second edition

# advanced practical organic chemistry

J. Leonard

B. Lygo

G. Procter

BLACKIE ACADEMIC & PROFESSIONAL
An Imprint of Chapman & Hall

# Advanced Practical Organic Chemistry

*Second edition*

J. LEONARD
B. LYGO
G. PROCTER
Department of Chemistry and Applied Chemistry
University of Salford

江苏工业学院图书馆
藏书章

BLACKIE ACADEMIC & PROFESSIONAL
An Imprint of Chapman & Hall
London · Glasgow · Weinheim · New York · Tokyo · Melbourne · Madras

**Published by Blackie Academic & Professional, an imprint of Chapman & Hall, Wester Cleddens Road, Bishopbriggs, Glasgow G64 2NZ**

---

Chapman & Hall, 2-6 Boundary Row, London SE1 8HN, UK

Blackie Academic & Professional, Wester Cleddens Road, Bishopbriggs, Glasgow G64 2NZ, UK

Chapman & Hall GmbH, Pappelallee 3, 69469 Weinheim, Germany

Chapman & Hall USA, One Penn Plaza, 41st Floor, New York NY 10119, USA

Chapman & Hall Japan, ITP-Japan, Kyowa Building, 3F, 2-2-1 Hirakawacho, Chiyoda-ku, Tokyo 102, Japan

DA Book (Aust.) Pty Ltd, 648 Whitehorse Road, Mitcham 3132, Victoria, Australia

Chapman & Hall India, R. Seshadri, 32 Second Main Road, CIT East, Madras 600 035, India

---

First edition 1990
Second edition 1995

© 1995 Chapman & Hall

Printed in Great Britain by The Alden Press, Osney Mead, Oxford

ISBN 0 7514 0200 1

Apart from any fair dealing for the purposes of research or private study, or criticism or review, as permitted under the UK Copyright Designs and Patents Act, 1988, this publication may not be reproduced, stored, or transmitted, in any form or by any means, without the prior permission in writing of the publishers, or in the case of reprographic reproduction only in accordance with the terms of the licences issued by the Copyright Licensing Agency in the UK, or in accordance with the terms of licences issued by the appropriate Reproduction Rights Organization outside the UK. Enquiries concerning reproduction outside the terms stated here should be sent to the publishers at the Glasgow address printed on this page.

The publisher makes no representation, express or implied, with regard to the accuracy of the information contained in this book and cannot accept any legal responsibility or liability for any errors or omissions that may be made.

A catalogue record for this book is available from the British Library

Library of Congress Catalog Card Number: 94-72928

Printed on acid-free text paper, manufactured in accordance with ANSI/NISO Z39.48-1992 (Permanence of Paper).

# Advanced Practical Organic Chemistry

*Dedicated to Professor Gilbert Stork*
*In recognition of the skills and enthusiasm for chemistry*
*gained in his laboratories*

试读结束：需要全本请在线购买： www.ertongbook.com

# Preface to Second Edition

The preparation of organic compounds is central to many areas of scientific research, from the most applied to the most academic, and is not limited to chemists. Any research which uses new organic chemicals, or those which are not available commercially, will at some time require the synthesis of such compounds.

This highly practical book continues to cover the most up-to-date techniques commonly used in organic synthesis and is based on our experience of establishing research groups in synthetic organic chemistry and our association with some of the leading laboratories in the field. It is not claimed to be a comprehensive compilation of information to meet all possible needs and circumstances; rather, the intention has been to provide sufficient guidance to allow the researchers to carry out reactions under conditions which offer the highest chance of success.

The book is written for postgraduate and advanced level undergraduate organic chemists and for chemists in industry, particularly those involved in pharmaceutical, agrochemical and other fine chemicals research. Biologists, biochemists, genetic engineers, material scientists and polymer researchers in university and industry will find the book a useful source of reference.

All the artwork for this second edition has been modernized and the chapters have been reorganized to allow for more expanded treatment of practical techniques.

# Contents


**1 General Introduction** 1

**2 Safety** 3

2.1 Safety is your primary responsibility 3
2.2 Safe working practice 4
2.3 Common hazards 4
2.4 Accident and emergency procedures 6
2.5 Bibliography 7

**3 Keeping records of laboratory work** 8

3.1 Introduction 8
3.2 The laboratory notebook 8
3.2.1 Why keep a lab book? 8
3.2.2 How to write a lab book 9
3.2.3 Suggested notebook format 10
3.3 Keeping records of data 13
3.3.1 Purity, structure determination and characterization 13
3.3.2 What type of data should be collected 14
3.3.3 Formats for data records 19
3.4 Some tips on report and thesis writing 24
3.4.1 Sections of a report or thesis 24
3.4.2 Planning a report or thesis 24
3.4.3 Writing the report or thesis 26

**4 Equipping the laboratory and the bench** 36

4.1 Introduction 36
4.2 Setting up the laboratory 36
4.3 General laboratory equipment 37

4.4 The individual bench 44
4.4.1 Routine glassware 44
4.4.2 Personal items 45
4.4.3 Specialized personal items 46

**5 Purification and drying of solvents 54**

5.1 Introduction 54
5.2 Purification of solvents 54
5.3 Drying agents 55
5.4 Drying of solvents 59
5.5 Solvent stills 65

**6 Reagents: Preparation, purification and handling 69**

6.1 Introduction 69
6.2 Classification of reagents for handling 70
6.3 Techniques for obtaining pure and dry reagents 71
6.3.1 Purification and drying of liquids 71
6.3.2 Purifying and drying solid reagents 74
6.4 Techniques for handling and measuring reagents 76
6.4.1 Storing liquid reagents or solvents under inert atmosphere 76
6.4.2 Bulk transfer of a liquid under inert atmosphere (cannulation) 78
6.4.3 Using cannulation techniques to transfer measured volumes of liquid under inert atmosphere 81
6.4.4 Use of syringes for the transfer of reagents or solvents 84
6.4.5 Handling and weighing solids under inert atmosphere 92
6.5 Preparation and titration of simple organometallic reagents 98
6.5.1 General considerations 98
6.5.2 Preparation of Grignard reagents 99
6.5.3 Preparation of organolithium reagents 100
6.5.4 Titration of lithium reagents 102
6.5.5 Preparation of lithium amide bases 102
6.6 Preparation of diazomethane 103
6.6.1 Safety measures 104
6.6.2 Preparation of diazomethane (a dilute ethereal solution) 104
6.6.3 General procedure for esterification of carboxylic acids 106

6.6.4 Titration of diazomethane solutions 106

**7 Gases 107**

7.1 Introduction 107
7.2 Use of gas cylinders 107
7.2.1 The procedure for fitting a regulator to a cylinder 109
7.3 Handling gases 110
7.4 Measurement of gases 113
7.4.1 Measurement of a gas using standardized solution 113
7.4.2 Measurement of a gas using a gas tight syringe 113
7.4.3 Measurement of a gas using a gas burette 114
7.4.4 Quantitative analysis of hydride solutions using a gas burette 115
7.4.5 Measurement of a gas by condensation 116
7.4.6 Measurement of as gas using a quantitative reaction 117
7.5 Inert gases 117
7.6 Reagent gases 118
7.6.1 Gas scrubbers 119
7.6.2 Methods for preparing some commonly used gasses 119

**8 Vacuum pumps 122**

8.1 Introduction 122
8.2 House vacuum systems 122
8.3 Medium vacuum systems 123
8.3.1 Water aspirators 123
8.3.2 Electric diaphragm pumps 123
8.4 High vacuum pumps 124
8.4.1 Rotary oil pumps 124
8.4.2 Vapour diffusion pumps 126
8.5 Pressure measurement and regulation 126
8.5.1 Units of pressure (vacuum) measurement 127

**9 Carrying out the reaction 128**

9.1 Introduction 128
9.2 Reactions with air sensitive reagents 129

| | | | |
|---|---|---|---|
| | 9.2.1 | Introduction | 129 |
| | 9.2.2 | Preparing to carry out a reaction under inert conditions | 129 |
| | 9.2.3 | Drying and assembling glassware | 130 |
| | 9.2.4 | Typical reaction set-ups using a double manifold | 131 |
| | 9.2.5 | Basic procedure for inert atmosphere reactions | 132 |
| | 9.2.6 | Modifications to basic procedure | 135 |
| | 9.2.7 | Use of balloons for holding an inert atmosphere | 140 |
| | 9.2.8 | The use of a 'spaghetti' tubing manifold | 143 |
| 9.3 | Reaction monitoring | | 144 |
| | 9.3.1 | Thin layer chromatography | 145 |
| | 9.3.2 | High performance liquid chromatography (hplc) | 152 |
| | 9.3.3 | Gas-liquid chromatography (gc, glc, vpc) | 156 |
| 9.4 | Reactions at other than room temperature | | 159 |
| | 9.4.1 | Low temperature reactions | 160 |
| | 9.4.2 | Reactions above room temperature | 163 |
| 9.5 | Driving equilibria | | 168 |
| | 9.5.1 | Dean and Stark traps | 169 |
| | 9.5.2 | High pressure reactions | 170 |
| 9.6 | Agitation | | 170 |
| | 9.6.1. | Magnetic stirring | 170 |
| | 9.6.2. | Mechanical stirrers | 172 |
| | 9.6.3. | Mechanical shakers | 174 |
| | 9.6.4. | Sonication | 175 |

**10 Working up the reaction** **177**

| | | | |
|---|---|---|---|
| 10.1 | Introduction | | 177 |
| 10.2 | Quenching the reaction | | 178 |
| | 10.2.1 | General comments | 178 |
| | 10.2.2 | Strongly basic non-aqueous reactions | 178 |
| | 10.2.3 | Neutral non-aqueous reactions | 179 |
| | 10.2.4 | Strongly acidic non-aqueous reactions | 180 |
| | 10.2.5 | Acidic or basic aqueous reactions | 180 |
| | 10.2.6 | Liquid ammonia reactions | 180 |
| 10.3 | Isolation of the crude product | | 181 |
| | 10.3.1 | General comments | 181 |
| | 10.3.2 | Very polar aprotic solvents | 182 |

**11 Purification** **184**

11.1 Introduction 184
11.2 Crystallization 184
11.2.1 Simple crystallization 184
11.2.2 Small scale crystallization 187
11.2.3 Crystallization at low temperature 189
11.2.4 Crystallization of air sensitive compounds 192
11.3 Distillation 193
11.3.1 Simple distillation 193
11.3.2 Distillation under inert atmosphere 194
11.3.3 Fractional distillation 196
11.3.4 Distillation under reduced pressure 197
11.3.4 Small scale distillation 201
11.4. Sublimation 203
11.5 Chromatographic purification of reaction product 204
11.6 Flash chromatography 205
11.6.1 Equipment required for flash chromatography 205
11.6.2 Procedure for running a flash column 208
11.6.3 Recycling procedure for flash chromatography 214
11.7 Dry-column flash chromatography 215
11.7.1 *Method for running a dry flash column* 215
11.8 Preparative tlc 217
11.9 Medium pressure liquid chromatography 217
11.9.1 Setting up an mplc system 218
11.9.2 Procedure for using mplc 221
11.10 Preparative hplc 224
11.10.1 Equipment required 224
11.10.2 Running a preparative hplc column 224

**12 Small scale reactions** **227**

12.1 Introduction 227
12.2 Reactions at or below room temperature 228
12.3 Reactions above room temperature 231
12.4 Reactions in nmr tubes 232
12.5 Purification of materials 233

试读结束：需要全本请在线购买： www.ertongbook.com

12.5.1 Distillation 233
12.5.2 Crystallization 234
12.5.3 Chromatography 234

**13 Large scale reactions 236**

13.1 Introduction 236
13.2 Carrying out the reaction 237
13.3 Purification of the products 237

**14 Special procedures 240**

14.1 Introduction 240
14.2 Catalytic hydrogenation 240
14.3 Photolysis 244
14.4 Ozonolysis 246
14.5 Flash vacuum pyrolysis 247
14.6 Liquid ammonia reactions 247

**15 Characterization 250**

15.1 Introduction 250
15.2 Nmr 251
15.3 Ir 253
15.4 Uv 254
15.5 Mass spectra 254
15.6 M.p. and b.p. 254
15.7 Optical rotation 255
15.8 Microanalysis 256
15.9 Keeping the data 257

**16 'Trouble shooting'; what to do when things don't work 258**

**17 The chemical literature 262**

17.1 The structure of the chemical information 262

17.1.1 Introduction 262
17.1.2 The structure of the literature 263
17.2 Some important paper-based sources of chemical information 264
17.2.1 Chemical Abstracts 264
17.2.2 Beilstein 265
17.2.3 Science Citation Index 266
17.3 Some important electronic-based sources of chemical information 267
17.3.1 Beilstein 269
17.3.2 CAS ON-LINE 269
17.3.3 CASREACT 269
17.3.4 SCI 269
17.3.5 Chemical Journals On-line (CJO) 270
17.3.6 REACCS (Molecular Design Ltd.) 270
17.3.7 Cambridge Structure Database 270
17.3.8 The World Wide Web 270
17.4 How to find chemical information 271
17.4.1 How to do searches 271
17.4.2 How to find information on specific compounds 272
17.4.3 How to find information on classes of compounds 273
17.4.4 How to find information on synthetic methods 274
17.5 Current awareness 275

**Appendices** **277**

Appendix 1. Properties of common solvents 277
Appendix 2. Properties of common gases 278
Appendix 3. Approximate pKa values for some common deprotonations compared to some common bases 279
Appendix 4. Lewis acids 280
Appendix 5. Common reducing reagents 281
Appendix 6. Common oxidizing reagents 285

**Index** **289**

CHAPTER 1

# General Introduction

The preparation of organic compounds is central to many areas of scientific research, from the most applied to the most "academic", and is not limited to chemists. Any research which uses new organic chemicals, or those which are not available commercially, will at some time require the synthesis of such compounds. Accordingly the biologist, biochemist, genetic engineer, materials scientist, and polymer researcher in university or industry all might find themselves faced with the task of carrying out an organic preparation, along with those involved in pharmaceutical, agrochemical, and other fine chemicals research.

These scientists share with the new organic chemistry graduate student a need to be able to carry out modern organic synthesis with confidence and in such a way as to maximize the chance of success. The techniques, methods, and reagents used in organic synthesis are numerous, and increasing every year. Many of these demand particular conditions and care at several stages of the process, and it is unrealistic to expect an undergraduate course to prepare the chemist for all the situations which might be met in the research laboratories. The non-specialist is even more likely not to be conversant with most modern techniques and reagents.

Nevertheless, it is perfectly possible for both the non-specialist and the graduate student beginning research in organic chemistry to carry out such reactions with success, provided that the appropriate precautions are taken and the proper experimental protocol is observed.

Much of this is common sense, given a knowledge of the properties of the reagents being used, as most general techniques are relatively straightforward. However, it is often very difficult for the beginner or non-specialist to find the appropriate information.

At Salford, we found ourselves handing out to students beginning research in organic chemistry a compilation of what we hoped was useful information on the practical aspects of organic synthesis, based on the authors' recent associations with some of the top synthetic organic research laboratories. We have gathered this information together in this book, and expanded it to cover some other areas, in the hope that it will be an aid to the specialist and non-specialist alike. Of course most research groups will have their own modifications and requirements, but on the whole the basic principles will remain the same.

This book is intended to be a guide to carrying out the types of reactions which are widely used in modern organic synthesis, and is concerned with basic technique. It is not intended to be a comprehensive survey of reagents and methods, but the appendix does contain some information on commonly used reagents.

If we have achieved our aims, users of this book should be able to approach their synthetic tasks with confidence. Organic synthesis is both exciting and satisfying, and provides opportunity for real creativity. If our book helps anyone along this particular path then our efforts will have been worthwhile.

CHAPTER 2

# Safety

## 2.1 Safety is your primary responsibility

Chemical laboratories are potentially dangerous workplaces and accidents in the laboratory can have serious and tragic consequences. However, if you are aware of potential hazards, and work with due care and attention to safety, the risk of accidents is small. Some general guidelines for safety in the laboratory are presented in this section. In addition to these principles you ***must*** be familiar with the safety regulations in force in your area and the rules and guidelines applied by the administrators of your laboratory.

Your supervisor has a responsibility to warn you of the dangers associated with your work, and you should always consult him/her, or a safety officer, if you are unsure about potential hazards. However, your own safety, and that of your colleagues in the lab, is largely determined by ***your*** work practices. Always work carefully, use your common sense, and abide by the safety regulations.

Some important general principles of safe practice are summarized in the following rules

1. ***Work carefully, do not take risks.***
   This covers basic rules such as always wearing safety spectacles, never working alone, and working neatly and unhurriedly.
2. ***Assess the possible hazards before carrying out a reaction.***
   Find out about the dangers of handling unfamiliar chemicals or apparatus and take note of any necessary precautions.
3. ***Know the accident and emergency procedures.***

It is vital to know what to do in case of an accident. This includes being familiar with the fire fighting and first aid equipment, and knowing how to get assistance from qualified personnel.

## 2.2 Safe working practice

It has been emphasized already that you should be familiar with the regulations and codes of practice pertaining in your laboratory. We will not discuss safety legislation here but some fundamental rules should be stressed. Never work alone in a laboratory. Always wear suitable safety spectacles and a cotton lab coat, and use other protection such as gloves, face masks, or safety shields if there is a particular hazard. Never eat, drink or smoke in a laboratory. Work at a safe, steady pace, and keep your bench and your lab clean and tidy. Familiarity breeds contempt; do not allow yourself to get careless with everyday dangers such as solvent flammability. Familiarize yourself with the location and operation of the safety equipment in your laboratory.

As regards specific hazards the chief rule is to carry out an assessment of the dangers involved before using an unfamiliar chemical or piece of apparatus. Some of the commonest hazards are described in the next section. Once you are aware of the possible dangers take all the necessary precautions, and ensure that you know what to do if an accident does occur.

Store your chemicals in clearly labelled containers, and abide by the regulations concerning storage of solvents and other hazardous materials. Dispose of waste chemicals safely, according to the approved procedures for your laboratory. Never pour organic compounds down the sink.

## 2.3 Common hazards

Always assess the risks involved ***before*** carrying out a reaction. Extensive compilations of information about the dangers posed by a large number of compounds are available (see Bibliography). Consult these references and your supervisor before using a compound or procedure which is new to you. In some areas safety legislation makes it mandatory to conduct such a safety audit, but even if it is not legally required, it should still be regarded as an essential preliminary before doing a reaction.

试读结束：需要全本请在线购买： www.ertongbook.com