

Supercritical Fluid

Methods and Protocols

Edited by

John R. Williams

Anthony A. Clifford



HUMANA PRESS

METHODS IN BIOTECHNOLOGY™

Supercritical Fluid Methods and Protocols

Edited by

John R. Williams

College of Science, Sultan Qaboos University, Sultanate of Oman

and

Anthony A. Clifford


School of Chemistry, Leeds, UK

Humana Press  Totowa, New Jersey

© 2000 Humana Press Inc.
999 Riverview Drive, Suite 208
Totowa, New Jersey 07512

All rights reserved. No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, microfilming, recording, or otherwise without written permission from the Publisher. Methods in Biotechnology™ is a trademark of The Humana Press Inc.

All authored papers, comments, opinions, conclusions, or recommendations are those of the author(s), and do not necessarily reflect the views of the publisher.

This publication is printed on acid-free paper. 
ANSI Z39.48-1984 (American Standards Institute) Permanence of Paper for Printed Library Materials.

Cover design by Patricia F. Cleary.

For additional copies, pricing for bulk purchases, and/or information about other Humana titles, contact Humana at the above address or at any of the following numbers: Tel: 973-256-1699; Fax: 973-256-8341; E-mail: humana@humanapr.com, or visit our Website at www.humanapress.com

Photocopy Authorization Policy:

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by Humana Press Inc., provided that the base fee of US \$10.00 per copy, plus US \$00.25 per page, is paid directly to the Copyright Clearance Center at 222 Rosewood Drive, Danvers, MA 01923. For those organizations that have been granted a photocopy license from the CCC, a separate system of payment has been arranged and is acceptable to Humana Press Inc. The fee code for users of the Transactional Reporting Service is: [0-89603-571-9/00 \$10.00 + \$00.25].

Printed in the United States of America. 10 9 8 7 6 5 4 3 2 1

Library of Congress Cataloging in Publication Data

Supercritical fluid methods and protocols / edited by John R. Williams and Anthony A. Clifford.
p. cm. -- (Methods in biotechnology ; 13)

Includes bibliographical references and index.

ISBN 0-89603-571-9 (alk. paper)

I. Supercritical fluid extraction--Laboratory manuals. 2. Supercritical fluid chromatography--Laboratory manuals. 3. Biomolecules--Separation--Laboratory manuals. I. Williams, John R., 1967- II. Clifford, Tony. III. Series.

QP519.9.S85 S87 2001
572'.36'028--dc21

00-024567

Supercritical Fluid Methods and Protocols

METHODS IN BIOTECHNOLOGY™

John M. Walker, SERIES EDITOR

13. **Supercritical Fluid Methods and Protocols**, edited by *John R. Williams and Anthony A. Clifford, 2000*
12. **Environmental Monitoring of Bacteria**, edited by *Clive Edwards, 1999*
11. **Aqueous Two-Phase Systems**, edited by *Rajni Hatti-Kaul, 1999*
10. **Carbohydrate Biotechnology Protocols**, edited by *Christopher Bucke, 1999*
9. **Downstream Processing Methods**, edited by *Mohamed A. Desai, 2000*
8. **Animal Cell Biotechnology**, edited by *Nigel Jenkins, 1999*
7. **Affinity Biosensors: Techniques and Protocols**, edited by *Kim R. Rogers and Ashok Mulchandani, 1998*
6. **Enzyme and Microbial Biosensors: Techniques and Protocols**, edited by *Ashok Mulchandani and Kim R. Rogers, 1998*
5. **Biopesticides: Use and Delivery**, edited by *Franklin R. Hall and Julius J. Menn, 1998*
4. **Natural Products Isolation**, edited by *Richard J. P. Cannell, 1998*
3. **Recombinant Proteins from Plants: Production and Isolation of Clinically Useful Compounds**, edited by *Charles Cunningham and Andrew J. R. Porter, 1998*
2. **Bioremediation Protocols**, edited by *David Sheehan, 1997*
1. **Immobilization of Enzymes and Cells**, edited by *Gordon F. Bickerstaff, 1997*

Preface

Over the last 15 years, there has been renewed interest in supercritical fluids owing to their unique properties and relatively low environmental impact. Greatest attention has been given to the extraction and separation of organic compounds. Supercritical fluids have also been successfully used for particle production, as reaction media, and for the destruction of toxic waste. Supercritical carbon dioxide has been the most widely used supercritical fluid, mainly because it is cheap, relatively nontoxic, and has convenient critical values. Supercritical fluids have also been used on analytical and preparative scales for many biological and other applications.

Many papers have been published on the use of supercritical fluids. However, few have acted as a detailed instruction manual for those wanting to use the techniques for the first time. We anticipate that this *Methods in Biotechnology* volume, *Supercritical Fluid Methods and Protocols* will satisfy the need for such a book.

Every chapter has been written by experienced workers and should, if closely followed, enable workers with some or no previous experience of supercritical fluids to conduct experiments successfully at the first attempt. The Introduction to each chapter gives the reader all the necessary background information. The Materials and Methods sections describe, in detail, the apparatus and steps needed to complete the protocol quickly, with a minimum of fuss. The Notes section, an acclaimed feature of the *Methods in Biotechnology* series, gives additional information not normally seen in published papers that enable the procedures to be conducted easily. Some of the chapters describe how the procedures can be modified for application to new situations. The first chapter is not a detailed procedure, but a theoretical, general introduction to the area of supercritical fluids intended to instruct novices in this branch of technology.

It is envisaged that *Supercritical Fluid Methods and Protocols* will be useful to both student and experienced research workers in biology and related areas. Our hope is that the experience gained when using these techniques will give these workers the confidence to explore new applications for supercritical fluids.

One can envisage a time in the future when the use of sub- and supercritical carbon dioxide and water becomes very important in laboratory work, with organic solvent use considerably reduced.

Finally, we would like to thank Professor John Walker for allowing us to edit this volume and for his cooperation during the compiling of this book. We would also like to acknowledge Professor E. D. Morgan of Keele University, UK for passing this opportunity on to us. We thank Thomas Lanigan and his colleagues at Humana for their help in seeing our book through press.

John R. Williams
Anthony A. Clifford

Contributors

- PAOLO ALESSI • *Dipartimento di Ingegneria Chimica, dell'Ambiente e delle Materie Prime, University of Trieste, Trieste, Italy*
- KEIICHI AOE • *Analytical Research Laboratory, Tanabe Seiyaku Co., Ltd., Osaka, Japan*
- VIDDESH R. BARI • *Department of Chemistry, Ismail Yusuf College of Arts, Commerce and Science, Mumbai, India*
- SUSANA BARREIROS • *Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Oeiras, Portugal*
- JOSÉ L. BERNAL • *Department of Analytical Chemistry, Faculty of Sciences, University of Valladolid, Valladolid, Spain*
- ALBERTO BERTUCCO • *Istituto di Impianti Chimici, University of Padova, Padova, Italy*
- CHRISTINA BORCH-JENSEN • *Department of Chemical Engineering, Technical University of Denmark, Lyngby, Denmark*
- DOUGLAS BRAY • *Department of Biological Sciences, University of Lethbridge, Lethbridge, Canada*
- FABIO CARLI • *Vectorpharma SPA, Trieste, Italy*
- ANTHONY A. CLIFFORD • *School of Chemistry, University of Leeds, Leeds, UK*
- PHILIPPE CHRISTEN • *Laboratoire de Chimie Analytique Pharmaceutique, Université de Genève, Genève, Switzerland*
- MICHAEL D. COLE • *Forensic Science Unit, University of Strathclyde, Glasgow, UK*
- MARIA L. COLOMBO • *Institute of Pharmacological Science, University of Milan, Milan, Italy*
- TERESA CORRÊA DE SAMPAIO • *Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Oeiras, Portugal*
- ANGELO CORTESI • *Dipartimento di Ingegneria Chimica, dell'Ambiente e delle Materie Prime, University of Trieste, Trieste, Italy*
- JOHN R. DEAN • *School of Applied and Molecular Sciences, University of Northumbria, Newcastle upon Tyne, UK*
- MARÍA J. DEL NOZAL • *Department of Analytical Chemistry, Faculty of Sciences, University of Valladolid, Valladolid, Spain*

- URMILA J. DHORDA • *Department of Chemistry, Ismail Yusuf College of Arts, Commerce and Science, Mumbai, India*
- WALTER FIDDLER • *Agricultural Research Service, Eastern Regional Research Center, US Department of Agriculture, Wyndmoor, PA*
- BRENDA S. FUERST • *Food Safety Inspection Service, Midwestern Laboratory, US Department of Agriculture, St. Louis, MO*
- MÁRIO S. GALHIANE • *Institute of Chemistry of São Carlos, University of São Paulo, São Carlos, Brazil*
- THOMAS GAMSE • *Institut für Thermische Verfahrenstechnik und Umwelttechnik, Technische Universität Graz, Graz, Austria*
- MICHAEL O. GAYLOR • *Department of Environmental Sciences, Virginia Institute of Marine Sciences, College of William and Mary, Gloucester Point, VA*
- RICKY L. GREEN • *Express Separations Limited, Leeds, UK*
- WERNER HAERDI • *Laboratoire de Chimie Analytique Pharmaceutique, Université de Genève, Pavillon des Isotopes, Genève, Switzerland*
- ROBERT C. HALE • *Department of Environmental Sciences, Virginia Institute of Marine Sciences, College of William and Mary, Gloucester Point, VA*
- KARI HARTONEN • *Laboratory of Analytical Chemistry, Department of Chemistry, University of Helsinki, Helsinki, Finland*
- CAROLYN HENRY • *Midwestern Laboratory, Food Safety Inspection Service, US Department of Agriculture, St. Louis, MO*
- RAINER HUOPALAHTI • *Department of Biochemistry and Food Chemistry, University of Turku, Turku, Finland*
- BROOKS M. HYBERTSON • *Webb-Waring Institute for Cancer, Aging and Antioxidant Research, University of Colorado Health Sciences Center, Denver, CO*
- EILA P. JÄRVENPÄÄ • *Department of Biochemistry and Food Chemistry, University of Turku, Turku, Finland*
- JUAN J. JIMÉNEZ • *Department of Analytical Chemistry, Faculty of Sciences, University of Valladolid, Valladolid, Spain*
- IRENEO KIKIC • *Dipartimento di Ingegneria Chimica, dell'Ambiente e delle Materie Prime, University of Trieste, Trieste, Italy*
- PASCAL KINTZ • *Institut de Médecine Légale, Cedex, France*
- MARCEL KOHLER • *Laboratoire de Chimie Analytique Pharmaceutique, Université de Genève, Pavillon des Isotopes, Genève, Switzerland*
- FERNANDO M. LANÇAS • *Institute of Chemistry of São Carlos, University of São Paulo, São Carlos, Brazil*
- KEITH L. LEVIEN • *Department of Chemical Engineering, Oregon State University, Corvallis, OR*

- ALAN R. LIGHTFIELD • *Eastern Regional Research Center, Agricultural Research Service, US Department of Agriculture, Wyndmoor, PA*
- BEN LIU • *Department of Pharmacy, Hubei College of Traditional Chinese Medicine, People's Republic of China*
- EDWIN LUDKIN • *School of Applied and Molecular Sciences, University of Northumbria, Ellison Building, Newcastle upon Tyne, UK*
- MAGNUS MAGNUSSEN • *Food and Environmental Institute, Thorshavn, Faroe Islands*
- KARIN E. MARKIDES • *Department of Analytical Chemistry, Uppsala University, Uppsala, Sweden*
- ROLF MARR • *Institut für Thermische Verfahrenstechnik und Umwelttechnik, Technische Universität Graz, Graz, Austria*
- MARÍA T. MARTÍN • *Department of Analytical Chemistry, Faculty of Sciences, University of Valladolid, Valladolid, Spain*
- ROBERT J. MAXWELL • *Eastern Regional Research Center, Agricultural Research Service, US Department of Agriculture, Wyndmoor, PA*
- HARALD MICHOR • *Institut für Thermische Verfahrenstechnik und Umwelttechnik, Technische Universität Graz, Graz, Austria*
- BRIAN MINTY • *School of Applied Sciences, University of Glamorgan, Glamorgan, UK*
- JØRGEN MOLLERUP • *Department of Chemical Engineering, Technical University of Denmark, Lyngby, Denmark*
- FUJIO MORISHITA • *Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoto, Japan*
- JEFFREY J. MORRELL • *Department of Forest Products, Oregon State University, Corvallis, OR*
- ANDREA MOSSA • *Institute of Pharmacological Science, University of Milan, Milan, Italy*
- NORIYUKI NISHIMURA • *Analytical Research Laboratory, Tanabe Seiyaku Co., Ltd., Osaka, Japan*
- HIDETAKA NORITOMI • *Department of Applied Chemistry, Graduate School of Engineering, Tokyo Metropolitan University, Tokyo, Japan*
- PAOLO PALLADO • *Exenia Group srl., Albignasego, Italy*
- JOHN W. PENSABENE • *Eastern Regional Research Center, Agricultural Research Service, US Department of Agriculture, Wyndmoor, PA*
- OWEN W. PARKS • *Eastern Regional Research Center, Agricultural Research Service, US Department of Agriculture, Wyndmoor, PA*
- EDWARD D. RAMSEY • *School of Applied Sciences, University of Glamorgan, Glamorgan, UK*
- ANTHONY T. REES • *Nycomed Amersham, Cardiff Laboratories, Cardiff, UK*

- MARJA-LIISA RIEKKOLA • *Laboratory of Analytical Chemistry, Department of Chemistry, University of Helsinki, Helsinki, Finland*
- SANDRA R. RISSATO • *Institute of Chemistry of São Carlos, University of São Paulo, São Carlos, Brazil*
- TADASHI SATO • *Analytical Research Laboratory, Tanabe Seiyaku Co., Ltd., Osaka, Japan*
- HELMUT SCHWAB • *Institut für Biotechnologie, Technische Universität Graz, Graz, Austria*
- FRANCISCO J. SEÑORÁNS • *Ciencia y Tecnología de Alimentos, Facultad de Ciencias, Universidad Autónoma de Madrid, Madrid, Spain*
- MARIA L. SERNA • *Department of Analytical Chemistry, Faculty of Sciences, University of Valladolid, Valladolid, Spain*
- ROXANNE J. SHADWELL • *Eastern Regional Research Center, Agricultural Research Service, US Department of Agriculture, Wyndmoor, PA*
- CHRISTIAN STAUB • *Institut de Médecine Légale, Genève, Switzerland*
- G. KIM STEARMAN • *Center for the Management, Utilization and Protection of Water Resources, Tennessee Technological University, Cookeville, TN*
- M. SUNDARESAN • *Department of Chemistry, C.B. Patel Research Centre for Chemistry and Biological Sciences, Mumbai, India*
- LAURA TORIBIO • *Department of Analytical Chemistry, Faculty of Sciences, University of Valladolid, Valladolid, Spain*
- JEAN-LUC VEUTHEY • *Laboratoire de Chimie Analytique Pharmaceutique, Université de Genève, Pavillon des Isotopes, Genève, Switzerland*
- JOHN R. WILLIAMS • *Department of Chemistry, College of Science, Sultan Qaboos University, Sultanate of Oman*
- KOJI YAKU • *Analytical Research Laboratory, Tanabe Seiyaku Co., Ltd., Osaka, Japan*

Contents

Preface	v
Contributors	xi
1 Introduction to Supercritical Fluids and Their Applications Anthony A. Clifford and John R. Williams	1
2 Supercritical Fluid Extraction of Caffeine from Instant Coffee John R. Dean, Ben Liu, and Edwin Ludkin	17
3 Supercritical Fluid Extraction of Nitrosamines from Cured Meats John W. Pensabene and Walter Fiddler	23
4 Supercritical Fluid Extraction of Melengestrol Acetate from Bovine Fat Tissue Robert J. Maxwell, Owen W. Parks, Roxanne J. Shadwell, Alan R. Lightfield, Carolyn Henry, and Brenda S. Fuerst	31
5 Supercritical Fluid Extraction of Polychlorinated Biphenyls from Fish Tissue Michael O. Gaylor and Robert C. Hale	41
6 Isolation of Polynuclear Aromatic Hydrocarbons from Fish Products by Supercritical Fluid Extraction Eila P. Järvenpää and Rainer Huopalahti	55
7 Supercritical Fluid Extraction of Mycotoxins from Feeds Rainer Huopalahti and Eila P. Järvenpää	61
8 Supercritical Fluid Extraction of Pigments from Seeds of <i>Eschscholtzia californica</i> Cham. Maria L. Colombo and Andrea Mossa	67
9 Supercritical Fluid Extraction of Flumetralin from Tobacco Samples Fernando M. Lanças, Mário S. Galhiane, and Sandra R. Rissato	75
10 Supercritical Fluid Extraction and High Performance Liquid Chromatography Determination of Carbendazim in Bee Larvae José L. Bernal, Juan J. Jiménez, and María T. Martín	83

11	Supercritical Fluid Extraction Coupled with Enzyme Immunoassay Analysis of Soil Herbicides G. Kim Stearman	89
12	The Supercritical Fluid Extraction of Drugs of Abuse from Human Hair Pascal Kintz and Christian Staub	95
13	Application of Direct Aqueous Supercritical Fluid Extraction for the Dynamic Recovery of Testosterone Liberated from the Enzymatic Hydrolysis of Testosterone- β -D-Glucuronide Edward D. Ramsey, Brian Minty, and Anthony T. Rees	105
14	Analysis of Anabolic Drugs by Direct Aqueous Supercritical Fluid Extraction Coupled On-Line with High-Performance Liquid Chromatography Edward D. Ramsey, Brian Minty, and Anthony T. Rees	113
15	Detection of Beta-Blockers in Urine and Serum by Solid-Phase Extraction–Supercritical Fluid Extraction and Gas Chromatography–Mass Spectrometry Kari Hartonen and Marja-Liisa Riekkola	119
16	On-Line SFE–SFC for the Analysis of Fat-Soluble Vitamins and Other Lipids from Water Matrices Francisco J. Señoráns and Karin E. Markides	127
17	Determination of Artemisinin in <i>Artemisia annua</i> L. by Off-Line Supercritical Fluid Extraction and Supercritical Fluid Chromatography Coupled to an Evaporative Light-Scattering Detector Marcel Kohler, Werner Haerdi, Philippe Christen, and Jean-Luc Veuthey	135
18	Analysis of <i>Cannabis</i> by Supercritical Fluid Chromatography with Ultraviolet Detection Michael D. Cole	145
19	Direct Chiral Resolution of Optical Isomers of Diltiazem Hydrochloride by Packed Column Supercritical Fluid Chromatography Koji Yaku, Keiichi Aoe, Noriyuki Nishimura, Tadashi Sato, and Fujio Morishita	149
20	Determination of Salbutamol Sulfate and Its Impurities in Pharmaceuticals by Supercritical Fluid Chromatography María J. del Nozal, Laura Toribio, José L. Bernal, and María L. Serna	157

21	Packed Column Supercritical Fluid Chromatographic Determination of Acetaminophen, Propyphenazone, and Caffeine in Pharmaceutical Dosage Forms Urmila J. Dhorda, Viddesh R. Bari, and M. Sundaresan	163
22	Analysis of Shark Liver Oil by Thin-Layer and Supercritical Fluid Chromatography Christina Borch-Jensen, Magnus Magnussen, and Jørgen Møllerup	169
23	Enzymatically Catalyzed Transesterifications in Supercritical Carbon Dioxide Rolf Marr, Harald Michor, Thomas Gamse, and Helmut Schwab	175
24	Transesterification Reactions Catalyzed by Subtilisin Carlsberg Suspended in Supercritical Carbon Dioxide and in Supercritical Ethane Teresa Corrêa de Sampaio and Susana Barreiros	179
25	Enzymatic Synthesis of Peptide in Water-Miscible Organic Solvent/Supercritical Carbon Dioxide Hidetaka Noritomi	189
26	Micronization of a Polysaccharide by a Supercritical Antisolvent Technique Alberto Bertucco and Paolo Pallado	193
27	Rapid Expansion of Supercritical Solutions Technology: Production of Fine Particles of Steroid Drugs Paolo Alessi, Angelo Cortesi, Ireneo Kikic, and Fabio Carli	201
28	Supercritical Fluid Aerosolized Vitamin E Supplementation Brooks M. Hybertson	209
29	Extraction of Biologically Active Substances from Wood Jeffrey J. Morrell and Keith L. Levien	221
30	The Deposition of a Biocide in Wood-Based Material Jeffrey J. Morrell and Keith L. Levien	227
31	Critical Point Drying of Biological Specimens for Scanning Electron Microscopy Douglas Bray	235
32	Staining of Fingerprints on Checks and Banknotes Using Ninhydrin Anthony A. Clifford and Ricky L. Green	245
	Index	251

Introduction to Supercritical Fluids and Their Applications

Anthony A. Clifford and John R. Williams

1. Pure Substances as Supercritical Fluids

Cagniard de la Tour showed in 1822 that there is a *critical temperature* above which a single substance can only exist as a fluid and not as either a liquid or gas. He heated substances, present as both liquid and vapor, in a sealed cannon, which he rocked back and forth and discovered that, at a certain temperature, the splashing ceased. Later, he constructed a glass apparatus in which the phenomenon could be more directly observed. These phenomena can be put into context by reference to **Fig. 1**, which is a phase diagram of a single substance. The diagram is schematic, the pressure axis is nonlinear, and the solid phase at high temperatures occurs at very high pressures. Further solid phases and also liquid crystal phases can also occur on a phase diagram. The areas where the substance exists as a single solid, liquid, or gas phase are labeled, as is the triple point where the three phases coexist. The curves represent coexistence between two of the phases. If we move upward along the gas–liquid coexistence curve, which is a plot of vapor pressure vs temperature, both temperature and pressure increase. The liquid becomes less dense because of thermal expansion, and the gas becomes more dense as the pressure rises. At the critical point, the densities of the two phases become identical, the distinction between the gas and the liquid disappears, and the curve comes to an end at the *critical point*. The substance is now described as a fluid. The critical point has pressure and temperature co-ordinates on the phase diagram, which are referred to as the critical temperature, T_c , and the critical pressure, p_c , and which have particular values for particular substances, as shown by example in **Table 1 (I)**.

In recent years, fluids have been exploited above their critical temperatures and pressures, and the term *supercritical fluids* has been used to describe these

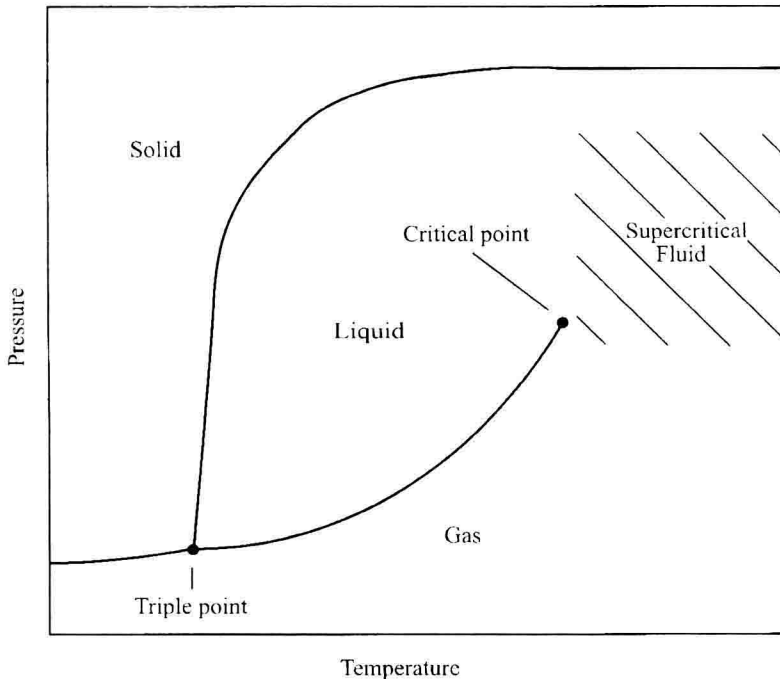


Fig. 1. The phase diagram of a single substance.

media. The greatest advantages of supercritical fluids are realized when they are used not too far above (say within 100 K of) their critical temperatures. Nitrogen gas in a cylinder is a fluid, but is not usually considered as a supercritical fluid, but more often described by an older term as a permanent gas. The region for supercritical fluids is the hatched area in **Fig. 1**. It has been shown to include a region a little below the critical pressure, as processes at these conditions are sometimes included in discussions as “supercritical.” Lower pressures are important in practice also because these conditions are relevant to separation stages in supercritical processes. There are no phase boundaries below and to the left of the supercritical region in **Fig. 1**, and behavior does not change dramatically on moving out of the hatched area in these directions. The liquid region to the left of the supercritical region has many of the characteristics of supercritical fluids and is exploited in a similar way. For this reason some people prefer the term *near-critical fluids* and the adjective *subcritical* is also used. The term supercritical fluid has, however, gained currency; is convenient and not problematic provided the definition is not too rigid. Supercritical fluids exhibit important characteristics, such as compressibility, homogeneity, and a continuous change from gaslike to liquidlike prop-

Table 1
Substances Useful as Supercritical Fluids

Substance	Critical Temperature, T_c (K)	Critical Pressure, p_c (bar)
Carbon dioxide	304	74
Water	647	221
Ethane	305	49
Ethene	282	50
Propane	370	43
Xenon	290	58
Ammonia	406	114
Nitrous oxide	310	72
Fluoroform	299	49

Parameters from Reid et al. (1).

erties. These properties are characteristic of conditions inside the hatched area in **Fig. 1** and, to different degrees, in the area around it.

Table 1 shows the critical parameters of some of the important compounds useful as supercritical fluids. One compound, carbon dioxide, has so far been the most widely used because of its convenient critical temperature, cheapness, chemical stability, nonflammability, stability in radioactive applications, and nontoxicity. Large amounts of carbon dioxide released accidentally could constitute a working hazard, given its tendency to blanket the ground, but hazard detectors are available. It is an environmentally friendly substitute for organic solvents. The carbon dioxide is obtained in large quantities as a by-product of fermentation, combustion, and ammonia synthesis and would be released into the atmosphere sooner rather than later, if it were not used as a supercritical fluid. Its polar character as a solvent is intermediate between a truly nonpolar solvent, such as hexane, and weakly polar solvents. Because the molecule is nonpolar, it is often classified as a nonpolar solvent, but it has some limited affinity with polar solutes because of its large molecular quadrupole. To improve its affinity with polar molecules further, carbon dioxide is sometimes modified with polar entrainers (*see Subheading 3.*). However, pure carbon dioxide can be used for many organic solute molecules even if they have some polar character. It has a particular affinity for fluorinated compounds and is useful for working with fluorinated metal complexes and fluoropolymers.

Carbon dioxide is not such a good solvent for hydrocarbon polymers and other hydrocarbons of high molar mass. Ethane, ethene, and propane become alternatives for these compounds, although they have the disadvantages of