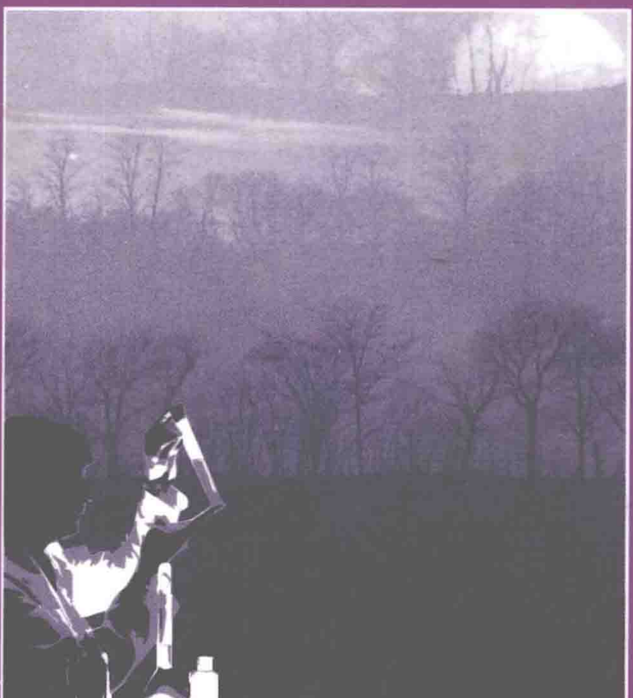
ACS SYMPOSIUM SERIES 767

Green Chemical Syntheses and Processes



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ACS SYMPOSIUM SERIES **767**

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Library of Congress Cataloging-in-Publication Data

Green chemical syntheses and processes / Paul T. Anastas, Lauren G. Heine, Tracy C. Williamson [editors].

p. cm.—(ACS symposium series ; 767)

Includes bibliographical references and index.

ISBN 0-8412-3678-X

1. Environmental chemistry—Industrial applications—Congresses. 2. Environmental management—Congresses.

I. Anastas, Paul T.., 1962- II. Heine, Lauren G., 1957– III. Williamson, Tracy C., 1963- IV. Title. V. Series.

TP155.2.E58 G75 2000
660′.28′6—dc21 00–41638

The paper used in this publication meets the minimum requirements of American National Standard for Information Sciences—Permanence of Paper for Printed Library Materials, ANSI Z39.48–1984.

Distributed by Oxford University Press

PRINTED IN THE UNITED STATES OF AMERICA

Foreword

THE ACS SYMPOSIUM SERIES was first published in 1974 to provide a mechanism for publishing symposia quickly in book form. The purpose of the series is to publish timely, comprehensive books developed from ACS sponsored symposia based on current scientific research. Occasionally, books are developed from symposia sponsored by other organizations when the topic is of keen interest to the chemistry audience.

Before agreeing to publish a book, the proposed table of contents is reviewed for appropriate and comprehensive coverage and for interest to the audience. Some papers may be excluded in order to better focus the book; others may be added to provide comprehensiveness. When appropriate, overview or introductory chapters are added. Drafts of chapters are peer-reviewed prior to final acceptance or rejection, and manuscripts are prepared in camera-ready format.

As a rule, only original research papers and original review papers are included in the volumes. Verbatim reproductions of previously published papers are not accepted.

ACS BOOKS DEPARTMENT

Preface

Scientific innovation is at the heart of Green Chemistry. The same flame of innovation that powered industry and economic growth since science's beginnings is now also powering the protection of human health and the environment. This book contains chapters by individuals from different disciplines, different sectors (industry, academia, and government), and different countries. In many cases, they worked together as teams toward the unified goal of sustainability through science. Through this past century, many goals have been set out as challenges to humanity including conquering many terrible diseases, combating hunger, and even going to the moon. Just as it has been that science and technology was the engine to achieve those noble goals, it too will provide the engine that takes us down the road toward sustainability.

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Chapter 1

Green Chemical Syntheses and Processes: Introduction

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Green chemistry is enjoying significant adoption by industry around the world and widespread activity from the research community (*1*). One reason for this is that not only does green chemistry address the fundamental scientific challenges of protecting human health and the environment at the molecular level, it accomplishes this in an economically beneficial way for industry (*2*). One measure of this is the fact that while there is not a single regulation requiring industry to engage in the specific practices or methodologies of green chemistry (*3*), there are nevertheless plentiful examples of excellent green chemistry techniques being commercialized. This can be seen by both the number and quality of the nominations and winners of the Presidential Green Chemistry Challenge Awards given annually at the National Academy of Sciences (*4*).

Green Chemistry, defined as the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances (*5*), has been referred to as pollution prevention at the molecular level. This emerging area recognizes that during the design phase of any chemical synthesis, product, or process, minimized hazard must be viewed as a performance criterion. Moreover, hazard must also be viewed as a physical/chemical property that is possible to manipulate and control at the molecular level.

By using the same skills, techniques, and expertise that is central to traditional chemistry, the practices of green chemistry are realizing some notable and in some cases, dramatic, results in the protection of human health and the environment.

This book presents a number of the innovations that have been developed recently in the emerging area of green chemistry. The chapters of the book are derived from presentations made at the Green Chemistry and Engineering Conference at the National Academy of Sciences, Washington, D.C. This conference was established to

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highlight the cutting edge science and engineering in this field being conducted in industry, academia and government.

Over the years, the Green Chemistry and Engineering Conference has had different themes. One of those themes was "Implementing Vision 2020 for the Environment". This theme was based on the document produced by the chemical industry to provide goals for the next twenty years, entitled "Vision 2020 for the Chemical Industry". Throughout this document, there was a common thread that was woven throughout the goals ranging from new chemical technologies to supply chain issues and this thread was the environment. Throughout all aspects of the chemical enterprise and all of the goals outlined in the report was the recurring and overarching recognition that the environmental impact of all activities must be among the fundamental considerations.

It is because of the ubiquitous need to consider environmental issues in all parts of the chemical industry that Vision 2020 was viewed as a good theme for the conference. It was recognized that the science and technology of Green Chemistry and Engineering was, in real time, implementing or beginning to implement many of the stated goals of 'Vision 2020'. By developing new separation techniques, new syntheses, new reaction processes, etc., and doing it while engaging in fundamental protection of human health and the environment, Green Chemistry and Engineering was accomplishing, or at least beginning to accomplish, those challenges outlined in 'Vision 2020'.

Another theme of a Green Chemistry and Engineering Conference was "Global Perspectives". This conference emphasized the fact that the science and engineering that are the topic of the conference know no boundaries. By featuring presentations from industry, academia, and government, the conference illustrated that Green Chemistry and Engineering is being actively pursued in both the public and private sectors. By featuring talks from disciplines ranging from organic synthesis to biology to electrical engineering and many others, it was demonstrated that this area is not limited by disciplinary bounds. The industrial sectors represented as well spanned well beyond the traditional chemical industry into electronics, pulp and paper, and pharmaceuticals, to name a few. Finally, it was shown that green chemistry and engineering know no national boundaries by representatives from eleven nations around the world taking part in the conference. Therefore, in several ways, one can see that a global perspective can be achieved through the practice of green chemistry and engineering.

Each year an organizing committee with representatives from all parts of the chemical enterprise convene to construct a conference that will represent some of the most recent, innovative and topical advances in green chemistry and engineering. Those organizations, American Chemical Society, American Institute of Chemical Engineers, Chemical Manufacturers Association, Council for Chemical Research, U.S. Department of Energy, U.S. Environmental Protection Agency, National Academy of Sciences, National Research Council, National Institute of Standards and Technology, and Organization for Economic Cooperation and Development, represent a breadth of essential elements of the discovery, demonstration, and commercialization of chemical technology. The fine work presented in this volume is a tribute to the work these organizations do in promoting, encouraging, funding, supporting and catalyzing the emerging area of Green Chemistry and Engineering.

Discussion of Book Sections

There are multiple ways to categorize approaches to green chemistry research. When considering chemicals that serve important social or industrial needs, some work focuses on their synthesis via environmentally friendly synthetic pathways or processes. Other work focuses on developing new benign replacements capable of achieving the desired performance without negative human or ecological impacts. Each section in this book contains chapters that are related by the principles that underlie the authors' work in green chemistry.

Designing Safer Chemicals

In this section, four chapters present work that shares the common goal of designing new products with safer and more benign impacts over their life-cycle. The topics range from the design and synthesis of environmentally friendly metal-complexed textile dyes that have the potential to eliminate the source of wastewater containing toxic metals, to a superior replacement for the current energy intensive and hazardous waste producing process of organic coating on metals. In the area of pest control, a chemically and mechanistically novel caterpillar control agent is described that has high target selectivity but poses minimal hazard to non-target organisms and the environment. There is also a chapter on a new methodology to produce highly selective, nontoxic insect sex pheromones. The purpose of this research is to facilitate the environmentally benign practice of insect control based on mating disruption by making it more economical. While these topics are disparate in their subject matter, they demonstrate the breadth of the application of green chemistry principles to the design of benign products and processes.

Green Chemical Synthesis

The chapters in this section focus on chemical reactions which utilize more environmentally benign reagents or are conducted in more benign reaction media. This approach has attracted more and more attention over the last decade, due in part to the desire for the development of more environmentally safe reaction processes. Dimethylcarbonate is discussed as an environmentally friendly substitute for dimethylsulfate and methyl halides in methylation reactions. In addition, the chapters by Paquette and Li illustrate that many reactions that are traditionally carried out in organic solvents can be carried out in water with additional interesting features. The focus of this work is on organometallic reactions in water, with a particular emphasis on indium-promoted coupling reactions by Paquette.

Biocatalysis and Biosynthesis

Biocatalysis and biosynthesis of chemicals has the potential to allow synthesis under environmentally friendly conditions while achieving high specificity and yield. Such reaction systems may also use renewable feedstocks and transform materials with low or negative economic value into fuels or chemicals with higher value. A biocatalytic process for the hydration of adiponitrile to 5-cyanovaleramide has been demonstrated which can be run to higher conversion, produce more product per weight of catalyst, and generate significantly less waste products than alternate chemical processes. Ho describes how her research successfully developed a genetically engineered recombinant *Saccharomyces* yeast that can effectively ferment both glucose and xylose to ethanol. This work has the potential to make the conversion of cellulosic biomass to ethanol technically viable. The chapter by Lima discusses the bioconversion of sugar cane vinnasse into microbial biomass by recombinant strains of Aspergillus nidulans transforms a waste product with ecologically detrimental impacts to a product with value as a fuel resource.

Environmentally Benign Catalysis

A principle of green chemistry contends that all other factors being equal, catalytic systems (as selective as possible) are superior to stoichiometric reagents (*3*). Using catalytic reagents creates opportunities for increased selectivity and the use of alternative reaction conditions. In this section, the effectiveness of both homogeneous and heterogeneous catalysis is expanded in some intriguing and practical ways.

Nikolopoulos *et al.* promote the condensation/hydrogenation of acetone to methyl isobutyl ketone (MIBK) using novel multi-functional heterogeneous catalysts. Bergbreiter and Vincent *et al.* focus on techniques to facilitate recovery and reuse of homogeneous catalysts. Some of the separation strategies described include soluble polymers that precipitate on cooling, soluble polymers that precipitate on heating, and polymers that dissolve selectively in fluorous or aqueous phases. A novel two phase homogeneous process called fluorous biphasic catalysis is discussed where a lower phase fluorocarbon solvent solubilizes the homogeneous catalyst, and a second upper solvent phase solubilizes the substrate alkane/alkene, the oxidant, and the products of alkane and alkene oxidation.

Photochemical oxidation is a potentially environmentally benign method for selective oxidation of hydrocarbons. Panov *et al.* compare the photooxidation of toluene with molecular oxygen using zeolites, BaX, BaY, CaY, BaZSM-5, and NaZSM-5. Sahle-Demessie and Gonzalez synthesize high-value organic compounds from linear and cyclic hydrocarbons by photocatalytic oxidation under mild conditions using the semiconductor material, titanium dioxide (TiO_2). TiO_2 photooxidation using gaseous phase reaction conditions eliminates the need for a separation step involving liquid solvents and minimizes the adsorption of products to the catalyst.

Green Solvent Systems

There is presently considerable interest in the development and utilization of more environmentally benign solvents and solventless systems that reduce or eliminate the use of toxic or environmentally hazardous solvents. In this section, concepts and tools for finding "green" solvent systems are described. The advantages of green solvents can be broadened to include the development and optimization of novel reaction conditions that can help to maximize product yield and minimize energy usage.

Zhao *et al.* describe the concepts and mathematical foundations for PARIS II software that designs solvent mixtures based on optimal solvent properties. The solvent property categories include performance requirements and environmental requirements (a VOC index and an environmental impacts index), and are based on general, dynamic, and equilibrium properties. The chapter by Nelson contains perspectives on the defining characteristics of green solvents, their desired characteristics (ecologically and economically) and a methodological approach to their selection.

Williams, of Dow Corning Corporation, discusses the properties of linear volatile methyl siloxanes, a class of mild solvents having an unusual combination of environmentally benign qualities, that have the potential to replace less benign solvents in applications such as coating formulations or the removal of particulates, oils, fluxes, and aqueous contaminants. The chapter details data showing that their solvency can be tailored to specific applications by using azeotropes, co-solvents and surfactants.

The use of supercritical carbon dioxide (sc-CO_2) is further expanded as an environmentally benign solvent for chemical synthesis and processing. Tanko *et al.* describe sc-CO_2 solvent effects on chemical reactivity for free radical reactions, providing a unique alternative to many conventional solvents for these reactions which are either carcinogenic or damaging to the environment. Tester *et al.* describe the results of fruitful collaboration between chemists and chemical engineers in understanding carbon-carbon bond forming reactions in supercritical fluids and in optimizing them to enable scaled-up designs for economically competitive processes.

Varma moves away from the use of solvents altogether by demonstrating microwave expedited solvent-free synthetic processes. He exposes neat reactants to microwave (MW) irradiation in the presence of supported reagents or catalysts on mineral oxides resulting in enhanced reaction rates, greater selectivity and experimental ease of manipulation.

Conclusion

The chapters in the book serve to illustrate some of the examples of green chemistry that are being researched and developed in academia, as well as being implemented in industry. Also recommended to the reader is an accompanying volume entitled, "Green Engineering and Processing" that provides a complementary treatment of the area of green engineering that works together integrally with green chemistry.

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Designing Safer Chemicals

Chapter 2

Tebufenozide: A Novel Caterpillar Control Agent with Unusually High Target Selectivity

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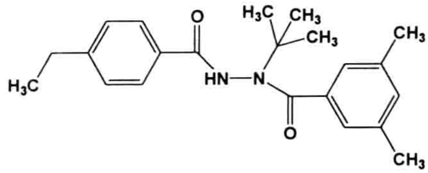
Tebufenozide is a chemically and mechanistically novel caterpillar control agent that poses very minimal hazard to non-target organisms and the environment. It can be used to selectively control a wide range of agriculturally important caterpillar pests, effectively replacing the use of many older more toxic and/or more environmentally persistent broad spectrum insecticides. Rohm and Haas Company was granted a Presidential Green Chemistry Award for the discovery and development of tebufenozide.

Introduction

A target selective insect control agent is one that is capable of controlling a specific insect pest, or small group of related insect pests, without causing significant harm to other non-target organisms in the ecosystem, including other non-target insects. Intuitively such agents would seem highly desirable, yet surprisingly few have actually reached the marketplace. Most highly target selective insect control agents currently in use are of biological, rather than synthetic, origin (Bt toxins, insecticidal viruses/ fungi, etc.) Unfortunately, such biologicals tend to have certain major deficiencies (lack of storage stability, lack of residuality in the field, poor formulation characteristics, very slow speed of kill, mediocre cost-efficacy, etc.) that have severely limited their success in the marketplace.

Tebufenozide (RH-5992) is one of the first examples of a highly target selective insecticide that has been produced by rational design and chemical synthesis (*1,2,3*). This chemically novel insecticide is the first commercial product to act as a potent mimic of 20-hydroxyecdysone (20E) in caterpillars (larval members of the insect order Lepidoptera). It very effectively controls a wide range of agriculturally important caterpillar pests at low use rate, yet it is almost as safe as the biologicals to a wide range of non-target organisms, including an impressive list of important beneficial and predatory insects. The following paper briefly describes the insecticidal and toxicological properties of tebufenozide and discusses the probable mechanistic basis for the remarkable target selectivity of this compound.

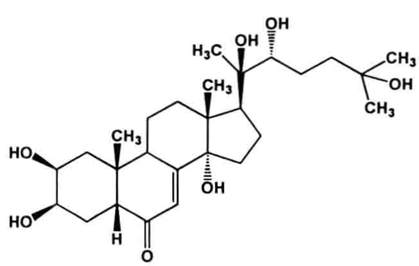


tebufenozide

20-Hydroxyecdysone and the Molting Process in Insects

Insects possess a characteristic laminar exoskeleton which gives them both great mechanical strength and impressive protection from physical and environmental stress. Insects certainly owe much of their evolutionary success to this distinctive body design. However, there is a serious drawback. The exoskeleton (cuticle) of insects is composed of a non-living polymeric material (chitin) which is relatively non-elastic and constrictive. Thus, in order to grow, the insect must periodically synthesize an entirely new and larger cuticle and then cast off the overlying old one. This reoccurring and highly complex process, called molting, is fraught with potential danger. Each time the insect molts, it must completely cease feeding, restrict its mobility, and initiate an intricate series of energy consuming physiological processes. This can make the insect temporarily more vulnerable to predation, mechanical injury, energy depletion, and/or desiccation.

Insects employ an unusual polyhydroxylated, cis-A/B ring-fused sterol to regulate molting. This substance, called 20-hydroxyecdysone (20E) or insect molting hormone, is biosynthesized by the insect from other simpler sterols extracted from the diet. It is released into, and removed from, the insect's blood during certain discrete stages of the insect's development. Precisely timed pulses of 20E concentration in the blood and tissues govern the key events of the molting cycle.



20-hydroxyecdysone (20E)