAZARDOUS CHEMICALS

General Reference: *Prudent Practices for Handling Hazardous Chemicals in Laboratories,* National Academy Press, Washington, D.C. 1983

Physical Hazards

Fire. Avoid open flames by use of electric heaters. Limit the quantity of flammable liquids stored in the laboratory. Motors should be of the nonsparking induction type.

Explosion. Use shielding when working with explosive classes such as acetylides, azides, ozonides, and peroxides. Peroxidizable substances such as ethers and alkenes, when stored for a long time, should be tested for peroxides before use. Only sparkless "flammable storage" refrigerators should be used in laboratories.

Electric Shock. Use 3-prong grounded electrical equipment if possible.

Chemical Hazards

Because all chemicals are toxic under some conditions, and relatively few have been thoroughly tested, it is good strategy to minimize exposure to all chemicals. In practice this means having a good, properly installed hood; checking its performance periodically; using it properly; carrying out most operations in the hood; protecting the eyes; and, since many chemicals can penetrate the skin, avoiding skin contact by use of gloves and other protective clothing.

Acute Effects. These effects occur soon after exposure. The effects include burn, inflammation, allergic responses, damage to the eyes, lungs, or nervous system (e.g., dizziness), and unconsciousness or death (as from overexposure to HCN). The effect and its cause are usually obvious and so are the methods to prevent it. They generally arise from inhalation or skin contact, so should not be a problem if one follows the admonition "work in a hood and keep chemicals off your hands." Ingestion is a rare route, being generally the result of eating in the laboratory or not washing hands before eating.

Chronic Effects. These effects occur after a long period of exposure or after a long latency period and may show up in any of numerous organs. Of the chronic effects of chemicals, cancer has received the most attention lately. Several dozen chemicals have been demonstrated to be carcinogenic in man and hundreds to be carcinogenic to animals. Although there is no direct correlation between carcinogenicity in animals and man, there is little doubt that a significant proportion of the chemicals used in laboratories have some potential for carcinogenicity in man. For this and other reasons, chemists should employ good practices.

The key to safe handling of chemicals is a good, properly installed hood, and the referenced book devotes many pages to hoods and ventilation. It recommends that in a laboratory where people spend much of their time working with chemicals there should be a hood for each two people, and each should have at least 2.5 linear feet (0.75 meter) of working space at it. Hoods are more than just devices to keep undesirable vapors from the laboratory atmosphere. When closed they provide a protective barrier between chemists and chemical operations, and they are a good containment device for spills. Portable shields can be a useful supplement to hoods, or can be an alternative for hazards of limited severity, e.g., for small-scale operations with oxidizing or explosive chemicals.

Specialized equipment can minimize exposure to the hazards of laboratory operations. Impact resistant safety glasses are basic equipment and should be worn at all times. They may be supplemented by face shields or goggles for particular operations, such as pouring corrosive liquids. Because skin contact with chemicals can lead to skin irritation or sensitization or, through absorption, to effects on internal organs, protective gloves are often needed.

Laboratories should have fire extinguishers and safety showers. Respirators should be available for emergencies. Emergency equipment should be kept in a central location and must be inspected periodically.

DISPOSAL OF CHEMICAL WASTE

General Reference: *Prudent Practices for Disposal of Chemicals from Laboratories*, National Academy Press, Washington, D.C. 1983

Effluents from synthetic organic chemistry fall into the following categories:

1. **Gases**

   1a. Gaseous materials either used or generated in an organic reaction.
   1b. Solvent vapors generated in reactions swept with an inert gas and during solvent stripping operations.
   1c. Vapors from volatile reagents, intermediates and products.

2. **Liquids**

   2a. Waste solvents and solvent solutions of organic solids (see item 3b).
   2b. Aqueous layers from reaction work-up containing volatile organic solvents.
   2c. Aqueous waste containing non-volatile organic materials.
   2d. Aqueous waste containing inorganic materials.

3. **Solids**

   3a. Metal salts and other inorganic materials.
   3b. Organic residues (tars) and other unwanted organic materials.
   3c. Used silica gel, charcoal, filter acids, spent catalysts and the like.

The operation of industrial scale synthetic organic chemistry in an environmentally acceptable manner* requires that all these effluent categories be dealt with properly. In small scale operations in a research or academic setting, provision should be made for dealing with the more environmentally offensive categories.

1a. Gaseous materials that are toxic or noxious, e.g., halogens, hydrogen halides, hydrogen sulfide, ammonia, hydrogen cyanide, phosphine, nitrogen oxides, metal carbonyls, and the like.
1c. Vapors from noxious volatile organic compounds, e.g., mercaptans, sulfides, volatile amines, acrolein, acrylates, and the like.
2a. All waste solvents and solvent solutions of organic waste.
2c. Aqueous waste containing dissolved organic material known to be toxic.

*An environmentally acceptable manner may be defined as being both in compliance with all relevant state and federal environmental regulations *and* in accord with the common sense and good judgement of an environmentally aware professional.

2d. Aqueous waste containing dissolved inorganic material known to be toxic, particularly compounds of metals such as arsenic, beryllium, chromium, lead, manganese, mercury, nickel, and selenium.

3. All types of solid chemical waste.

Statutory procedures for waste and effluent management take precedence over any other methods. However, for operations in which compliance with statutory regulations is exempt or inapplicable because of scale or other circumstances, the following suggestions may be helpful.

Gases

Noxious gases and vapors from volatile compounds are best dealt with at the point of generation by "scrubbing" the effluent gas. The gas being swept from a reaction setup is led through tubing to a (large!) trap to prevent suck-back and on into a sintered glass gas dispersion tube immersed in the scrubbing fluid. A bleach container can be conveniently used as a vessel for the scrubbing fluid. The nature of the effluent determines which of four common fluids should be used: dilute sulfuric acid, dilute alkali or sodium carbonate solution, laundry bleach when an oxidizing scrubber is needed, and sodium thiosulfate solution or diluted alkaline sodium borohydride when a reducing scrubber is needed. Ice should be added if an exotherm is anticipated.

Larger scale operations may require the use of a pH meter or starch/iodide test paper to ensure that the scrubbing capacity is not being exceeded.

When the operation is complete, the contents of the scrubber can be poured down the laboratory sink with a large excess (10–100 volumes) of water. If the solution is a large volume of dilute acid or base, it should be neutralized before being poured down the sink.

Liquids

Every laboratory should be equipped with a waste solvent container in which *all* waste organic solvents and solutions are collected. The contents of these containers should be periodically transferred to properly labeled waste solvent drums and arrangements made for contracted disposal in a regulated and licensed incineration facility.*

Aqueous waste containing dissolved toxic organic material should be decomposed *in situ*, when feasible, by adding acid, base, oxidant, or reductant. Otherwise, the material should be concentrated to a minimum volume and added to the contents of a waste solvent drum.

Aqueous waste containing dissolved toxic inorganic material should be evaporated to dryness and the residue handled as a solid chemical waste.

*If arrangements for incineration of waste solvent and disposal of solid chemical waste by licensed contract disposal services are not in place, a list of providers of such services should be available from a state or local office of environmental protection.

Solids

Soluble organic solid waste can usually be transferred into a waste solvent drum, provided near-term incineration of the contents is assured.

Inorganic solid wastes, particularly those containing toxic metals and toxic metal compounds, used Raney nickel, manganese dioxide, etc. should be placed in glass bottles or lined fiber drums, sealed, properly labeled, and arrangements made for disposal in a secure landfill.* Used mercury is particularly pernicious and small amounts should first be amalgamated with zinc or combined with excess sulfur to solidfy the material.

Other types of solid laboratory waste including used silica gel and charcoal should also be packed, labeled, and sent for disposal in a secure landfill.

Special Note

Since local ordinances may vary widely from one locale to another, one should always check with appropriate authorities. Also, professional disposal services differ in their requirements for segregating and packaging waste.

*If arrangements for incineration of waste solvent and disposal of solid chemical waste by licensed contract disposal services are not in place, a list of providers of such services should be available from a state or local office of environmental protection.

PREFACE

Beginning a new tradition for *Organic Syntheses*, collective volumes will be compiled every 5 years instead of the previous 10. Thus Collective Volume VIII contains procedures previously published in annual volumes 65–69 (1987–1990) but revised and updated in the light of experience and advances since their first appearance. This new format reflects in part the increased pace of research in organic chemistry and our belief that *Organic Syntheses* should be publishing the most up-to-date and significant procedures for the use of our readership. The Editor is grateful to the submitters for their cooperation in reviewing and updating their procedures. In a few instances the Editor has revised the original title so that each procedure has a title compound.

Through the efforts of Assistant Editor Theodora Greene the nomenclature, presentation of spectroscopic data and other variable elements of style have been standarized during the preparation of recent annual volumes. She reexamined those volumes published before her association with the enterprise to ensure as much conformity as possible in this compendium.

In accord with past practice, extensive hazard warnings have been included. In addition we are now soliciting from submitters any information needed for special disposal problems. The Board of Editors is discouraging the use of potentially hazardous solvents such as benzene and hexamethylphosphoric triamide (HMPA) by asking submitters to replace them with others. In the particular case of HMPA procedures involving that solvent have been rechecked with a replacement.

Following the practice of Collective Volumes VI and VII, the table of contents has been arranged alphabetically by title compound (not by the name of the method). Since this listing is probably the least used, this ordering, while often not keeping related procedures adjacent to each other, is likely to have the least effect on users. The concordance listing introduced in Collective Volume VI, which relates the title to the annual volume in which it first appears, is retained in the contents section. If one has a literature citation to an annual volume, the concordance index at the end of the volume allows the reader to find the latest version.

In this volume the Editor has followed the practice reintroduced in Collective Volume VII of multiple indices. Where names of title compounds, isolated intermediates, and uncommon reagents appear, they are accompanied by *Chemical Abstracts* registry numbers. In the titles in the text, the *Chemical Abstracts* name, which is usually different, is given below the main title name in brackets. The practice introduced in recent annual volumes of following each procedure with an appendix of *Chemical Abstracts* registry numbers and names has been dropped in this collective volume to save space, but, as indicated above, this information is retained in the indices.

The editors of *Organic Syntheses* welcome corrections, suggestions, and procedures being submitted for consideration by the Board of Editors. Prospective submitters should consult the section entitled "Submission of Preparations" at the front of one of the latest annual volumes for guidance. Correspondence should be addressed to the current Secretary of the Board of Editors of *Organic Syntheses*, Dr. Jeremiah P. Freeman, Department of Chemistry, University of Notre Dame, Notre Dame, IN 46556.

The Editor is grateful to the submitters, checkers, and editors of annual volumes 65–69 who made this collective volume possible. He is indebted to previous editors Richard E. Benson, Robert M. Coates, and the late William E. Sheppard for the useful Style Guide for *Organic Syntheses*, and to Theodora Greene, whose careful attention to the detail of this guide and whose skill in the use of *Chemical Abstracts*, provides us with accurate nomenclature, registry numbers and conformity of style. The major burden of this work as well as the preparation of the annual volumes in recent years has fallen to my secretary, Mrs. Myra Martin, whose diligence and passion for thoroughness has left these volumes as error-free as is humanly possible.

JEREMIAH P. FREEMAN

Notre Dame, Indiana
November, 1992

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