

Edited by Paul T. Anastas

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Green Processes



Volume 9: Designing Safer Chemicals

Volume Editors:
Robert Boethling
Adelina Voutchkova



Handbook of Green Chemistry

Volume 9

Designing Safer Chemicals

Edited by

Robert Boethling and Adelina Voutchkova



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The Editor

Prof. Dr. Paul T. Anastas

Yale University
Center for Green Chemistry & Green Engineering
225 Prospect Street
New Haven, CT 06520
USA

Volume Editors

Dr. Robert Boethling

U.S. Environmental Protection
Agency
1200 Pennsylvania Ave. N.W.
Washington, DC 20460
USA

Dr. Adelina Voutchkova

Yale University
Department of Chemistry
225 Prospect Street
New Haven, CT 06520
USA

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About the Editors

Series Editor



Paul T. Anastas joined Yale University as Professor and serves as the Director of the Center for Green Chemistry and Green Engineering there. From 2004–2006, Paul was the Director of the Green Chemistry Institute in Washington, D.C. Until June 2004 he served as Assistant Director for Environment at the White House Office of Science and Technology Policy where his responsibilities included a wide range of environmental science issues including furthering international public-private cooperation in areas of Science for Sustainability such as Green Chemistry. In 1991, he established the industry-government-university partnership Green Chemistry Program, which was expanded to include basic research, and the Presidential Green Chemistry Challenge Awards. He has published and edited several books in the field of Green Chemistry and developed the 12 Principles of Green Chemistry.

Volume Editors



Robert S. Boethling has been at the US Environmental Protection Agency headquarters in Washington, DC, Office of Pollution Prevention and Toxics (OPPT) since 1980. After earning his PhD degree in microbiology at UCLA (1976) he spent 2 years in Martin Alexander's soil microbiology lab at Cornell University, and came to EPA as it began its implementation of the Toxic Substances Control Act (TSCA). For many years he led environmental fate review for new chemical (Premanufacture Notice) substances under TSCA, the program from which predictive capabilities, tools and software in environmental chemistry emerged starting in the 1980s. He was a principal contributor in the development of several widely used computer programs, notably EPI

Suite, the PBT Profiler, and the BLOWIN biodegradability estimation program. He is the recipient of many EPA medals for distinguished service and several EPA Science and Technology Achievement Awards (STAA), including awards for review of new chemical substances under TSCA and the *Handbook of Property Estimation Methods for Chemicals: Environmental Health Sciences* (Lewis/CRC, 2000, with Don Mackay).



Adelina Voutchkova is an Assistant Professor at the Department of Chemistry at the George Washington University. She received her Ph.D. from Yale University and subsequently joined the Center for Green Chemistry and Green Engineering at Yale as a research associate. Dr. Voutchkova's current research interests span both facets of green chemistry - the design of tools that chemists can apply to the rational design safer industrial chemicals, and the development of greener metal-catalyzed organic transformations.

List of Contributors

Paul Anastas

Yale University
Department of Chemistry
225 Prospect Street
New Haven, CT 06520
USA

Fred Arnold

U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Nicholas A. Ashford

Massachusetts Institute of Technology
Technology and Law Program
77 Mass Avenue, Room E40-239
Cambridge, MA 02139
USA

Charles Auer

Charles Auer & Associates, LLC
17116 Campbell Farm Road
Poolesville, MD 20837
USA

Sajida Bakhtyar

Curtin University
Department of Environment and
Agriculture
Kent Street
Perth, WA 6845
Australia

Ian Beadham

Dublin City University
School of Chemical Sciences
Collins Avenue
Dublin 9
Ireland

Robert S. Boethling

U.S. Environmental Protection Agency
Office of Pollution Prevention and
Toxics
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Mary Cushmac (Retired)

U.S. Environmental Protection Agency
Design for the Environment Program
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Clive Davies

U.S. Environmental Protection Agency
Design for the Environment Program
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Stephen C. DeVito

U.S. Environmental Protection Agency
Office of Environmental Information
Toxics Release Inventory Program
1200 Pennsylvania Avenue NW
Washington, DC 20004
USA

David DiFiore

U.S. Environmental Protection Agency
Design for the Environment Program
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Nicholas J. Dixon

Innospec Ltd.
Oil Sites Road
Ellesmere Port, Cheshire CH65 4EY
UK

Marthe Monique Gagnon

Curtin University
Department of Environment and
Agriculture
Kent Street
Perth, WA 6845
Australia

Nicholas Gathergood

Dublin City University
School of Chemical Sciences
Collins Avenue
Dublin 9
Ireland

Fadri Gottschalk

EMPA – Swiss Federal Laboratories for
Materials Science and Technology
Technology and Society Laboratory
Lerchenfeldstrasse 5
9014 St. Gallen
Switzerland

**Kelly Grant (Former AAAS Science and
Technology Policy Fellow)**

U.S. Environmental Protection Agency
Design for the Environment Program
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Monika Gurbisz

Dublin City University
School of Chemical Sciences
Collins Avenue
Dublin 9
Ireland

Mark Hanson

University of Manitoba
Department of Environment and
Geography
Winnipeg, MB R3T 2N2
Canada

Katherine Hart

U.S. Environmental Protection Agency
Design for the Environment Program
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Carol Hetfield

U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Philip H. Howard

SRC, Inc.
7502 Round Pond Road
North Syracuse, NY 13212
USA

Russell S. Jones

U.S. Environmental Protection Agency
 Biopesticides and Pollution Prevention
 Division
 Office of Pesticide Programs
 1200 Pennsylvania Avenue NW
 Washington, DC 20460
 USA

Richard Judson

U.S. Environmental Protection Agency
 National Center for Computational
 Toxicology
 109 T.W. Alexander Drive
 Research Triangle Park, NC 27711
 USA

Jakub Kostal

Yale University
 Department of Chemistry
 225 Prospect Street
 New Haven, CT 06520
 USA

Klaus Kümmerer

Leuphana University Lüneburg
 Institute of Sustainable and
 Environmental Chemistry
 Scharnhorststraße 1
 21335 Lüneburg
 Germany

David Y. Lai

U.S. Environmental Protection Agency
 Office of Pollution Prevention and
 Toxics
 Risk Assessment Division
 1200 Pennsylvania Avenue NW
 Washington, DC 20460
 USA

Emma Lavoie

U.S. Environmental Protection Agency
 Design for the Environment Program
 1200 Pennsylvania Avenue NW
 Washington, DC 20460
 USA

Chuantung Lin

U.S. Environmental Protection Agency
 Office of Pollution Prevention and Toxics
 1200 Pennsylvania Avenue NW
 Washington, DC 20460
 USA

**Meghan Marshall (Former Student
Career Experience Program Intern)**

U.S. Environmental Protection Agency
 Design for the Environment Program
 1200 Pennsylvania Avenue NW
 Washington, DC 20460
 USA

Michael McDavit

U.S. Environmental Protection Agency
 Biopesticides and Pollution Prevention
 Division
 Office of Pesticide Programs
 1200 Pennsylvania Avenue NW
 Washington, DC 20460
 USA

Laura Morlacci

SRC, Inc.
 2451 Crystal Drive, Suite 475
 Arlington, VA 22202
 USA

Nicole C. Mueller

EMPA – Swiss Federal Laboratories for
 Materials Science and Technology
 Technology and Society Laboratory
 Lerchenfeldstrasse 5
 9014 St. Gallen
 Switzerland

John L. Nelson

Eastern Michigan University
Chemistry Department
Ypsilanti, MI 48197
USA

Bernd Nowack

EMPA – Swiss Federal Laboratories for
Materials Science and Technology
Technology and Society Laboratory
Lerchenfeldstrasse 5
9014 St. Gallen
Switzerland

Thomas G. Osimitz

Science Strategies, LLC
Citizens Commonwealth Center
300 Preston Ave
Charlottesville, VA 22902
USA

Keith R Solomon

University of Guelph
Centre for Toxicology and School of
Environmental Sciences
2120 Bovey Building
Gordon Street
Guelph, ON N1G 2W1
Canada

Claudia Som

EMPA – Swiss Federal Laboratories for
Materials Science and Technology
Technology and Society Laboratory
Lerchenfeldstrasse 5
9014 St. Gallen
Switzerland

Elizabeth Sommer

U.S. Environmental Protection Agency
Design for the Environment Program
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Kathleen Vokes

U.S. Environmental Protection Agency
Office of Air and Radiation
Office of Atmospheric Programs
Climate Protection Partnership Division
ENERGY STAR Labeling Branch
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Adelina Voutchkova

Yale University
Department of Chemistry
225 Prospect Street
New Haven, CT 06520
USA

Melanie Vrabel

U.S. Environmental Protection Agency
Design for the Environment Program
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Yin-tak Woo

U.S. Environmental Protection Agency
Office of Pollution Prevention and
Toxics
Risk Assessment Division
1200 Pennsylvania Avenue NW
Washington, DC 20460
USA

Preface

Design is a statement of human intention. You can't design by accident. It has to be a conscious decision. To make the design decisions you need considerations; you need criteria. If you want to design molecules for reduced hazard, those criteria need to be based on an understanding of the molecular basis of hazard. Fortunately, there are data from the world of molecular toxicology that provide us with insights for the foundations for our problems and concerns around chemicals. At some level, the only reason to deeply understand a problem is to use that understanding to inform and empower the solution to the problem. That is what this volume of *Designing Safer Chemicals* is about; solving (and avoiding) problems.

Synthetic chemistry is a highly advanced field, and chemists have developed the expertise in designing chemicals for specific industrial or pharmaceutical functions. Unfortunately, even today relatively little systematic consideration is given to rationally minimizing undesired toxic and environmental effects at the design stage.

Principle 4 of the Twelve Principles of Green Chemistry, "**Designing safer chemicals**," stresses preserving useful function while reducing toxicity, and is an emerging field. This volume highlights illustrative examples of how chemicals have been designed, or redesigned, to minimize toxicity, and provides some basic guidelines for minimizing some types of unintended biological activity. It also underscores the important need for research and development focusing on design strategies that are based on mechanisms of biological action and relevant physical and chemical properties.

If we consider the design of commercial chemicals that are not only benign to humans but also to the environment, we see that toxicity is not the only consideration. In fact, we can broadly segregate hazards into three types, as shown in Figure 1: toxicological (human and environmental), physical (such as explosivity, material corrosion and flammability) and global (large scale effects on our planet: influencing climate change, causing an increased loading of persistent and bioaccumulative chemicals). The majority of this text focuses on toxicological hazards, but several chapters, such as Chapter 16 (Howard/Boethling) and Chapter 17 (Ashford) introduce the topic of global and physical hazards.

The idea of deriving molecular design strategies for reduced intrinsic hazard may seem idealistic to chemists, who are trained to think of all chemicals as potentially

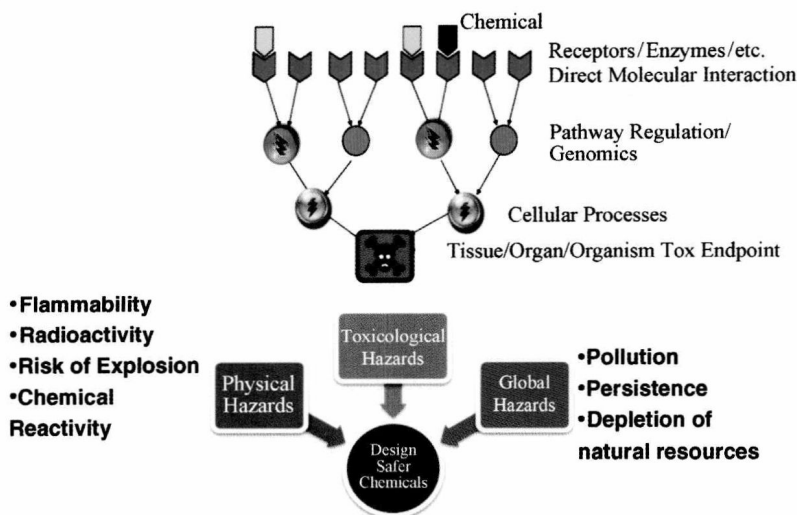


Figure 1. Classification of intrinsic chemical hazard into physical, toxicological and global.

hazardous. However, the achievements of the field of medicinal chemistry has shown us that it is possible to design chemicals with highly specific and desirable biological activity, and those lessons can be extended to inform the design of other commercial chemicals for reducing undesirable biological activity. Although this is unquestionably challenging due to the plethora of possible biological mechanisms of action, this text aims to show that there are strategies that can be applied.

The focus of this text, therefore, is minimization—at the molecular level—of potential health and environmental chemical hazard. This is distinct from *risk assessment*, which seeks to characterize the probability of harm. Implicit in risk assessment is knowledge of the potential toxicity and associated dose-response relationships, as well as a reasonable estimate of the exposure that an organism will receive under certain circumstances (the external dose). While risk assessment is a useful tool in evaluating comparative risks of existing chemicals and the identification of risk management strategies when needed, we submit that the focus for new chemicals should be on the reduction of *intrinsic hazard*, as exposure cannot always be predicted or controlled. “Benign by design” is the ultimate precautionary approach and this volume seeks to empower that approach.

The current understanding of how to design safer chemicals is an emerging field of research and application. Prior to this volume, there have been foundational treatments of the topic that laid the conceptual framework for how this idea can be developed and implemented. It is the hope of the editors and chapter authors that this text is built upon by others with further explorations that demonstrate how commercial chemicals can be rationally designed to minimize biological and environmental activity.

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