SOURCEBOOK OF ADVANCED ORGANIC LABORATORY PREPARATIONS

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ACADEMIC PRESS, INC.
Harcourt Brace Jovanovich, Publishers
San Diego New York Boston London Sydney Tokyo Toronto

This book is a guide to provide information concerning its subject matter. Synthesis of chemicals is a rapidly changing field. The reader should consult current product specifications for state-of-the-art instructions and applicable government safety regulations. The Publisher and the authors do not accept responsibility for any misuse of this book, including its use as a source of product specifications or other specific information.

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Academic Press, Inc.
1250 Sixth Avenue, San Diego, California 92101-4311

United Kingdom Edition published by
Academic Press Limited
24-28 Oval Road, London NW1 7DX

Library of Congress Cataloging-in-Publication Data

Sandler, Stanley R., date
Sourcebook of advanced organic laboratory preparations / Stanley R. Sandler, Wolf Karo.
p. cm.
Includes indexes.
ISBN 0-12-618506-9
1. Organic compounds-Synthesis. I. Karo, Wolf, date. II. Title.
QD262.S24 1992
547.2'078-dc20 92-13631
CIP

PRINTED IN THE UNITED STATES OF AMERICA
92 93 94 95 96 97 EB 9 8 7 6 5 4 3 2 1

PREFACE

The purpose of this laboratory text is to provide a ready source of reliable procedures for those involved in organic synthesis in either academic or industrial laboratories. It will be useful to instructors and students seeking to find additional reliable organic or polymer preparations. The introductory material in each chapter gives a brief synopsis of the synthesis of a given functional group or class of compounds. Industrial chemists will also appreciate the convenient source of procedures as well as the tables found in the text. The numerous polymer preparations will also be helpful to those needing a reliable procedure for their synthesis.

This text gives selections of some of the procedures found in two series of books by the authors. These books are listed in the Introduction to this text and should be referred to for additional details and references that cover both patents and journals.

Unique features of this book are the Name Reaction Index with procedures for most reactions and the Appendix titled *Documentation of Product and Process Research and Development*, which explains, with examples, methods for proper documentation in the laboratory notebook.

The procedures described in this sourcebook are based primarily on the literature. Many were developed long before our current concerns of exposure to chemicals, "right-to-know" laws, occupational health and safety, environmental effects, pollution, material disposal, and so on. As a result, all of the syntheses given herein must be re-evaluated in the light of ever-changing regulations (see, for example, "U.S. Courts Overturn Regulatory Shortcuts," *Chemical Engineering News*, July 13, 1992, page 7.)

In this book, many examples have been given that use *benzene* as a reagent or solvent. However, since benzene is a cancer-suspect agent, its use must be severely restricted and efforts must be made to eliminate this

solvent from the workplace completely. In some cases, possible substitutes for benzene may be *toluene*, *heptane*, or *cyclohexane*. In other situations, totally different systems may need to be developed. Similar problems exist for other materials. The reader must, therefore, be constantly alert to the shifting regulations on handling materials and the real and/or anticipated health hazards. While the so-called "Material Safety Data Sheets" required for all chemicals are of some value, the reader should keep in mind that the information given there is not always based on solid experimental data.

We would like to express our appreciation to our families for their encouragement in this work. We also would like to thank the staff of Academic Press for all their efforts in guiding this work through the publication process.

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INTRODUCTION

Sourcebook of Advanced Organic Laboratory Preparations has been designed as a convenient source for synthetic procedures of wide utility for both students and industrial chemists.

In the case of students, this laboratory preparations manual can be used to find additional experiments to illustrate concepts in synthesis and to augment existing laboratory texts. A Name Reaction Index is also included to direct the reader to the location where specific reactions appear in this manual.

The industrial chemist is frequently required to prepare a variety of compounds, and this manual can serve as a convenient guide to choose a synthetic route.

Each chapter describes the synthesis of a given class of compound or functional group type (hydrocarbons, olefins, acetylenes, carboxylic acids, polymers of various types, mercaptans, etc.) and gives a brief summary of the available routes that can be used. A few representative preparations are illustrated because of their wide applicability. For more details the reader is referred to review the following six books from which these preparations came:

Organic Functional Group Preparations, Volumes I, II, and III, second editions, by Stanley R. Sandler and Wolf Karo, Academic Press, Inc. (1983, 1986, 1989).

Polymer Syntheses, Volume I, 2d ed. and Volumes II and III by Stanley R. Sandler and Wolf Karo, Academic Press, Inc. (1992, 1977, 1980).

One unique feature of this laboratory manual is that emphasis is placed not only on simple organic compounds but also on polymers of high molecular weight. This topic usually is not covered in as much detail in other laboratory texts of this type. In the present

manual the topic of polymers is introduced early on as in the case of Chapter 1, Hydrocarbons, as well as throughout the other chapters.

This laboratory manual assumes that the student has already mastered the introductory laboratory techniques in an introductory course on organic chemistry involving the typical glassware normally used in these preparations. Careful record keeping is a must and is covered in the Appendix. Experience in the various analytical techniques described is also assumed. Experience in distillations, both at atmospheric pressure and under reduced pressure, is also assumed.

1: SCALE OF OPERATIONS AND MONITORING OF REACTIONS

Most preparations cited can be scaled *down* provided microware is available. The advantage is that less waste disposal is required.

Preparations should *not* be scaled up unless this is done *gradually* to determine if the exothermic reaction can be safely tolerated by the equipment being used. All glassware should be free of cracks.

The reactions in most cases can be easily monitored by gas chromatography, infrared spectroscopy, ultraviolet spectroscopy, and thin layer chromatography. Where available a nuclear magnetic resonance (NMR) instrument can also be very effectively used to follow the course of the reaction and to determine the structures of the products.

A. SAFETY

All experiments should be carried out in a good fume hood with due personal protection involving safety eye glasses, a laboratory coat or apron, and the use of gloves.

All experiments should first be studied in detail and outlined. A senior chemist or laboratory supervisor should oversee that all details have been understood before starting the laboratory preparation. The nature of each chemical used should be thoroughly understood by examining in detail the appropriate Material Safety Data Sheet (MSDS) and then signed off before using.

Several **CAUTIONS** are a must to review and are mentioned here again for emphasis:

1. Read all the Material Safety Data Sheets for the raw materials that you plan to use. Contact the supplier if you have any questions.

2. Read all the toxicity information.
3. Use good personal protective equipment such as eye protection, laboratory coats, and gloves (respirators when necessary). The type of gloves and eye protection must be suitable for the operation.
4. Use a well-ventilated hood.
5. Use traps to control toxic vapors or other volatile by-products.
6. Always work with someone else nearby in the same laboratory. *Never work alone!*
7. Read and reread all preparations. Write out equations and understand the chemistry involved.
8. Never scale-up experiments unless you are sure this will not lead to a highly exothermic uncontrollable reaction.
9. When uncertain, ask questions of your instructor or other professional who is qualified.

B. WASTE DISPOSAL

For the disposal of waste chemicals consult your supervisor or the Safety Director.

Broken glassware and paper towels used to mop up chemicals should be segregated also by placing them in special containers or plastic bags. Check with your laboratory instructor for the proper guidelines that you are to follow.

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HYDROCARBONS: PARAFFINIC AND AROMATIC

1. INTRODUCTION

Hydrocarbons are conveniently prepared in the laboratory by reduction, condensation, elimination, or hydrolysis reactions. Isomerization, oxidation, and photochemical reactions are less common on a preparative scale.

From S. R. Sandler and W. Karo, *Organic Functional Group Preparations*, Vol. I, 2d ed. (New York, 1983), 1–37, by permission of Academic Press, Inc.

The reduction methods depend on converting a given functional group to a methylene group. For example, olefins, aromatic rings, alcohols, aldehydes, ketones, and halides give hydrocarbons on reduction. These methods allow the preparation of hydrocarbons of known structure. The Clemmensen (zinc amalgam and hydrochloric acid) and Wolff–Kishner (hydrazine and base) methods can be used to reduce aldehydes and ketones. Catalytic hydrogenation methods can be used to reduce olefins and aromatic compounds. The catalytic hydrogenation method can also be used for ketones, provided that a high-pressure apparatus is available. Nickel and platinum are the most commonly used catalysts.

The use of sodium borohydride with palladium chloride has been described for the reduction of olefins in excellent yields. The method is quite reliable and it has been applied as an analytical technique for the quantitative estimation of the degree of unsaturation of a compound or of a mixture.

$$RCH{=}CH_2 + NaBH_4 \xrightarrow[H^+]{PdCl_2} RCH_2{-}CH_3 \qquad (1)$$

Condensation reactions are used to synthesize a hydrocarbon from two or more compounds which may or may not be the same as described in Eq. (2)

$$R{-}Y + RX \longrightarrow R{-}R + XY \qquad (2)$$

where X or Y may be a hydrogen, halogen, diazo, or organometallic group. The Friedel–Crafts, the Wurtz, the Wurtz–Fittig, organometallic coupling, Ullmann, and Pschorr syntheses are some representative condensation reactions. The Friedel–Crafts reaction and the coupling of organometallics with halides are the most useful laboratory syntheses of hydrocarbons, especially branched-chain hydrocarbons such as neohexane.

The hydrolysis of the Grignard reagent is a useful method of preparing hydrocarbons from halides [Eq. (3)].

$$ROH \xrightarrow{HX} RX \xrightarrow{Mg} RMgX \xrightarrow{H_2O} RH \qquad (3)$$

The yields by this method are usually excellent and pure hydrocarbons are obtained. The chloromethylation reaction can thus be used as a step in the addition of a methyl group to an aromatic nucleus.

Carboxylic acids eliminate carbon dioxide when heated with soda lime or electrolyzed to produce paraffins (Kolbe reaction). The former is a more useful method in the laboratory.

Aldehyde, diazo, and sulfuric acid groups are a few of the other groups that can be eliminated and replaced by hydrogen to give hydrocarbons.

Cyclodehydration of aromatic alcohols and ketones gives tetralins, anthracenes, phenanthrenes, and other ring systems.

The Jacobsen reaction involves the isomerization by sulfuric acid of an aromatic system containing several alkyl halo groups to give vicinal derivatives.

Olefins can also be hydroborated to organoboranes which are then converted to the hydrocarbon by refluxing with propionic acid [1]. This procedure is a convenient noncatalytic laboratory method for the hydrogenation of olefins.

$$3\,RCH{=}CH_2 + NaBH_4 + BF_3 \longrightarrow (RCH_2CH_2)_3B \xrightarrow{C_2H_5COOH} 3\,RCH_2CH_3 \quad (4)$$

Terminal olefins are readily hydroborated but internal olefins require additional reaction time and heating prior to refluxing with propionic acid. Substituents such as active sulfur, chlorine, or nitrogen are not affected by this hydrogenation procedure.

2. REDUCTION REACTIONS

1-1. Conversion of 1-Hexene to *n*-Hexane by Hydroboration Method [1]

$$3\,CH_3(CH_2)_3{-}CH{=}CH_2 + NaBH_4 + BF_3 \longrightarrow [CH_3(CH_2)_3CH_2CH_2]_3B \longrightarrow 3\,CH_3(CH_2)_4CH_3 \quad (5)$$

To a three-necked flask equipped with a mechanical stirrer, dropping funnel, and reflux condenser with attached drying tube are added 16.8 gm (0.20 mole) of 1-hexene and 2.0 gm of sodium borohydride (0.055 mole) in 55 ml of diglyme. While stirring under nitrogen, 10.0 gm (0.075 mole) of boron trifluoride etherate in 25 ml of diglyme is added during a period of 1.5 hr. Then 22.2 gm (0.3 mole) of propionic acid is added and the mixture is refluxed for 2 hr while ether and the product distill over. The product is washed with sodium bicarbonate solution, then water, dried, and fractionally distilled