INTRODUCTION

Most biological agents can be inactivated by treating them with formaldehyde, ethylene oxide, or moist heat, and radioactive materials will decay with the passage of sufficient time, but there are no destruction techniques that are universally applicable to chemical agents. The availability of destruction techniques for specific hazardous chemical agents would be particularly helpful because of the dangers associated with their handling and disposal. In addition, being able to destroy or inactivate the hazardous materials where they are used is advantageous because the user should be familiar with the hazards of these materials and the precautions required in their handling.

Here, we present summaries of destruction procedures for a variety of hazardous chemicals. Many of the procedures have been validated, some by international collaborative testing. We have drawn on information available in the literature[1–13] through the end of 2010 with some later publications and on our own published and unpublished work. It is a cause of regret that technological changes have essentially resulted in the closing of many scientific libraries to the general public. It is unfortunate that a work such as this can no longer be written without the access provided by an institutional affiliation.

Destruction of Hazardous Chemicals in the Laboratory, Third Edition. George Lunn and Eric B. Sansone.

About This Book

This book is a collection of techniques for destroying a variety of hazardous chemicals. It is intended for those whose knowledge of the chemistry of the compounds covered is rather sophisticated; that is, for those who are aware not only of the obvious dangers, such as the toxic effects of the compounds themselves and of some of the reagents and other materials used in the methods but also of the potential hazards represented, for example, by the possible formation of diazoalkanes when *N*-nitrosamides are treated with base. If you are not thoroughly familiar with the potential hazards and the chemistry of the materials to be destroyed and the reagents to be used, do not proceed.

In this edition of the book, we have expanded the number of monographs that deal with the destruction of hazardous compounds that are derived from biological sources, for example, ricin, tetrodotoxin, but we do not deal with the destruction of biological organisms themselves. However, it should be noted that guidelines for handling biological materials in the laboratory have been described and specific procedures for their destruction have been published. A survey of the existing literature on this subject is beyond our scope, but overviews of biological safety are available from the Centers for Disease Control and Prevention,[14] the World Health Organization,[15] the National Research Council,[16] and the American Society for Microbiology.[17] Each of these publications deals to a greater or lesser extent with the destruction of biological materials. For a more encyclopedic approach, see McDonnell.[18] Note that steam sterilization, a method of choice for the treatment of much biological waste in laboratories, hospitals, and commercial establishments, does not eliminate all the potential hazards from antineoplastic drug residues.[19]

The destruction methods are organized in what we believe to be rational categories. These categories are listed in the Table of Contents. It is quite likely, however, that others would have categorized these methods differently, so we have provided five indexes. We have assembled many synonyms of the compounds covered into a Name Index. In each case, the page number given is the first page of the monograph in which the destruction of that compound is discussed. In some cases, the compound itself may not have been studied; it may have been referred to in the Related Compounds section. Since it is not possible to cite every synonym and every variation in spelling, we have also provided a CAS Registry Number Index and a Molecular Formula Index. With these aids one should be able to find

the appropriate destruction method for the compound in question. Pharmaceuticals are referred to in the monographs and in the Name Index mostly by their United States Adopted Name (USAN). However, we recognize that many people may be more familiar with these pharmaceuticals by their Trade Names or by their International Nonproprietary Name (INN) or by some other name, so we have provided a Cross-Index of Pharmaceutical Names, which you should consult if you cannot find the name you are looking for in the Name Index. In a similar fashion, many dyes and biological stains have multiple names so in the monograph we have used a common name for each dye and provided a Cross-Index for the various other names that are used.

One of the difficulties in preparing a book such as this is deciding what should be included and what should be excluded from the text. We have tried to make the method descriptions and the supporting references complete, but at the same time not include unnecessary details. We also tried to eliminate ambiguity wherever possible, going so far as to repeat almost verbatim certain procedures for some compounds rather than noting a minor change and referring to another section and so risking a wrong page number or a misinterpretation. Some general safety precautions are given below. These are not repeated for each group of compounds; in some cases, unusual hazards are noted. For many of the destruction procedures we use the word "discard" in connection with the final reaction mixture. This *always* means "discard in compliance with all applicable regulations".

Although we have included all the validated destruction procedures known to us, we realize that there may be other procedures in the literature or in development. Thus, we would be pleased to hear from readers who have any information or suggestions.

Properties of a Destruction Technique

We have already indicated the advantages of destroying hazardous chemicals at the place where they were generated. It is also useful to consider the desirable properties of a destruction technique for hazardous chemicals.

- Destruction of the hazardous chemical should be complete.
- A substantially complete material accountance should be available, with the detectable products being innocuous materials. (This accountance is often difficult to accomplish. In the absence of a complete material accountance, an assessment of the mutagenic activity of the

reaction mixture may provide useful information concerning the potential biological hazards associated with the decomposition products.)

- The effectiveness of the technique should be easy to verify analytically.
- The equipment and reagents required should be readily available, inexpensive, and easy and safe to use. The reagents should have no shelf-life limitations.
- The destruction technique should require no elaborate operations (such as distillation or extraction) that might be difficult to contain; it must be easy to perform reliably and should require little time.
- The method should be applicable to the real world; that is, it should be capable of destroying the compound itself, solutions in various solvents, and spills.

These properties characterize an ideal destruction technique. Most techniques cannot meet all of these criteria, but they represent a goal toward which one should strive.

Contents of a Monograph

Each monograph usually contains the following information:

- An introduction describes the various properties of the compound or class of compounds being considered.
- The principles of destruction section details, in general terms, the chemistry of the destruction procedures, the products, and the efficiency of destruction.
- The destruction procedures section may be subdivided into procedures for bulk quantities, solutions in water, organic solvents, and so on.
- The analytical procedures section describes one or more procedures that may be used to test the final reaction mixtures to ensure that the compound has been completely degraded. The techniques usually involve packed column gas chromatography (GC) or reverse phase high-performance liquid chromatography (HPLC), but colorimetric procedures and thin-layer chromatography (TLC) are also used in some cases.
- The mutagenicity assays section describes the data available on the mutagenic activity of the starting materials, possible degradation products, and final reaction mixtures. The data were generally

obtained from the plate incorporation technique of the *Salmonella*/mammalian microsome mutagenicity assay (see below).

- The related compounds section describes other compounds to which the destruction procedures should be applicable. The destruction procedures have not usually been validated for these materials, however; they should be fully investigated before adopting them.
- References identify the sources of the information given in the monograph.

For pharmaceuticals and nonspecific methods of destruction, however, the nature of the material has led us to take a different approach, and the organization of these monographs is based on the type of reaction under consideration, for example, potassium permanganate oxidation, photolysis.

Mutagenicity Assays

In many cases the residues produced by the destruction methods were tested for mutagenicity. Unless otherwise specified, the reaction mixtures from the destruction procedures and some of the starting materials and products were tested for mutagenicity using the plate incorporation technique of the *Salmonella*/mammalian microsome assay essentially as recommended by Ames et al.[20] with the modifications of Andrews et al.[21] Some or all of the tester strains TA98, TA100, TA1530, TA1535, TA1537, and TA1538 of *Salmonella typhimurium* were used with and without S9 rat liver microsomal activation. The reaction mixtures were neutralized before testing. In general, basic reaction mixtures were neutralized by adding acetic acid. Acidic reaction mixtures were neutralized by adding solid sodium bicarbonate. Reaction mixtures containing potassium permanganate were decolorized with sodium ascorbate before neutralization. A 100 μL aliquot of the solution (corresponding to varying amounts of undegraded material) was used per plate. Pure compounds were generally tested at a level of 1 mg per plate in either dimethyl sulfoxide (DMSO) or aqueous solution. To each plate were added 100 μL of these solutions. The criterion for significant mutagenicity was set at more than twice the level of the control value. The control value was the average of the cells only and cells plus solvent runs. Unless otherwise specified, residues did not exhibit mutagenic activity. The absence of mutagenic activity in the residual solutions, however, does not necessarily imply that they are nontoxic or have no other adverse biological or environmental effects.

Analytical Procedures

For the most part, unless otherwise specified, the analytical equipment used for the work carried out by the authors consisted of the following. For HPLC, a dual pump computer-controlled solvent delivery system (Rainin Instrument Co., Woburn, MA) was used with ultraviolet (UV) detection using either a Knauer Model 87 variable wavelength detector (Rainin) or an ABI 1000S diode array detector (Applied Biosystems, Foster City, CA). The injection volume was 20 μL and the flow rate was 1 mL/min. The column was a 250 × 4.6-mm i.d. column of Microsorb 5 μm C8 fitted with a 15 × 4.6-mm guard column of the same material. For GC a Hewlett Packard HP 5880A instrument was fitted with a 1.8-m × 2-mm i.d. × 0.25-in. o.d. packed silanized glass column. The column was fitted with a guard column packed with the same material. The guard column was changed periodically. The injector temperature was 200°C and the flame ionization detector temperature was 300°C. The carrier gas was nitrogen flowing at 30 mL/min. Injection was by syringe and sample volumes were in the 1–5 μL range. For each instrument an electronic integrator was used to determine peak areas automatically.

In some cases, we found that injecting unneutralized reaction mixtures onto the hot GC column caused degradation of the material for which we were analyzing. Thus, it might be that degradation was incomplete but the appropriate peak was not observed in the chromatogram because the compound was degraded on the GC column. Spiking experiments can be used to determine if this is a problem. In a spiking experiment a small amount of the original compound is added to the final reaction mixture and this spiked mixture is analyzed. If an appropriate peak is observed, compound degradation on the GC column is not a problem. If an appropriate peak is not observed, it may be necessary to neutralize the reaction mixture before analysis and/or use a different GC column. Similar problems may be encountered when using HPLC because of the formation of salts or the influence of the sample solvent; again, spiking experiments should be employed. We have indicated in the monographs some instances where problems such as these were encountered (see, e.g., Halogenated Compounds monograph) but spiking experiments should be used routinely to test the efficacy of the analytical techniques.

Spills

Before starting work, have a plan for dealing with spills or accidents; coming up with a good plan on the spur of the moment is difficult. At a

minimum have the appropriate decontaminating or neutralizing agents prepared and close at hand. Small spills can probably be cleaned up by the researcher. In the case of larger spills, the area should be evacuated and help sought from those experienced and equipped for dealing with spills, for example, your institutional safety department.

The initial step in dealing with a spill should be the removal of as much of the spill as possible by using a high efficiency particulate air (HEPA) filter equipped vacuum cleaner for solids and absorbents for liquids or solutions. The residue should be decontaminated as described in the monographs.

Whereas solutions or bulk quantities may be treated with heterogeneous [e.g., nickel–aluminum (Ni–Al) alloy reduction] or homogeneous methods [e.g., potassium permanganate/sulfuric acid ($KMnO_4/H_2SO_4$) oxidation], decontamination of glassware, surfaces, and equipment and the treatment of spills is best accomplished with homogenous methods. These methods allow the reagent, which is in solution, to contact all parts of the surface to be decontaminated. At the end of the cleanup, it is frequently useful to rub the surface with a wipe moistened with a suitable solvent, for example, water, methanol, acetone, and analyze the wipe for the spilled compound.

Applicability of Procedures

Methods that successfully degrade some compounds may not affect other compounds of the same class or other classes of compounds. For example, oxidation with $KMnO_4$ in H_2SO_4 solution has been successfully applied to the destruction of several classes of compounds such as aromatic amines[8] and polycyclic aromatic hydrocarbons.[4] This method gave satisfactory results with some of the antineoplastic agents but not with others, including most of the *N*-nitrosourea drugs.[9] Sodium hypochlorite treatment, often recommended as a general destruction technique, failed to give satisfactory results with doxorubicin and daunorubicin[9] and polycyclic aromatic hydrocarbons,[4] and estrones.[22] However, it was satisfactory for the destruction of aflatoxins.[2] Nickel–aluminum alloy in dilute base worked well for *N*-nitrosamines[3] but was unsatisfactory for the destruction of polycyclic aromatic hydrocarbons.[4]

Chromic acid is an attractive oxidizing agent and has been used successfully to degrade many compounds, but the spent chromium compounds are potentially carcinogenic. These compounds are also environmentally hazardous and may not be discharged into the sewer. For this reason, we have not recommended the use of chromic acid for degrading

any of the compounds we have covered. Potassium permanganate/sulfuric acid degradation appears to be as efficient and has fewer hazards.

Safety Considerations

A first step in minimizing risks associated with hazardous chemicals is to prepare a set of guidelines regulating such work. Many organizations have produced such guidelines and many texts have been written on the subject of laboratory safety,[1, 14–17, 23–29] preventing exposure to hazardous drugs,[30] and the hazardous properties of chemicals.[31–36] A recent paper shows that implementing procedures for the safe handling of antineoplastic drugs led to a drop in worker exposure over a 10 year period.[37]

The American Chemical Society maintains an index of the chemical safety letters that have appeared in Chemical and Engineering News at http://www.pubs.acs.org/cen/safety/. The full text of each letter can be accessed through this index.

Such documents will provide many useful suggestions when preparing guidelines for any laboratory situation. It is important that the guidelines "fit" the management and administrative structure of the institution and that any particular work requirements be taken into account. Obviously, all national and local laws should be obeyed as well as all institutional regulations. Controlled substances are regulated by the Drug Enforcement Administration. By law, Material Safety Data Sheets must be readily available. All laboratories should have a Chemical Hygiene Plan [29CFR Part 1910.1450] and institutional safety officers should be consulted as to its implementation. Help is (or should be) available from your institutional Safety Office. Use it.

To ensure the safety of those working with hazardous materials of any kind, policies, responsibility, and authority must be clearly defined. The responsibilities of the laboratory director, the supervisor, the employee, and the safety committee should be clearly spelled out.

It is important that potentially hazardous materials are handled only by those workers who have received the appropriate training. For that reason, glassware and equipment should be decontaminated in the laboratory before they are transferred to any central washing system.

Obviously, it is important to consider the waste disposal aspects of one's work before the work begins. Experiments should always be designed to use the minimum quantities of potentially hazardous materials, and plans should be made in advance to minimize the wastes generated by any

experimentation. Equally when purchasing material for the laboratory consideration should be given as to its eventual disposal. Although buying large quantities may result in a lower unit cost this may be no bargain if you must eventually pay to have large quantities of unused material disposed of. Consideration should also be given to purifying and using existing stocks rather than discarding the old material and buying fresh. A recent book describes the purification of laboratory chemicals.[38] As an example see the Monograph on Butyllithium where methods of retitrating solutions of uncertain concentration are described. In addition, Appendix I describes procedures for drying organic solvents. These procedures may help to reduce the need to discard older materials.

Although we concentrate here on laboratory methods for destroying or decontaminating hazardous chemicals, it is valuable to briefly discuss some other approaches to handling chemical wastes. Regardless of the disposal approach selected, only completely decontaminated wastes producing no adverse biological effects should be discarded. Procedures for disposing of hazardous chemicals must comply with all applicable regulations. It is obviously undesirable to deliberately dispose of hazardous chemicals through the sewage system or by evaporation into the atmosphere, unless one has solid evidence that their subsequent degradation is extremely rapid, irreversible, complete, and produces safe degradation products.

It is impossible to provide a concise summary of safety practices for handling hazardous chemicals in the laboratory. For a complete discussion, the reader is advised to consult readily available references.[1, 14, 23–36, 39–46] Each institution and facility should tailor its program to meet its needs. It is important that the safety program include procedures for working with chemicals, biological materials, compressed gases, high-voltage power supplies, radioisotopes, and so on.

The following descriptions are designed to give a sufficiently complete guide to the destruction methods available to allow one to implement them successfully. The user may wish to consult the sources cited in order to determine the exact reaction conditions, limitations, and hazards that we have not been able to list because of space limitations. In some cases more than one procedure is listed. In these instances all the procedures should be regarded as equally valid unless restrictions on applicability are noted. In the course of collaborative testing, we have occasionally found that the efficacy of the same technique varies between laboratories and may also depend on the batch of reagents being used. Thus, we strongly recommend that these methods be periodically validated to ensure that the chemicals are

actually being destroyed. These methods have been tested on a limited number of compounds. The efficiency of the destruction techniques must be confirmed when they are applied to a new compound.

The details of analytical techniques are also included. It should be noted that even if 99.5% of a compound is destroyed, the remaining amount may still pose a considerable hazard, particularly if the original reaction was performed on a large scale. The efficiency of degradation is generally indicated by giving the limit of detection, for example, <0.5% of the original compound remained. This means that **none** of the original compound could be detected in the final reaction mixture. However, because of the limitations of the analytical techniques used, it is possible that traces of the original compound, which were below the limit of detection, remained. If this is the case, to use the example given above, the quantity that remained was less than 0.5% of the original amount.

The reactions described were generally performed on the scale specified. If the scale is greatly increased unforeseen hazards may be introduced, particularly with respect to the production of large amounts of heat, which may not be apparent in a small-scale reaction. Extra care should therefore be exercised when these reactions are performed on a large scale.

In addition to the potential hazards posed by the compounds themselves, many of the reagents used in degradation procedures are hazardous. *Acids and bases are corrosive and should be prepared and used carefully. As noted below, the dilution of concentrated H_2SO_4 is a very exothermic process, which can result in splattering if carried out incorrectly.* All reactions should be carried out in a properly functioning chemical fume hood, which is vented to the outside. Laminar flow cabinets or other recirculating hoods with or without filters are not appropriate. The performance of the hood should be checked by qualified personnel at regular intervals. Hoods should be equipped with an alarm that sounds if the airflow drops below a preset value.

Dissolving concentrated H_2SO_4 in H_2O is a very exothermic process and appropriate protective clothing, including eye protection, should be worn. Concentrated H_2SO_4 should **always** be added to H_2O and **never** the other way around (otherwise splashing of hot concentrated H_2SO_4 may occur). To prepare H_2SO_4 solutions, the appropriate quantity of concentrated H_2SO_4 is slowly and cautiously added to about 500 mL of H_2O, which is stirred in a 1 L flask. When addition is complete, H_2O is added to bring the volume up to 1 L and the mixture is allowed to cool to room temperature before use. To prepare a 1 M H_2SO_4 solution, use 53 mL of

concentrated H_2SO_4 and to prepare a 3 M H_2SO_4 solution, use 160 mL of concentrated H_2SO_4.

Appropriate protective clothing should be worn.[40,41] This clothing includes, but is not limited to, eye protection (safety glasses or face shield), lab coat, and gloves. Rubber gloves generally allow the passage of organic liquids and solutions in organic solvents; they should not be allowed to routinely come into contact with them. Protective clothing should be regarded as the last line of defense and should be changed immediately if it becomes contaminated.

Wastes should be segregated into solid, aqueous, nonchlorinated organic, and chlorinated organic material and disposed of in accordance with local regulations.

In the introductions to the monographs, we did not try to give an exhaustive listing of the toxicity data [e.g., LD_{50} (the dose that is lethal for 50% of the animals tested) or TLV (threshold limit values) data] or other hazards associated with the compounds under consideration. Instead, we attempted to give some indication of the main hazards associated with each compound or class of compounds. Extensive listings of all the *known* hazards associated with these compounds can be found elsewhere.[31,34,35]

All organic compounds discussed in this book should be regarded as flammable and all volatile compounds should be regarded as having the capacity of forming explosive mixtures in confined spaces. In many cases the toxic properties of many of these compounds have simply not been adequately investigated. Prudence dictates that, unless there is good reason for believing otherwise, all of the compounds discussed in this book should be regarded as volatile, highly toxic, flammable, human carcinogens, and should be handled with great care.

Other hazards are introduced by the reagents needed to perform the destruction procedures. Examples are the use of Ni–Al alloy and the use of $KMnO_4$.

Safety Considerations with Nickel–Aluminum Alloy

In the course of the reaction Ni–Al alloy reacts with base to produce hydrogen, a flammable gas that forms explosive mixtures with air. Providing the reactions are done in a fume hood this should not be a problem. It has been found that this reaction frequently exhibits an induction period.[47] There is an initial temperature rise when the Ni–Al alloy is first added but the temperature soon declines to ambient levels. Typically, after about 3 h, a

much larger temperature rise occurs and the reaction mixture has frequently been observed to boil at this stage. For this reason, the reaction should be carried out in a flask that is certainly no more than one-half full. In some cases, we have observed that considerable foaming occurs and that an even larger flask is required. These instances are mentioned in the monographs (see, e.g., page 577). We have found it convenient to perform these reactions in a round-bottom flask fitted with an air condenser. The reaction also produces finely divided nickel, which is potentially pyrophoric. This product does not appear to be a problem, however, as long as it is allowed to dry on a metal tray away from flammable solvents for 24 h before being discarded.

Safety Considerations with Potassium Permanganate

It has been pointed out[48] that when $KMnO_4$ in H_2SO_4 was used to degrade hazardous compounds mutagenic reaction mixtures were produced because manganese was left in solution. The Ames test was used with tester strain *S. typhimurium* TA102 (which was most sensitive to manganese) to assess mutagenic activity. Mutagenic activity was also detected with strain TA100 but at a lower level. Manganese is also known to be a carcinogen.[49, 50] Thus, disposal of reaction mixtures that contain manganese is not desirable. However, by manipulating the workup conditions, $KMnO_4$ can be used to degrade hazardous reagents and the manganese can subsequently be removed from solution.[51] These procedures have been incorporated into the monographs. A fuller account of the procedures that can be used to remove manganese from solution can be found in Appendix II.

A number of potential hazards have been identified. We have made no attempt to provide comprehensive guidelines for safe work, however, and it is essential that workers follow a code of good practice.

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