Ali Mohammad · Inamuddin *Editors*

Green Solvents I

Properties and Applications in Chemistry

Springer

Green Solvents I

Ali Mohammad · Inamuddin
Editors

Green Solvents I

Properties and Applications in Chemistry

Springer

Editors
Ali Mohammad
Department of Applied Chemistry
Faculty of Engineering and Technology
Aligarh Muslim University
Aligarh, India

Inamuddin
Department of Applied Chemistry
Faculty of Engineering and Technology
Aligarh Muslim University
Aligarh, India

ISBN 978-94-007-1711-4 e-ISBN 978-94-007-1712-1
DOI 10.1007/978-94-007-1712-1
Springer Dordrecht Heidelberg New York London

Library of Congress Control Number: 2012933835

© Springer Science+Business Media Dordrecht 2012
This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law.
The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

The fast-growing process of urbanization, industrialization, and unethical agriculture that has been implemented until recently has neither taken in consideration nor foreseen its effect on the environment, flora and fauna, and peoples' health and safety. Thus, over the last decade, green chemistry research has been focusing on finding and using safer and more environmentally friendly solvents.

Indeed, every process in chemistry, physics, biology, biotechnology, and other interdisciplinary fields of science and technology makes use of *solvents, reagents, and energy* that not only are highly toxic but also produce a great amount of undesirable waste, damaging irreparably our environment.

However, according to one of the green chemistry principles, the use of solvents should either be avoided or limited as much as possible, and although sometimes this is not possible, we ought to try to use greener alternatives to toxic solvents.

Green Solvents Volume I and II has been compiled to broadly explore the developments in the field of Green Solvents.

Written by 87 leading experts from various disciplines, these remarkable volumes cover the most comprehensive, in-depth, and state-of-the-art research and reviews about green solvents in the fields of science, biomedicine, biotechnology, biochemistry, chemical engineering, applied chemistry, metallurgical engineering, environmental engineering, petrochemicals engineering, etc.

With more than 3,000 references, 325 figures, 95 tables, and 25 equations, *Green Solvents Volume I and II* will prove to be a highly useful source for any scientists working in the fields of organic synthesis, extraction and purification of bioactive compounds and metals, industrial applications of green solvents, bio-catalysis, acylation, alkylation and glycosylation reactions, oxidation of alcohols, carbon nanotube functionalization, hydrogen sulfide removal, pharmaceutical industry, green polymers, nanofluids coolants, high-performance liquid chromatography, and thin layer chromatography. Based on thematic topics, the book edition contains the following 14 chapters:

Chapter 1 provides an overview of the use of green solvent systems such as water, superficial fluids, ionic liquids, room temperature ionic liquids, and fluorinated solvents for a wide range of chemical applications including synthetic chemistry, extraction and material science.

Chapter 2 reviews green solvent extraction and purification of few marker compounds from propolis and rice bran using supercritical carbon dioxide (SC-CO_2). The central composite response surface methodology (RSM) was applied to predict the optimal operating conditions and to examine the significance of experimental parameters by a statistic analysis.

Chapter 3 focuses on coupling the attractive properties of green solvents with the advantages of using enzymes for developing biocatalytic processes.

Chapter 4 reviews the use of ionic liquids in the pharmaceutical industry and the production of fine chemicals.

Chapter 5 presents a complete picture of current knowledge on a useful and green bio-solvent "*d*-limonene" obtained from citrus peels through a steam distillation procedure followed by a deterpenation process.

Chapter 6 investigates selected examples of potential uses of glycerol in organic reactions as well as the advantages and disadvantages of such a green methodology.

Chapter 7 deals with the use of water as medium in synthetic processes based on the epoxide ring opening. Water has been presented as effective reaction medium to realize green epoxide–based processes.

Chapter 8 reviews the various aspects of ionanofluids together with their thermophysical properties for their potential applications as heat transfer fluids and novel media for green energy technologies.

Chapter 9 offers an overview of the polymerization of methyl methacrylate (MMA) to poly methyl methacrylate (PMMA) using ionic liquids, surfactants, and fluorous media as green solvents.

Chapter 10 analyzes the recent trends in converting fatty acids into green polymers and green composite materials in addition to providing insights to future trends.

Chapter 11 examines the work performed on the use of green solvents in the analysis of organic and inorganic substances by thin layer chromatography (TLC) during 2005–2010. The chapter discusses the usefulness of water, ethylene glycol, ethyl acetate, surfactants, etc., as green solvents in TLC analyses.

Chapter 12 explores the most important uses of dimethyl carbonate as solvent in supercapacitors, lithium batteries, and other emerging devices for energy storage and a dual behaviour as methylating and carbamoylating reagent.

Chapter 13 discusses supercritical carbon dioxide (SC-CO_2) extraction of triglycerides from powdered *Jatropha curcas* kernels and seeds, followed by CO_2 subcritical hydrolysis and supercritical methylation of the extracted (SC-CO_2) oil to obtain a 98.5% purity level of biodiesel.

Chapter 14 reviews experimental investigations on two major cooling features: convective and boiling heat transfer of nanofluids together with critical review of recent research progress in important areas of nanofluids. Nanofluids development along with their potential benefits and applications are also briefly discussed.

Aligarh, India

Ali Mohammad
Inamuddin

Editors' bios

Ali Mohammad is Professor of Chemistry in the Department of Applied Chemistry, Faculty of Engineering and Technology, Aligarh Muslim University, Aligarh, India. His scientific interests include physico-analytical aspects of solid-state reactions, micellar thin layer chromatography, surfactants analysis, and green chromatography. He is the author or coauthor of 230 scientific publications including research articles, reviews, and book chapters. He has also served as editor of *Journal, Chemical and Environmental Research* being published from India since 1992 and as the Associate Editor for Analytical Chemistry section of the *Journal of Indian Chemical Society*. He has been the member of editorial boards of Acta Chromatographica, Acta Universitatis Cibiniensis Seria F. Chemia, Air Pollution, and Annals of Agrarian Science. He has attended as well as chaired sessions in various international and nation conferences. Dr. Mohammad obtained his M.Phil. (1975), Ph.D. (1978), and D.Sc. (1996) degrees from Aligarh Muslim University, Aligarh, India. He has supervised 51 students for Ph.D./M.Phil. and M.Tech. degrees.

Inamuddin is currently working as Assistant Professor in the Department of Applied Chemistry, Aligarh Muslim University (AMU), India. He received his Master of Science degree in Organic Chemistry from Chaudhary Charan Singh (CCS) University, Meerut, India, in 2002. He received his Master of Philosophy and Doctor of Philosophy degrees in Applied Chemistry from AMU in 2004 and 2007, respectively. He has extensive research experience in multidisciplinary fields of Analytical Chemistry, Material Chemistry, and Electrochemistry and, more specifically, Renewable Energy and Environment. He has worked on different projects funded by University Grant Commission (UGC), Government of India, and Council of Scientific and Industrial Research (CSIR), Government of India. He has received Fast Track Young Scientist Award of Department of Science and Technology, India, to work in the area of bending actuators and artificial muscles. He has published 28 research articles and four book chapters of international repute. He is editing one more book entitled *Ion-Exchange Technology: Theory, Materials and Applications* to be published by Springer, United Kingdom. Recently, he edited a book entitled *Advanced Organic-Inorganic Composites: Materials, Devices* *and Allied Applications* published by Nova Science Publishers, Inc. He is presently working as editor in chief of *The Journal of Chemical and Environmental Research* published from The Muslim Association for the Advancement of Science, which is published in India. He has worked as a Postdoctoral Fellow leading a research team at Creative Research Initiative Center for Bio-Artificial Muscle, Hanyang University, South Korea, in the field of renewable energy, especially biofuel cells. He has also worked as Postdoctoral Fellow at Center of Research Excellence in Renewable Energy, King Fahd University of Petroleum and Minerals, Saudi Arabia, in the field of polymer electrolyte membrane fuel cells and computer fluid dynamics of polymer electrolyte membrane fuel cells. He is a life member of the *Journal of the Indian Chemical Society*.

Acknowledgments

We are most indebted to the grace of the Almighty “One Universal Being,” who inspires the entire Humanity to knowledge and who has given us the required favor to complete this work.

These books are the outcome of the remarkable contribution of experts from various interdisciplinary fields of science and cover the most comprehensive, in-depth, and up-to-date research and reviews. We are thankful to all the contributing authors and their coauthors for their esteemed work. We would also like to thank all publishers, authors, and others who granted us permission to use their figures, tables, and schemes.

We would like to express our deep gratitude to Prof. T. Urushadze (Georgia State Agriculture University, Georgia), Prof. K. Aoki (Toyohashi University of Technology, Japan), Prof. Rajeev Jain (Jiwaji University, India), Prof. S. Shtykov (Saratov State University, Russia), Prof. M. M. Srivastava (Dayal Bagh University, India), Prof. M. C. Chattopadhyaya (Allahabad University, India), Prof. U. S. Roy (Visva-Bharti Santiniketan, India), Dr. Ajay Taneja (Dr. B. R. Ambedkar University, Agra, India), Prof. A. P. Gupta (Delhi Technological University, India), Prof. Anca Sipos (Lucian Blaga University of Sibiu, Romania), Prof. J. K. Rozylo (Maria Curie-Skloclowska, Poland), Prof. P. K. Sharma (JNV University, Jodhpur), Prof. Ravi Bhusan (I.I.T. Roorkee, India), Prof. Ibraheem (Jamia Millia Islamia, India), Prof. El-Sayed Ali Abdel-Aal (CMRDI, Cairo, Egypt), Dr. Ajay Taneja (Dr. B. R. Ambedkar University, India), Dr. Reeta Mehra (MDS University, Ajmer), Prof. M. Kidwai (University of Delhi, India), Prof. M. S. Chauhan (Himachal Pradesh University, India), Prof. A. S. Aswar (SGB Amaravati University, India), Dr. Anees Ahmad and Prof. Syed Ashfaq Nabi (Department of Chemistry, Aligarh Muslim University (A.M.U.), India), Prof. J. Sherma (USA) and Prof. M. Mascini (University of Firenze, Italy), Prof. Ishtiaq Ahmad and Prof. Rakesh Kumar Mahajan (Department of Chemistry, Guru Nanak Dev University, Amritsar, India), Dr. B. D. Malhotra (Scientist-F, NPL, New Delhi, India), Dr. Raju Khan (Scientist-C, NEIST, Assam, India), Prof. Seon Jeon Kim (Hanyang University, South Korea), Prof. Kenneth I. Ozoemena (University of Pretoria, South Africa), Prof. Saleem-ur-Rahman and Prof. S. M. J. Zaidi (King Fahd University of Petroleum and Minerals, Saudi Arabia), Prof. Gaber Eldesoky

and Prof. Zeid-AL-Othman (King Saud University, Saudi Arabia), Prof. Sheikh Raisuddin (Jamia Hamdard University, New Delhi, India), Byong-Hun Jeon (Yonsei University, South Korea), and Prof. A. I. Yahya (Nizwa University, Oman) for their valuable suggestions, guidance, and constant inspiration.

It is with immense gratitude that we thank our departmental colleagues Prof. M. Mobin, Prof. Asif Ali Khan, Prof. R. A. K. Rao, Prof. Faiz Mohammad, Dr. M. Z. A. Rafiqui, Dr. Abu Nasar, Dr. Rais Ahmad, and Dr. Yasser Azim, without whose continuous encouragement these books would have not been completed. Dr. Inamuddin cannot thank enough his friends and colleagues Dr. M. M. Alam (USA), Dr. Amir-Al-Ahmad (KFUPM, Saudi Arabia), Dr. Zafar Alam, Dr. Mu. Naushad, Dr. Mohammad Luqman, Dr. Salabh Jain, Dr. Hemendra Kumar Tiwari, Dr. Adesh Bhadana, Dr. Shakeel Ahmad Khan, Satish Singh, and others, for their timely help, good wishes, encouragement, and affections. The help received from our research group (Arshi Amin, Asma Siddiq, Nida Khan, and Sardar Hussain) is appreciatively acknowledged.

Finally, we feel short of words and full of emotions in thanking our family members for their constant inspiration and gracious support.

Ali Mohammad and Inamuddin

Contents

Contributors

Mercedes Alvaro Departamento de Química, Instituto Universitario de Tecnología Química, Universidad Politécnica de Valencia, Valencia, Spain

V. Calvino-Casilda Instituto de Catálisis y Petroleoquímica, CSIC, Catalytic Spectroscopic Laboratory, Madrid, Spain

Carla C.C.R. de Carvalho Department of Bioengineering, Instituto Superior Técnico (IST), Universidade Técnica de Lisboa, Lisbon, Portugal

Institute for Biotechnology and Bioengineering, Centre for Biological and Chemical Engineering, IST, Lisbon, Portugal

Carlos A. Nieto de Castro Centre for Molecular Sciences and Materials, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Lisbon, Lisbon, Portugal

Chieh-Ming J. Chang Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Farid Chemat Université d'Avignon et des Pays de Vaucluse, INRA, Avignon, France

Smain Chemat Centre de Recherche Scientifique et Technique en Analyses Physico-chimiques (CRAPC), Algiers, Algeria

Chao-Rui Chen Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Chemical Engineering Division, Institute of Nuclear Energy Research, Lungtan, Taoyuan, Taiwan, ROC

Ching-Hung Chen Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Wei-Heng Chen Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Gaber E. El-Desoky Department of Chemistry, College of Science, King Saud University, Riyadh, Saudi Arabia

Pedro Fernandes Department of Bioengineering, Instituto Superior Técnico (IST), Universidade Técnica de Lisboa, Lisbon, Portugal

Institute for Biotechnology and Bioengineering, Centre for Biological and Chemical Engineering, IST, Lisbon, Portugal

Belen Ferrer Departamento de Química, Instituto Universitario de Tecnología Química CSIC-UPV, Universidad Politécnica de Valencia, Valencia, Spain

João M.P. França Centre for Molecular Sciences and Materials, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Lisbon, Lisbon, Portugal

Hermenegildo Garcia Departamento de Química, Instituto Universitario de Tecnología Química CSIC-UPV, Universidad Politécnica de Valencia, Valencia, Spain

Instituto Universitario de Tecnología Química, Universidad Politécnica de Valencia, Valencia, Spain

Shih-Lan Hsu Education and Research Department, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

Inamuddin Department of Applied Chemistry, Faculty of Engineering and Technology, Aligarh Muslim University, Aligarh, India

Shih-Ming Lai Department of Chemical and Materials Engineering, National Yunlin University of Science and Technology, Touliu, Yunlin, Taiwan, ROC

Daniela Lanari Laboratory of Green Synthetic Organic Chemistry, CEMIN–Dipartimento di Chimica, Università di Perugia, Perugia, Italy

Miau-Rong Lee Department of Biochemistry, China Medical University, Taichung, Taiwan, ROC

Ying-Nong Lee Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Manuel L.M. Lopes Centre for Molecular Sciences and Materials, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Lisbon, Lisbon, Portugal

J. López-Sanz Departamento de Química Inorgánica y Química Técnica, Universidad Nacional de Educación a Distancia, UNED, Madrid, Spain

Maria J.V. Lourenço Centre for Molecular Sciences and Materials, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Lisbon, Lisbon, Portugal

Nuno M.T. Lourenço Department of Bioengineering, Instituto Superior Técnico (IST), Universidade Técnica de Lisboa, Lisbon, Portugal

Institute for Biotechnology and Bioengineering, Centre for Biological and Chemical Engineering, IST, Lisbon, Portugal

Shadpour Mallakpour Organic Polymer Chemistry Research Laboratory, Department of Chemistry, Isfahan University of Technology, Isfahan, I. R. Iran

Nanotechnology and Advanced Materials Institute, Isfahan University of Technology, Isfahan, I. R. Iran

Marco P.C. Marques Department of Bioengineering, Instituto Superior Técnico (IST), Universidade Técnica de Lisboa, Lisbon, Portugal

Institute for Biotechnology and Bioengineering, Centre for Biological and Chemical Engineering, IST, Lisbon, Portugal

Rosa María Martín-Aranda Departamento de Química Inorgánica y Química Técnica, Universidad Nacional de Educación a Distancia, UNED, Madrid, Spain

Ershad Mistri School of Materials Science and Engineering, Bengal Engineering and Science University, Shibpur, Howrah, West Bengal, India

Ali Mohammad Department of Applied Chemistry, Faculty of Engineering and Technology, Aligarh Muslim University, Aligarh, India

S. Krishna Mohan Material Development Division (MDD), Directorate of Engineering (DOE), Defence Research & Development Laboratory (DRDL), Hyderabad, India

S.M. Sohel Murshed Centre for Molecular Sciences and Materials, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Lisbo, Lisbon, Portugal

Mu. Naushad Department of Chemistry, College of Science, King Saud University, Riyadh, Saudi Arabia

Oriana Piermatti Laboratory of Green Synthetic Organic Chemistry, CEMIN–Dipartimento di Chimica, Università di Perugia, Perugia, Italy

Ferdinando Pizzo Laboratory of Green Synthetic Organic Chemistry, CEMIN–Dipartimento di Chimica, Università di Perugia, Perugia, Italy

Zahra Rafiee Department of Chemistry, Yasouj University, Yasouj, I. R. Iran

Dipa Ray Department of Polymer Science & Technology, University of Calcutta, Kolkata, West Bengal, India

Fernando J.V. Santos Centre for Molecular Sciences and Materials, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Lisbon, Lisbon, Portugal

Ikumei Setsu Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Chun-Ting Shen Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Asma Siddiq Department of Applied Chemistry, Faculty of Engineering and Technology, Aligarh Muslim University, Aligarh, India

Valérie Tomao Université d'Avignon et des Pays de Vaucluse, INRA, Avignon, France

Chien-Hsiun Tu Department of Applied Chemistry, Providence University, Taichung, Taiwan, ROC

Luigi Vaccaro Laboratory of Green Synthetic Organic Chemistry, CEMIN–Dipartimento di Chimica, Università di Perugia, Perugia, Italy

Chih-Hung Wang Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Ling-Ya Wang Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Jia-Jiuan Wu Department of Chemical Engineering, National Chung Hsing University, Taichung, Taiwan, ROC

Department of Nutrition, China Medical University, Taichung, Taiwan, ROC

Hsin-Ling Yang Department of Nutrition, China Medical University, Taichung, Taiwan, ROC

Chapter 1
Green Solvents Fundamental and Industrial Applications

Shadpour Mallakpour and Zahra Rafiee

Abstract The toxicity and volatile nature of many organic solvents, widely utilized in huge amounts for organic reactions, have posed a serious threat to the environment. Thus, the principles of green chemistry direct to use safer and environmentally friendly solvents. The alternative solvent systems such as water, supercritical fluids, ionic liquids, and fluorinated solvents are employed for a wide range of chemical applications including synthetic, extractions, and materials chemistry. This chapter provides an overview about the use of these alternative solvents in various academic and industrial fields.

1.1 Introduction

Most chemical reactions of organic substances conducted in the laboratory as well as in industry need conventional organic solvents as reaction media. The use of these organic solvents such as benzene, toluene, xylene, methanol, and ethanol in many industrial chemical processes is an issue of great environmental concern. These solvents are characterized by high volatility and limited liquidus ranges (at atmospheric pressure, ~85–200°C). As a result, about 20 million tons per year of volatile organic compounds (VOCs) are discharged into the atmosphere owing to

---

S. Mallakpour (✉)
Organic Polymer Chemistry Research Laboratory, Department of Chemistry,
Isfahan University of Technology, Isfahan 84156-83111, I. R. Iran

Nanotechnology and Advanced Materials Institute, Isfahan University of Technology,
Isfahan 84156-83111, I. R. Iran
e-mail: mallakpour84@alumni.ufl.edu; mallak@cc.iut.ac.ir; mallak777@yahoo.com

Z. Rafiee
Department of Chemistry, Yasouj University, Yasouj 75914-353, I. R. Iran

A. Mohammad and Inamuddin (eds.), *Green Solvents I: Properties and Applications in Chemistry*, DOI 10.1007/978-94-007-1712-1_1,

industrial processes [1], contributing to global climatic changes, air pollution, and human health-related issues [2]. Therefore, the concept of green chemistry is becoming one of the main goals of designing process and reaction [3, 4]. Green chemistry is the utilization of a set of principles that will help to reduce the use and generation of hazardous substances during the manufacture and application of chemical products. Use of safer solvents and auxiliaries is one of the important principles of green chemistry. However, there is no perfect green solvent that can apply to all circumstance. Over the past several years, a number of alternative solvents such as water, supercritical fluids (SCFs), fluorous solvents, and ionic liquids (ILs) have been reported [5–8]. The utilization of these alternative solvents has inherent benefits such as enhanced rates of reaction, more readily isolated side products and main product recovery.

1.2 Solvent-Free Reactions

Obviously, the solvents are the ideal medium to transport heat to and from endo- and exothermic chemical reactions. On dissolution of solutes, solvents break the crystal lattice of solid reactants, dissolve liquid or gaseous reactants, and exert a significant influence on reaction rates and on the positions of chemical equilibrium. Additionally, the reactants can interact efficiently when they are in a homogeneous solution, which facilitates stirring, shaking, or other forms of agitation, whereby the reactant molecules come together rapidly and continuously [9–11].

Furthermore, uniform heating or cooling of the mixture in solution can be carried out easily. The role of a solvent in respect of organic reactions is complex. A solvent has the power to increase or decrease the speed of a reaction, sometimes extremely. Changing the solvent can influence the rate of reaction, and it can even alter the course of reaction. This may manifest in altered yields and ratios of products. Therefore, a solvent can be deeply and inseparably associated with the process of an organic reaction through the solvation of the reactants, products, transition state, or other intervening species.

Environmental concerns about solvent-based chemistry have stimulated a renewed interest in the study of chemical reactions under solvent-free conditions. Solvent-free organic syntheses are gaining increasing attention from the viewpoints of green chemistry [12–15]. One noticeable route to reduce waste involves generation of chemicals from reagents in the absence of solvents. However, by far the best green alternative is, of course, to avoid the use of any solvent. Moreover, the exclusion of solvents can offer access to new products and materials that are not readily accessible by conventional solution methods. In many solvent-free reactions, one of the reagents is a liquid and is sometimes present in excess. This liquid is often acting as the solvent and making a homogeneous reaction solution. In other solvent-free reactions, there may be a liquid, for example, water, formed during the course of the reaction, and this liquid assists the reaction at the interface between the reagents and acts like a solvent.

In comparison to reactions in organic solvents, benefits of solvent-free reactions include (1) there is no reaction medium to collect, purify, and recycle; (2) the compounds formed are often sufficiently pure to avoid extensive purification by chromatography, and in some cases, there is not even the require for recrystallization; (3) sequential solvent-free reactions are possible; (4) the reactions are often quick, sometimes reaching completion in several minutes as compared to hours with organic solvents; (5) energy usage may be considerably lower; (6) functional group protection-deprotection can be avoided; (7) there may be lower capital outlay for equipment when setting up industrial processes; and (8) significant batch-size reduction and processing cost savings, production of solvent-free protocols is not only more environmentally benign but also more economically feasible [9, 16].

There are some disadvantages to solvent-free reactions, which can be minimized by developments in engineering reactor technology [17]. Objections to the use of solvent-less reaction conditions include the formation of hot spots and the possibility of runaway reactions. Instead of operating in the old paradigm, notably the employment of a reaction medium or solvent as a heat sink or heat transfer agent, consideration could be given to applying developments in reactor design either for continuous flow or for batch systems. If highly exothermic reactions are identified, which are otherwise suited to solvent-less conditions, the problem could be addressed through advanced reactor design. Another objection can be difficulties in handling solid or highly viscous material. Again this can be overcome by advances in engineering and innovative reactor design. Solvent-less reactions may be more suitable for small volume commodity chemicals rather than high throughput, although it is possible to envisage extrusion type continuous reactors [16].

Traditionally, solvent-free reactions have been performed using a mortar and pestle, but recently high speed ball milling (HSBM) has shown to be a more attractive alternative. In the HSBM method, a ball bearing is placed inside a vessel that is shaken at high speeds. The high speed achieved by the ball bearing has enough force to create an atmosphere which can facilitate a chemical reaction. The use of commercial ball mills has allowed these reactions to be scaled up to industrial levels. The use of this methodology can significantly reduce solvent waste [18].

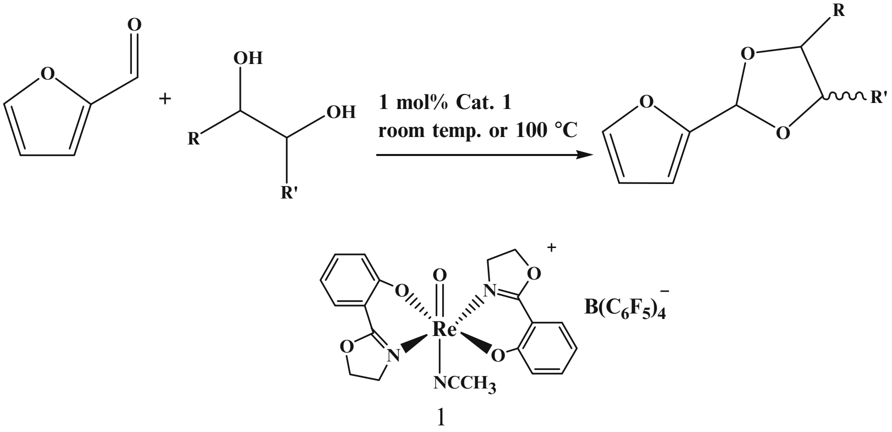
1.2.1 Organic Synthesis

The development of solvent-free green processes has gained significant attention in organic synthesis owing to certain advantages such as high efficiency and selectivity, easy separation and purification, mild reaction conditions, reduction in waste, and benefits to the industry as well as the environment [11]. Solvent-free organic reactions based on grinding two macroscopic particles together mostly involve the formation of a liquid phase prior to the reaction, that is, formation of a eutectic melt of uniform distribution where the reacting components being in proximity are capable to react in a controlled way [19].

1.2.1.1 Protection/Deprotection Reactions

The protection/deprotection reaction sequences form an integral part of organic manipulations such as the preparation of monomer building blocks, fine chemicals, and precursors for pharmaceuticals, and these reactions often involve the utilization of acidic, basic, or hazardous and corrosive reagents and toxic metal salts.

Aldehydes and diols have been transformed into 1,3-dioxolane in excellent yields using oxorhenium(V) oxazoline as a catalyst under solvent-free conditions at mild temperatures (Scheme 1.1) [20]. The reaction is applicable to biomass-derived furfural and glycerol. The obtained cyclic acetals may find use as value-added chemicals and/or oxygenate fuel additives.



Scheme 1.1 1,3-Dioxolane formation from furfural and diols catalyzed by oxorhenium(V) 1 (Reprinted from Ref. [20]. With kind permission of The American Chemical Society)

In the presence of mesoporous strong acidic cation-exchange resin as the catalyst, solvent-free reaction between methacrolein and acetic anhydride led to the formation of 2-methylallylidene diacetate [21].

The solvent-free selective demethylation and debenzylation of aryl methyl/benzyl ethers have been reported using magnesium iodide to synthesize natural flavone and biphenyl glycosides [22].

1.2.1.2 Tishchenko Reaction

The conversion of aldehydes to their dimeric esters, better known as the Tishchenko reaction, has been known for more than a 100 years. This reaction is heavily used in industry, and it is inherently environmentally benign since it utilizes catalytic conditions and is 100% atom economic.

Using solvent-free ball-milling conditions, the Tishchenko reaction for aryl aldehydes has been developed in the presence of sodium hydride as the catalyst in high yields in 0.5 h [18].

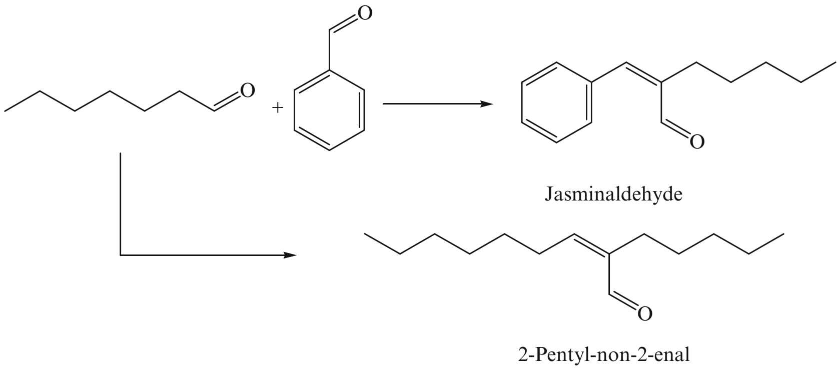
1.2.1.3 Condensation Reactions

The formation of kinetic and thermodynamic enolates has been reported under solvent-free HSBM conditions. The thermodynamic or kinetic enolate in high selectivity was obtained using 2-methylcyclohexanone as the substrate and sodium hydroxide or lithium hexamethyldisilazide as the base [23].

The application of methanesulfonic acid/morpholine catalyst to Knoevenagel condensation of ketones with malononitrile has been described under solvent-free conditions [24]. Ylidenemalononitriles were obtained with good yields in short reaction time.

The mechanochemical reaction of malononitrile with various aldehydes was investigated to achieve quantitative stoichiometric conversion in absence of any solvents and catalysts in vibration and planetary ball mills as well as in a melt under microwave irradiation [25]. A successful quantitative conversion appeared to be substrate dependent.

The synthesis of jasminaldehyde has been reported by the condensation of 1-heptanal with benzaldehyde using chitosan as a solid base catalyst under solvent-free conditions (Scheme 1.2) [26]. Jasminaldehyde was obtained with maximum conversion of >99% and 88% selectivity at 160°C.



Scheme 1.2 Synthesis of jasminaldehyde (Reprinted from Ref. [26]. With kind permission of Elsevier)

The aryl-*14H*-dibenzo [*a.j*] xanthenes have been synthesized via the condensation of β-naphthol with aromatic aldehydes using cellulose sulfuric acid as a catalyst under solvent-free conditions in excellent yields and short reaction times [27].

1.2.1.4 Aldol Reaction

The direct aldol reaction has been extensively used in industry either in bulk or in fine chemical manufacture and pharmaceutical target production to prepare polyoxygenated architectures from two carbonyl compounds.

The utilization of polystyrene-supported binam-prolinamide as catalyst has been studied in the aldol reaction between several ketones and aldehydes in the presence of benzoic acid under solvent-free or aqueous conditions [28]. Under these conditions, the corresponding aldol product was obtained in high yields, regio-, diastereo-, and enantioselectivity.

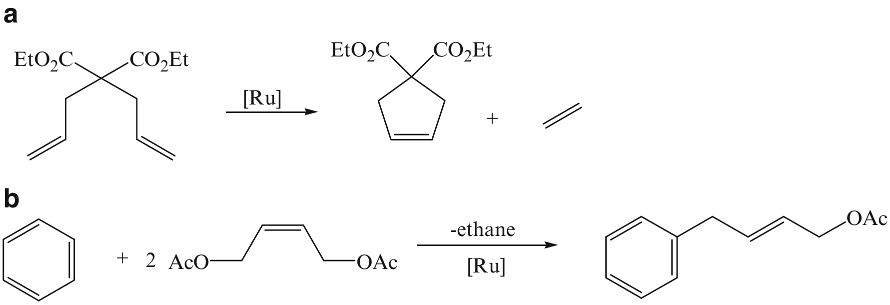
1.2.1.5 Sonogashira Reaction

The Sonogashira coupling of aryl halides with aryl and alkyl-substituted acetylenes has been studied without the use of copper or additional ligands and in the presence of $Pd(OAc)_2$ or $Pd(PPh_3)_4$ in combination with 1,4-diazabicyclo[2.2.2]octane as catalysts and base, respectively, in a planetary ball mill [29]. All coupling reactions exhibited high selectivity according to the desired Sonogashira products.

The solvent-free Sonogashira coupling of a variety of *para*-substituted aryl halides with trimethylsilylacetylene or phenylacetylene has been reported using HSBM [30]. Iodo- and bromo-substituted aromatics successfully undergo Sonogashira coupling, while chloro- and fluoro-substituted aryl compounds were unreactive.

1.2.1.6 Metathesis Reactions

The cross-metathesis of allyl benzene with *cis*-1,4-diacetoxy-2-butene and the ring-closing metathesis of diethyl diallylmalonate have been investigated under solvent-free media (Scheme 1.3) [31]. It was found that only the bulk conditions permitted a simple 25-fold reduction of the amount of metathesis catalyst for both studied metathesis reactions.

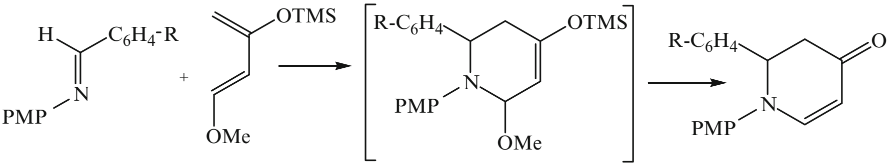


Scheme 1.3 (**a**) Ring-closing metathesis of diethyl diallylmalonate, (**b**) cross-metathesis of allyl benzene with *cis*-1,4-diacetoxy-2-butene (Reprinted from Ref. [31]. With kind permission of The Royal Society of Chemistry)

1.2.1.7 Diels-Alder Reactions

Diels-Alder reactions have been reported via heating a mixture of dicyclopentadiene and a dienophile under solvent-free conditions [32]. Cyclopentadiene, generated in situ, reacted with the dienophile in a thermodynamically controlled reaction.

The aza-Diels-Alder reaction between a variety of benzaldimines and Danishefsky's diene has been described in solvent-free conditions using porous zirconium hydrogen phosphate in the presence of sodium dodecyl sulfate at 30°C with excellent yields (Scheme 1.4) [33].



PMP = pOMe-C_6H_4
R = H, *p*Cl, *m*Cl, *o*Cl, *p*Br, *p*F, *p*NO_2, *p*SMe, *p*OMe, *p*Me, *p*CN

Scheme 1.4 Aza-Diels-Alder reaction of benzaldimines with Danishefsky's diene (Reprinted from Ref. [33]. With kind permission of Elsevier)

1.2.1.8 Heck Reaction

The use of Pd catalyst supported on 1,1,3,3-tetramethylguanidinium-modified molecular sieve SBA-15 has been introduced for Heck arylation of olefins with aryl halides in solvent-free conditions [34].

1.2.1.9 Mannich Reaction

The Mannich-type reactions provide one of the most classical and useful methods for the preparation of β-amino ketones and aldehydes, which constitute various pharmaceuticals, natural products, and versatile synthetic intermediates.

The one-pot three-component Mannich reaction of aromatic aldehydes, aromatic ketones, and aromatic amines has been investigated in the presence of an acidic catalyst, pyridinium trifluoroacetate under solvent-free conditions at room temperature [35]. The resulting β-amino carbonyl compounds were obtained in reasonably good yields.

1.2.1.10 Hydrogenation

The hydrogenation of quinolines has been reported using phosphine-free chiral cationic catalyst under solvent-free or highly concentrated conditions with high levels of enantioselectivities (>97%) and excellent yields only at 0.02–0.10 mol% catalyst loading [36].

The solvent-free hydrogenation of solid alkenes and nitro-aromatic compounds has been developed in the presence of Pd nanoparticles entrapped in aluminum oxyhydroxide to obtain corresponding alkanes and aromatic amines in nearly quantitative yields [37].

1.2.1.11 Esterification

The solvent-free direct esterification of various carboxylic acids with alcohols has been described in the presence of 5 mol% surfactant-catalyst, *para*-dodecylbenzene sulfonic acid, or copper para-dodecylbenzene sulfonate at room temperature with moderate to excellent yield [38].

1.2.1.12 Meyers' Lactamization

Meyers' lactamization is a typical bielectrophile-binucleophile reaction that produces quaternary centers, most of the time in a stereoselective manner. It is a well-known tool for the synthesis of natural products, especially alkaloids. This stereoselective reaction is the first step to access erythrina and amaryllidaceae alkaloids.

The solvent-free microwave-assisted synthesis of Meyers' bicyclic lactams has been introduced to obtain chiral lactams in good yield with high diastereoselectivity in short times [39].

1.2.1.13 Synthesis of 1,3,5-Triarylbenzene

1,3,5-Triarylbenzenes are very useful compounds used as electroluminescent materials, electrode devices, or conducting polymers. These compounds can also serve as versatile intermediates for the synthesis of buckminsterfullerenes, pharmaceuticals, and conjugated star polyaromatics.

The synthesis of 1,3,5-triarylbenzenes from acetophenones in the presence of *p*-toluenesulfonic acid as a catalyst under solvent-free conditions has been described as a chemoselective method without using any metal catalyst or solvent [40].

1.2.1.14 Hydroaminovinylation of Olefins

Olefin hydroaminovinylation is a valuable atom-economical domino reaction combining terminal alkene hydroformylation with in situ formation of enamine/imine, the firstly generated aldehyde reacting in a second step with an amine. When carrying out the reaction with secondary amines, hydroaminovinylation is often followed by another reaction, namely, the formation of amines through catalytic hydrogenation. A current industrial challenge is to stop the reaction at stage of the formation of the enamine. It is worth mentioning here that the linear selectivity in enamine mainly depends upon the regioselectivity of the hydroformylation step.

The solvent-free hydroaminovinylation of α-olefins using rhodium complexes containing hemispherical diphosphites based on a calix[4]arene skeleton as a catalyst allows access to high proportions of linear enamines/amines or imines [41]. A comparison of standard solvent vs. solvent-free reactions was undertaken. Under solvent-free conditions with an Rh/olefin ratio of 1:5,000, the reaction turned out to be about 15 times faster than when operating in toluene at the same Rh/olefin ratio and at an olefin concentration of 6.6 mol L^{-1}.

1.2.1.15 Synthesis of Diynes

The acid-treated K10 montmorillonite has been used as a catalyst in the solvent-free nucleophilic substitution of propargylic alcohols with alkynylsilanes to afford 1,4-diynes [42].

Using catalytic amounts of $CuCl_2$ and triethylamine, an environmentally friendly, efficient method has been reported for transforming terminal acetylenes into 1,3-diynes that are very important materials in the fields of biology and materials science [43].

1.2.1.16 Synthesis of Lactic Acid

The microwave-assisted conversion of sugar source into lactic acid has been reported under solvent-free conditions using alumina-supported potassium hydroxide (KOH) [44]. The reaction proceeded in yielding 75C% of lactic acid starting from D-glucose using 1.5 equiv of KOH at 180°C.

1.2.1.17 Synthesis of Thioglycosides

The synthesis of thioglycosides from a range of readily available glycosyl halides has been described in the ball mill in excellent yields [45].

1.2.1.18 Synthesis of Lipidyl-Cyclodextrins

The lipase-catalyzed amidation reaction between fatty acyl donors and mono-6-amino-permethylated β-cyclodextrin has been studied under solvent-free conditions [46].

1.2.1.19 Synthesis of Unsaturated Ketones

Under solvent-free conditions, unsaturated ketones have been synthesized with high conversion and good selectivity via Saucy-Marbet reactions of unsaturated alcohols with unsaturated ethers catalyzed by simple ammonium ILs [47].

1.2.1.20 Synthesis of Nitrotoluene

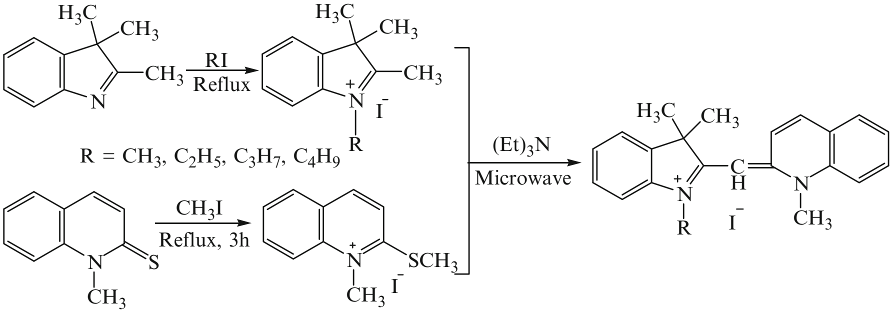
Solvent-free nitration of toluene has been carried out in the presence of sulfated titania as the catalyst at ambient temperature and atmospheric pressure to yield nitrotoluenes with good selectivity [48].

1.2.1.21 Synthesis of Quinazoline-2,4(1*H*,3*H*)-Diones

An efficient approach for the synthesis of quinazoline-2,4(1*H*,3*H*)-diones has been described via chemical fixation of carbon dioxide to 2-aminobenzonitriles catalyzed by low amounts of organic guanidines without the need of any additional solvent [49].

1.2.1.22 Synthesis of Monomethine Indocyanine Dyes

The solvent-free condensation of indole quaternary salts with 2-methylthio quinoline quaternary salt has been developed in the presence of triethylamine under microwave irradiation to obtain asymmetric monomethine indocyanine dyes (Scheme 1.5) [50].



Scheme 1.5 Synthesis of monomethine indocyanine dyes (Reprinted from Ref. [50]. With kind permission of Elsevier)

1.2.1.23 Synthesis of Acetyl Salicylic Acid

The solvent-free synthesis of acetyl salicylic acid has been reported by acetylation of salicylic acid with acetic anhydride using solid acid catalysts such as sulfated metal oxides, zeolites, and K-10 clay [51]. Among the catalysts applied, nanocrystalline-sulfated zirconia exhibited highest catalytic activity and was found to be efficient in minimal amount to obtain acetyl salicylic acid crystals with excellent yield.

1.2.1.24 Oxidation

The asymmetric oxidation of sulfides has been investigated using aluminum (salalen) complex as a catalyst under solvent-free or highly concentrated conditions [52]. Under these conditions, optically active sulfoxides were resulted in high yields with excellent enantioselectivity in the presence of only 0.002–0.01 mol% catalyst.

Microwave-assisted oxidation of secondary alcohols using *tert*-butylhydroperoxide as the oxidant in the presence of copper(II) 2,4-alkoxy-1,3,5-triazapentadienato complexes under solvent-free conditions, providing ketones with >100% yields, >890 turnover numbers (TON)s, and >1,780 h^{-1} turnover frequencies (TOF)s, has been reported [53].

A facile method for the aerobic oxidation of benzyl alcohol to benzaldehyde has been developed using Pd/organoclay catalysts [54]. Under base- and solvent-free conditions and in the presence of 0.2 wt% Pd/organoclay, a remarkably high TOF (up to 6,813 h^{-1}) was obtained.

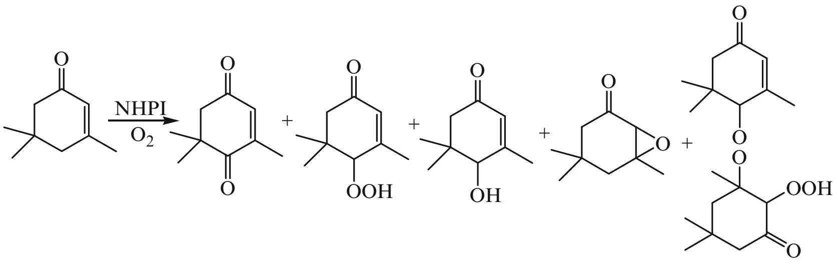
The supported gold nanoparticles as a green and reusable catalyst have been employed for the oxidation of various alcohols to the corresponding carbonyl compounds in the presence of aqueous hydrogen peroxide as an environmentally benign oxidant [55]. The reaction proceeded with good yields for nonactivated alcohols under base-free conditions.

The use of iodine-pyridine-*tert*-butylhydroperoxide as a catalytic system has been described for the solvent-free oxidation of benzylic methylenes and primary amines under quite mild conditions [56]. The oxidation of benzylic methylenes led to formation of the corresponding ketones in excellent yields with complete chemoselectivity, while the oxidation of primary amines was complete in several minutes, affording various nitriles in moderate to good yields.

The solvent-free oxidation of benzyl alcohol has been studied using supported gold palladium bimetallic nanoparticles and comparing their activity and performance with monometallic catalysts [57]. It found that the Au-Pd catalysts are all more active than the corresponding monometallic supported Au or Pd catalysts.

Ni^{2+}-containing IL, 1-methyl-3-[(triethoxysilyl)propyl] imidazolium chloride immobilized on silica has been developed as catalyst for the oxidation of styrene to benzaldehyde in the presence of H_2O_2 as the oxidant under solvent-free conditions as well as in the presence of acetonitrile [58]. Under solvent-free conditions, the conversion of styrene could reach 18.5% and the selectivity to benzaldehyde could be as high as 95.9%.

The solvent-free aerobic oxidation of α-isophorone to ketoisophorone has been reported using *N*-hydroxy phthalimide (NHPI) as the catalyst without a cocatalyst at 60°C for 10 h (Scheme 1.6) [59]. Under these conditions, the isomerization process of α-isophorone to β-isophorone was eliminated.



Scheme 1.6 The oxidation of α-isophorone catalyzed by NHPI with dioxygen (Reprinted from Ref. [59]. With kind permission of Elsevier)

The use of nanosize gold particles deposited on MgO with excellent reusability for the solvent-free selective oxidation of benzyl alcohol to benzaldehyde, providing very high catalytic activity with nearly 100% conversion in a short reaction period (0.5 h), has been reported [60].

Layered Sn(IV) phosphonate materials have been designed as catalysts for the Baeyer-Villiger oxidation of aromatic aldehydes using 30% aqueous H_2O_2 solution as the oxidant under solvent-free conditions [61].

The solvent-free oxidative dehydrogenation of **γ**-terpinene in the presence of alumina as a grinding auxiliary, with $KMnO_4$ as the oxidant in a planetary ball mill, led to formation of *p*-cymene in quantitative yields after 5 min [62].

1.2.1.25 Reduction

The catalytic use of IL-supported organotin reagent (down to 0.1 mol%) has been reported for the direct solvent-free reductive amination of aldehydes and ketones mediated by phenylsilane [63]. This method facilitated purification of the products, thus minimizing the contamination by tin.

1.2.1.26 Synthesis of Heterocyclic Compounds

A solvent-free process has been developed for the synthesis of a series of NH-pyrazoles involving the reaction of β-dimethylaminovinylketones and hydrazine sulfate in solid state on grinding, using *p*-toluenesulfonic acid as a catalyst [64]. The short reaction time coupled with the simplicity of the reaction procedure made this method one of the most efficient methods for the synthesis of this class of compounds.

1,4-Dihydropyridine derivatives have been synthesized from various aldehydes, β-dicarbonyl compounds, and amines using supported heteropoly acids as catalysts under solvent-free conditions [65].

1.2.2 Inorganic and Materials Synthesis

A facile chemical method has been developed for the fabrication of nonionic nanofluid hybrid material of multiwall carbon nanotubes (MWNT)s decorated with silica nanoparticles under solvent-free conditions [66]. Colloidal silica was dispersed in a 3-(trimethoxysilyl)-1-propanethiol aqueous solution to enhance silica nanoparticle dispersion and then the solvent-free nonionic nanofluid hybrid material consisting of MWNTs and silica nanoparticles were fabricated by carboxylic MWNTs and poly(ethylene oxide)-*block*-poly(propylene oxide)-*block*-poly(ethylene oxide).

The synthesis of magnetite octahedral microcrystals of Fe_3O_4 has been investigated from the thermolysis of single $Fe_3(CH_3COO)_6(OH)_2CH_3COO$ precursor in a closed reactor at 700°C without using catalyst under solvent-free conditions [67].

The one-pot, solvent-less synthesis process for the fabrication of lanthanum hydroxycarbonate superstructures decorated with carbon spheres has been reported which involved the thermal dissociation of the lanthanum acetate hydrate single precursor using autogenic pressure at elevated temperature [68].

The solvent-free sublimation has been used for the preparation of fibrillar nanostructures from low molecular weight organogelators with one-dimensional morphologies [69]. This methodology seems to be highly convenient in order to avoid uncontrollable solvent effects.

The solvent-free production of nanoscale zero-valent iron (nZVI) has been reported using a precision milling system with major physicochemical properties consistent with, in some cases superior to, those of the chemically synthesized [70]. The proposed milling method is completely scalable for large quantity production of nZVI, delivers nearly 100% yield of iron, uses no hazardous materials, and produces no waste in the production process. A series of reactive hydrogen-bonded crystalline supermolecules has been formed via solvent-free and liquid-assisted grinding [71].

High-density Co_3O_4 nanowire arrays have been produced via a simple, solvent-free synthesis method using narrow pores of the anodic alumina oxide template [72]. An amorphous coordination polymeric networked Pd(II) catalyst based on 3,5-bis(diphenylphosphino)benzoic acid has been synthesized through a mechanochemistry approach [73].

1.2.3 Polymerization

The living and highly stereoselective ring-opening polymerization of rac-lactide under solvent-free conditions using zirconium- and hafnium-based initiators supported by amine tris(phenolate) ligands, providing an unprecedented combination of high stereocontrol and high activity in <30 min, has been reported [74]. The solvent-free polymerization of cyclic ester monomers and lactides has been studied using bis(imino)phenoxide complexes of zirconium as initiators [75]. *N*-Heterocyclic carbine [1,3-bis-(diisopropyl)imidazol-2-ylidene] has been employed for the metal- and solvent-free ring-opening polymerization of propylene oxide at 50°C to afford well-defined α,ω-heterodifunctionalized poly(propylene oxide) oligomers [76].

The solvent-free lipase-catalyzed synthesis of long-chain starch esters with a high degree of substitution has been reported using microwave heating [77].

1.3 Water

Water is a green solvent with much to contribute to this steadily growing field. Organic synthesis in water is a rapidly growing area of research since it holds great promise for the future in terms of the cheap and environmentally friendly production of chemicals [78–82]. The use of water has numerous benefits in terms of reactivity and selectivity that are not achieved in organic solvents. In addition, in water, phase separation is facile because most of the organic compounds are not soluble in water, therefore, can easily be separated from aqueous phase. Water, due to its small size, high polarity, and the three-dimensional hydrogen-bonded network system of bulk water, offers some unique properties, which include large cohesive energy density, a high surface tension, and hydrophobic effect. Another important aspect is the development of chemical reactions in water that can achieve the desired chemical transformations without the need for the protection-deprotection of reactive functional groups or for generation of anhydrous conditions. This fact is particularly important in industrial scale-up processes to replace the use of hazardous and flammable organic solvents. Water is, obviously, the cleanest and safest available solvent, but it is not commonly used, as most organic compounds are poorly soluble in water. This issue can be overcome by using superheated water (>100°C) under microwave irradiation. Water is a good absorber for microwave energy and has been successfully employed as a solvent for various microwave-promoted organic syntheses.

1.3.1 Organic Synthesis

1.3.1.1 Suzuki-Miyaura Reactions

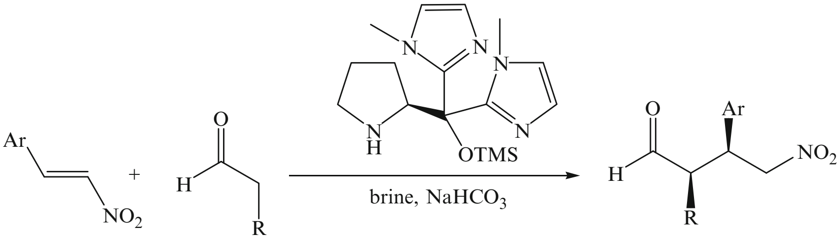
The ligand-free Suzuki-Miyaura reactions using stilbene-4,4′-bis[(1-azo)-3,4-dihydroxybenzene]-2,2′-disulfonic acid diammonium salt as a promoter in water have been reported. The desired carbon-carbon bond formation proceeded under mild conditions with high efficiency and good functional group tolerance [83].

The one-pot chemoenzymatic enantioselective synthesis of chiral biaryl alcohols has been reported via Suzuki-Miyaura cross-coupling catalyzed by protein-stabilized palladium nanoparticles under aerobic conditions in water [84]. The highly efficient heterogeneous palladium catalyst has been prepared for the Suzuki-Miyaura cross-coupling reaction in water via a simple procedure [85]. The polystyrene-supported palladium catalyst can be recycled up to ten times without significant loss of activity. The Suzuki-Miyaura C-C cross-coupling reactions of several *para*-substituted bromobenzenes with excellent yields have been reported using $[Pd(HQS)_2]$ (HQS = 8-hydroxyquinoline-5-sulfonic acid) as a catalyst in neat water under relatively mild conditions in the absence of phosphine or other additive [86].

The palladium-catalyzed Suzuki-Miyaura reactions of potassium aryltrifluoroborates with 5-iodo-1,3-dioxin-4-ones using *n*-Bu_4NOH as base in water have been utilized to get 5-aryl-1,3-dioxin-4-ones in good yields [87]. The obtained products were transformed into corresponding α-aryl-β-ketoesters by reaction with an alcohol in the absence of solvent.

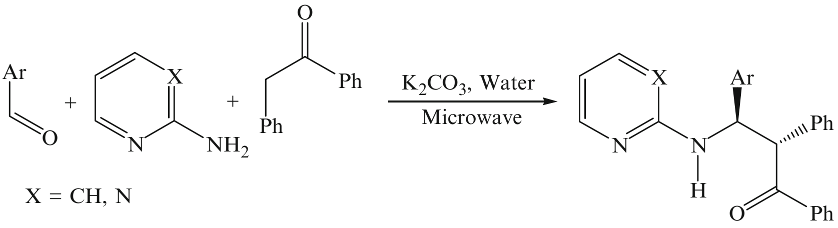
1.3.1.2 Michael Reactions

The highly enantioselective Michael addition reactions of aldehydes with nitroolefins have been developed in the presence of water-soluble catalyst di(methylimidazole) prolinol silyl ether using water as solvent in high yields (Scheme 1.7) [88].



Scheme 1.7 Organocatalytic asymmetric Michael reaction using aldehydes and nitroolefins (Reprinted from Ref. [88]. With kind permission of The American Chemical Society)

Microwave-assisted Mannich reaction for highly stereoselective synthesis of β-aminoketones has been studied by controlling the steric hindrance of the substituents using potassium carbonate as a catalyst and water as the reaction medium (Scheme 1.8) [89].



Scheme 1.8 The synthesis of β-aminoketones (Reprinted from Ref. [89]. With kind permission of The Royal Society of Chemistry)

The Michael addition reactions of β-ketoesters have been reported using 4-(dimethylamino)pyridine-related organocatalysts such as 4-(didecylamino)pyridine in water in the absence of cosolvents to afford Michael adducts in good to high yields [90]. The nitro-Michael addition of indoles and pyrroles has been developed using a combination of water and microwave irradiation without any catalyst [91].

1.3.1.3 Knoevenagel Reactions

4-Aza-1-azoniabicyclo[2.2.2]-octane-base ILs have been employed as recyclable catalysts for the Knoevenagel condensation reactions of a wide range of aldehydes (aromatic/aliphatic/heterocyclic/α,β-unsaturated) and aliphatic ketones using water as solvent [92]. The tetraketones have been synthesized via a simple, environmentally friendly, tandem Knoevenagel condensation and Michael addition of cyclic-13-diketones and a variety of aldehydes in water [93]. In this method, water as solvent itself catalyzes the reaction by hydrogen bonding, hence avoiding the utilization of any other catalysts.

1.3.1.4 Aldol Reactions

The direct asymmetric aldol reaction of various cyclic ketones with aryl aldehydes has been developed using primary-tertiary diamine-Brønsted acid as a catalyst in the presence of water [94]. The direct asymmetric aldol reactions between cyclic ketones and aromatic aldehydes have been reported using natural tryptophan as a catalyst in the presence of water [95]. Solvent studies demonstrated that water is the best reaction medium for the described direct asymmetric aldol reactions, and the desired products can be obtained with excellent *anti*selectivity and good enantioselectivity.

The direct aldol reactions of cyclic ketones with several aromatic aldehydes have been described in the presence of 4-*tert*-butyldimethylsiloxy-substituted organocatalysts. The resulting products were obtained with excellent diastereoselectivity and enantioselectivity using low-catalyst loadings (only 3 mol%), without using any additional additives [96].

1.3.1.5 Telomerisation Reactions

Two-phase telomerisation reactions with methanol, diethylamine, ethylene glycol, and glycerol and recycling of the homogeneous palladium catalysts have been studied using water as a solvent [97].

1.3.1.6 Amination Reactions

The palladium-catalyzed allylic aminations of allylic alcohols have been described in the presence of nanomicelle-forming amphiphile polyoxyethanyl α-tocopheryl sebacate in pure water [98].

1.3.1.7 Alkylation

The direct alkylation of amines with alcohols has been described using $[Cp^*IrI_2]_2$ (Cp^* = pentamethylcyclopentadienyl) as a catalyst in water in the absence of base or other additives [99].

The direct mono-*N*-alkylation of aromatic amines has been described by alkyl halides in water under microwave irradiation without any catalyst [100].

1.3.1.8 Cycloaddition Reactions

The 1,3-dipolar cycloaddition reactions of several hydrophobic nitrones have been investigated in both homogenous organic solutions and aqueous suspensions [101]. Reactions in water suspensions exhibited great rate accelerations over homogenous solutions. Small changes were also observed to the stereoselectivity of the reactions. Hydrophobic interactions are invoked for the observed behavior.

1.3.1.9 Hydroxylation

Copper-catalyzed direct hydroxylation of aryl halides has been investigated in the presence of lithium pipecolinate as a ligand in water with yields up to 92% [102].

1.3.1.10 Alkynylation

Alkynylation of terminal alkynes with aryl halides has been demonstrated in the presence of perfluoro-tagged palladium nanoparticles immobilized on silica gel under aerobic, copper-, and phosphine-free conditions in water with high yields [103].

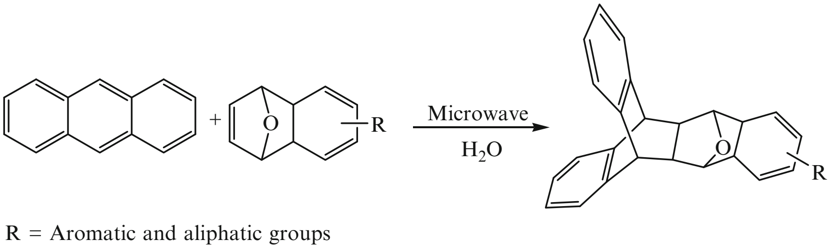
1.3.1.11 Condensation Reactions

A one-pot three-component condensation of an amine, carbon disulfide, and an aryl iodide or styrenyl bromide has been reported using copper nanoparticles as a catalyst in water under ligand- and base-free conditions. The (*E*)- and (*Z*)-styrenyl bromides produced the corresponding (*E*)- and (*Z*)-styrenyl dithiocarbamates in high diastereoselectivities [104].

1.3.1.12 Diels-Alder Reactions

Extended triptycenes have been prepared with high efficiencies via Diels-Alder reactions of anthracene and endoxides in water under microwave radiation (Scheme 1.9) [105].

C_2-symmetric 3,3′-dialkoxy-2,2′-bipyrrolidines catalysts have been employed for asymmetric Diels-Alder reactions of α,β-unsaturated aldehydes [106]. Lower chemical yields and enantioselectivity were attained in organic solvents, while, using water as solvent, the reaction rate was remarkably accelerated. The reaction completed within 2 h and afforded the Diels-Alder adduct in 95% yield with good enantioselectivity and moderate exoselectivity.



Scheme 1.9 Diels-Alder reactions between anthracene and various endoxides under microwave radiation in water (Reprinted from Ref. [105]. With kind permission of Elsevier)

The synthesis of β-aminophosphoryl compounds has been reported via the aza-Michael reaction in water without using catalyst or cosolvent in excellent yields over short reaction times [107].

1.3.1.13 Mannich Reactions

The diastereoselective synthesis of β-amino ketones has been investigated via three-component Mannich-type reaction of benzaldehyde, aniline, and cyclohexanone using $Cs_{2.5}H_{0.5}PW_{12}O_{40}$ as a catalyst in water [108].

The one-pot three-component Mannich reaction involving aldehydes, aromatic amines, and cycloalkanones has been studied using boric acid and glycerol in water to obtain major syn diastereoselectivity [109]. These reactions, which proceed very slowly in organic solvents, become quite faster in water.

1.3.1.14 Condensation Reactions

The synthesis of benzo[*c*]xanthene derivatives has been investigated via a one-pot condensation of α-naphthol, aldehydes, and cyclic 1,3-dicarbonyl compounds in the presence of proline triflate as a catalyst in water with good yields [110].

The three-component condensation reactions of primary amines with alkyl propiolates have been reported in the presence of alloxan derivatives in water for the high-yielding preparation of alkyl 2-(5-hydroxy-2,4,6-trioxohexahydro-5-pyrimidinyl)-3-(alkyl or arylamino)-2-propenoates [111].

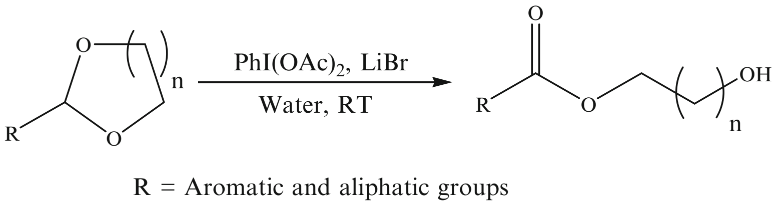
1.3.1.15 Sonogashira-Hagihara Reaction

The palladium-catalyzed Sonogashira-Hagihara of aryl halides coupling has been reported using 2-aminophenyl diphenylphosphinite ligand in water under copper-free condition [112].

The Sonogashira coupling of various aryl halides with terminal acetylenes has been developed in the presence of an amphiphilic polystyrene-poly-(ethylene glycol) resin-supported palladium-phosphine complex in water under copper-free conditions to offer the corresponding biarylacetylene derivatives in high yields [113].

1.3.1.16 Hydrolysis

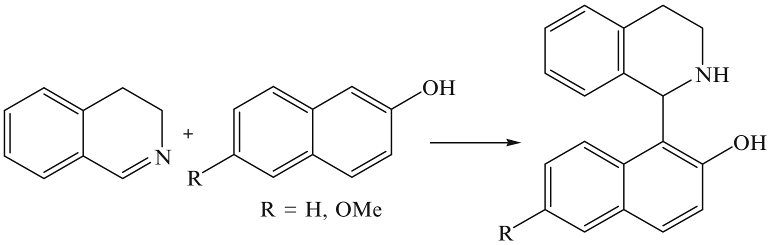
The oxidative hydrolysis of cyclic acetals by (diacetoxy)iodobenzene ($PhI(OAc)_2$) in the presence of lithium bromide (LiBr) in water, providing the corresponding hydroxyalkyl carboxylic esters in good to excellent yields at a short reaction time under mild reaction conditions, has been reported (Scheme 1.10) [114].



Scheme 1.10 Oxidation of acetals with $PhI(OAc)_2$/LiBr in water (Reprinted from Ref. [114]. With kind permission of Elsevier)

1.3.1.17 Aza-Friedel-Crafts Reaction

The synthesis of 1-naphthoyl tetrahydroisoquinolines has been reported via an aza-Friedel-Crafts reaction under solvent-free conditions or in/on water with 100% atom economy in the absence of any additional catalyst (Scheme 1.11) [115]. Yields were increased using water as a solvent.



Scheme 1.11 The reaction between 3,4-dihydroisoquinoline and 2-naphthol or 6-methoxy-2-naphthol (Reprinted from Ref. [115]. With kind permission of Elsevier)

1.3.1.18 Cyanation of Aryl Iodides

The cyanation of aryl iodides has been investigated using copper iodide as the catalyst, $K_4[Fe(CN)_6]$ as the cyanide source, and small quantities of water and tetraethylene glycol as the solvent within 30 min under microwave heating at 175°C [116].

1.3.1.19 Suzuki Reaction

The Suzuki cross-coupling reaction in water in the presence of a chitosan-g-(methoxy triethylene glycol)- or (methoxy polyethylene glycol)-supported palladium (0) catalyst has been described without additional phase transfer reagents [117].

1.3.1.20 Cycloaddition Reactions

The 1,3-dipolar cycloadditions of a galacto-configured cyclic nitrone with arabino- or galacto-furanosides containing a C-vinyl or O-allyl substituent have been found to produce galactofuranose-disaccharide analogues having a 1,4-dideoxy-1,4-imino-D-galactitol moiety [118]. The cycloadditions could be performed efficiently and stereoselectively in water using unprotected nitrone and sugar-derived dipolarophile as reaction partners.

1.3.1.21 Aminohalogenation Reaction

The aminohalogenation reaction of olefins has been reported with $TsNH_2$ and *N*-bromosuccinimide as nitrogen and bromine sources, respectively, in pure water in the presence of $PhI(OAc)_2$ as a catalyst [119]. This aqueous reaction permitted the aminobromination of olefins to proceed smoothly and efficiently, giving the useful vicinal bromoamines with high yields and selectivity.

1.3.1.22 Photooxygenation of Furans

The dye-sensitized photooxygenation of furans has been investigated in aqueous solution in the presence of ILs [120]. The reaction was generally selective, and the final products derive from rearrangement of the intermediate endoperoxides, depending mainly on the polarity and/or nucleophilic nature of the solvent.

1.3.1.23 Electrooxidation

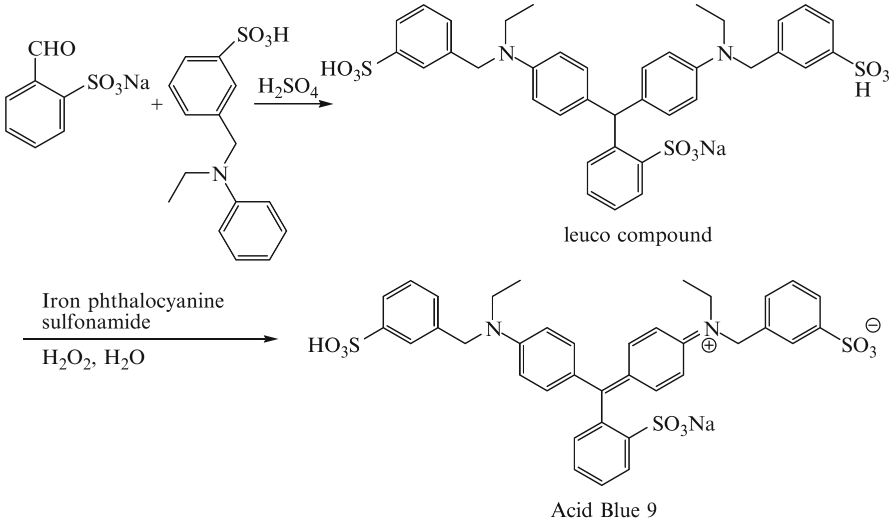
The *N*-oxyl-mediated electrooxidation of nanoemulsion-forming alcohols has been reported in the oil-in-water nanoemulsion system to form the corresponding carboxylic acids [121].

1.3.1.24 Synthesis of 1,8-Dioxo-9,10-Diaryldecahydroacridines

The Brønsted acidic imidazolium salts containing perfluoroalkyl tails have been employed as a highly effective catalyst for three-component one-pot synthesis of 1,8-dioxo-9,10-diaryldecahydroacridines in water in good to excellent yields [122].

1.3.1.25 Oxidation

The production of Acid Blue 9 has been reported via catalytic oxidation using hydrogen peroxide as an oxidant and iron phthalocyanine sulfonamide as a catalyst in aqueous media at room temperature within 3 h in high yield (Scheme 1.12) [123]. The reaction was successfully scaled up in a 3,000-L reactor, and the product was free from toxic metal impurities.



Scheme 1.12 The production process for Acid Blue 9 (Reprinted from Ref. [123]. With kind permission of The American Chemical Society)

Selective aerobic oxidation of styrene to benzaldehyde has been investigated using a green and water-soluble palladium(II) complex as a catalyst under neutral, chloride-, and base-free conditions in aqueous phase [124].

The metal-free aqueous oxidation of alcohols using the combination of the trivalent iodine reagents and tetraethylammonium bromide in water, offering ketones without racemization in good yields, has been reported [125].

The mild and selective aerobic oxidation of benzyl alcohols to benzaldehydes has been developed in water catalyzed by aqua-soluble multicopper(II) triethanolaminate compounds using air (or O_2) as oxidant at 50°C [126]. Molar yields of benzaldehydes up to 99% with high selectivity were reported. Hydroxyapatite-supported gold nanoparticles have been employed for the oxidation of a wide range of silanes into the corresponding silanols using water [127].

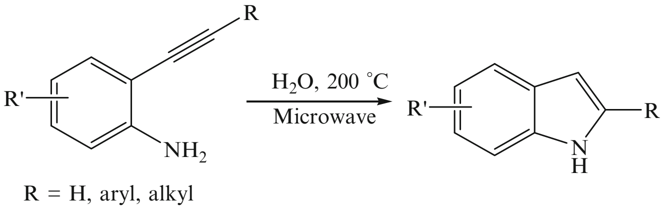
1.3.1.26 Reduction

A comparison between the microorganism- and ruthenium-based catalysts has been undertaken at the enantioselective reduction of ketoesters in water [128].

1.3.1.27 Synthesis of Heterocyclic Compounds

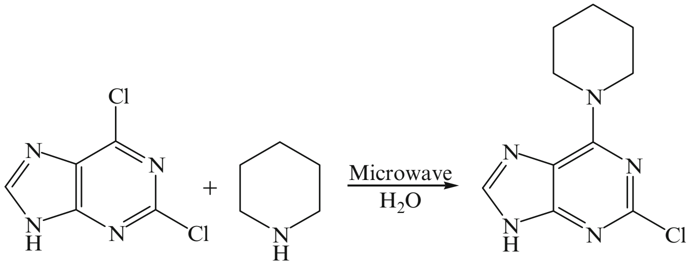
A series of 2-imidazolines with ability to inhibit the activity of the A and B isoforms of monoamine oxidase has been synthesized by condensation of aldehydes and ethylenediamine in the presence of *N*-bromosuccinimide in water as solvent under ultrasonic irradiation in high yields within short reaction times [129].

Microwave-assisted synthesis of indole and azaindole derivatives has been described via cycloisomerization of 2-alkynylanilines and alkynylpyridinamines in the presence of amines or catalytic amounts of neutral or basic salts in water (Scheme 1.13) [130].



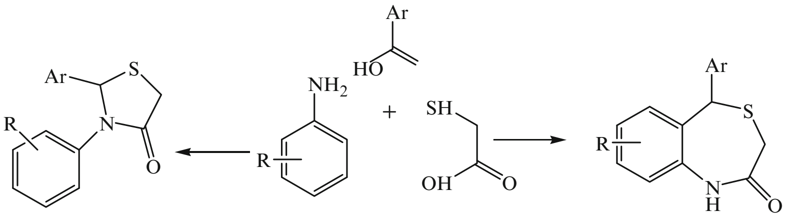
Scheme 1.13 Synthesis of indole derivatives (Reprinted from Ref. [130]. With kind permission of Elsevier)

Microwave-promoted synthesis of C6-cyclo secondary amine-substituted purine analogues in neat water, providing a rapid, efficient, and convenient method for the preparation of acyclic nucleosides, has been recommended (Scheme 1.14) [131].



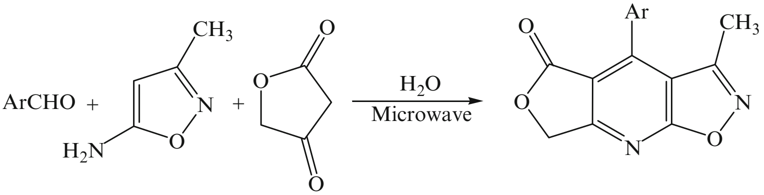
Scheme 1.14 Microwave promoting nucleophilic substitution reaction of 2,6-dichloropurine with piperidine (Reprinted from Ref. [131] with kind permission of The Royal Society of Chemistry)

Microwave-assisted three-component reaction between an aromatic aldehyde, aniline, and mercaptoacetic acid has been reported for the synthesis of benzo[*e*][1, 4]thiazepin-2(1*H*,3*H*,5*H*)-ones in aqueous media (Scheme 1.15) [132].



Scheme 1.15 The synthetic route to the benzothiazepinones and thiazolidinones (Reprinted from Ref. [132]. With kind permission of The Royal Society of Chemistry)

The one-pot synthesis of a series of polycyclic-fused isoxazolo[5,4-*b*]pyridines has been studied under microwave irradiation in water and organic solvents, without use of additional reagent or catalyst (Scheme 1.16) [133]. Water showed a superior advantage not only in promoting the reaction but also in isolation procedure, and the best yield was achieved.



Scheme 1.16 The synthesis of novel polycyclic-fused isoxazolo[5,4-*b*]pyridines under microwave irradiation in water (Reprinted from Ref. [133]. With kind permission of The American Chemical Society)

1.3.2 Synthesis of Metal Nanoparticles

The synthesis of silver nanoparticles as well as other noble metals has been described using glutathione as both a reducing and capping agent under microwave irradiation in aqueous medium within 30–60 s at a power level as low as 50 W [134].

1.4 Supercritical Fluids

Supercritical fluid (SCF) technology has rapidly grown as an alternative to some of the conventional methods of extraction, separation, reaction, fractionation, materials processing, particle formation processes, and analysis [135–148]. SCFs may be defined as the state of a compound, mixture, or element above its critical pressure (P_c) and critical temperature (T_c), but below the pressure required to condense it into a solid. In this region, the SCF exists in an intermediate phase between liquid and gas phases. The macroscopic appearance of the SCF is a homogeneous and opalescent system without phase separation (single phase) because of identical values of the densities of the gas and liquid. Nevertheless, a SCF does not show a specific aggregation state. These fluids have liquid-like density with gas-like transport properties and moderate solvent power, which moreover can be adjusted with changes in pressure and temperature.

Carbon dioxide (CO_2), water, ethane, ethene, propane, xenon, ammonia, nitrous oxide, and fluoroform are some of the significant compounds useful as SCFs. CO_2 is the most common candidate for use as a SCF due to its low toxicity, flammability, and cost, ready availability, stability, and environmental acceptability. In addition, the critical point conditions of 304 K (31°C) and 74 bar are readily attainable. As such, supercritical CO_2 (SC-CO_2) has been employed in a diverse range of applications, including polymer synthesis, drug delivery, powder production (e.g., proteins and ceramics), and powder coating. Water has good environmental and other advantages, although need more extreme conditions of T_c 647 K (374°C) and P_c 221 bar. SCF water is being used, at a research level, as a medium for the oxidative destruction of toxic waste. There is a particular attention in both supercritical and near-critical water owing to the behavior of its polarity.

The properties of SCFs (e.g., solubility, diffusivity, viscosity, and heat capacity) are different from those of ordinary liquids and gases and are tunable simply by changing the pressure and temperature. In particular, the density and viscosity change drastically at conditions close to the critical point.

The expected advantages of the reactions in SCFs are the increased reaction rates and selectivity resulting from the high solubility of the reactant gases, rapid diffusion of solvents, weakening of the solvation around the reacting species, and the local clustering of reactants or solvents. It is also fascinating to note, in a practical sense, that these fluids are easily recycled and allow the separation of dissolved compounds by a gradual release of pressure.

1.4.1 Extraction

The SCF extraction (SCFE) of lycopene from tomato juice has been studied without the need to dry the raw material [149]. The extraction of microbial phospholipid fatty acids (PLFA)s from activated sludge has been described using SC-CO_2 extraction [150]. It was found that the application of SC-CO_2 extraction to microbial PLFA analysis has the potential to drastically reduce the amount of solvent used and extraction time needed and could simplify the procedure.

The mesoporous TiO_2 crystals have been synthesized via the combination of a sol–gel process and surfactant-assisted templating method [151]. Either conventional calcinations or SC-CO_2 extraction was applied to remove surfactant from the as-synthesized material. The results showed that the SCFE approach provided materials with good crystallinity, considerably higher mesoporosity, and environmentally friendly.

The extraction of phenolic and phosphorus antioxidants from low-density and high-density polyethylene has been described using SCFE, conventional reflux, and automatic Soxhlet system [152]. SCFEs of polymer were successfully carried out, and these were associated with better recoveries (>94.9%), simplicity, and speed of the extraction process. The extraction of trivalent lanthanides with oxa-diamides has been described in SC-CO_2 [153].

1.4.2 Organic Synthesis

The SCFs have been employed as reaction media in the ethylbenzene disproportionation on ZSM-5 [154]. The oxidation of oleic acid with ozone and potassium permanganate has been studied in SC-CO_2 [155]. The Schiff base macrocycles have been synthesized using SC-CO_2 as both solvent and acid catalyst [156]. The designed SC route is not only a greener and safer method than the classical procedure but also a one-stage process that would lead to high yield, thus allowing a sustainable use of resources. The synthesized Schiff bases had an empty core, not filled with solvent molecules, since the SC-CO_2 was eliminated as a gas during depressurization.

The production of linear alkane has been described with >99% selectivity via hydrogenative ring opening of a furfural-derived compound in SC-CO_2 using Pd/Al-MCM-41 catalyst [157]. The self-stabilized dispersion nitroxide-mediated polymerization of methyl methacrylate has been investigated in SC-CO_2 in the presence of a CO_2-philic perfluorinated stabilizer generated in situ [158]. The hydrosilylation of alkenes has been reported using $Rh(PPh_3)_3Cl$ as a catalyst in a SC-CO_2/IL system [159]. No hydrogenation by-product (alkane) was detected in the SC-CO_2/IL system. During hydrosilylation in the SC-CO_2/IL system, the reactants were possibly transferred into the IL phase by SC-CO_2, in which the catalyst was dissolved. The products can be flushed with SC-CO_2 after the reaction and the catalyst/IL system reused.

The oxidation reactions using photochemically generated singlet oxygen have been performed in the presence of fluorous surfactants and a cosolvent to solubilize more polar photosensitizers and reactants in SC-CO_2 [160].

1.4.3 Materials Synthesis and Modifications

Cross-linking of starch blends has been described by phosphorylation using reactive SCF extrusion [161]. SC-CO_2-based expansion offered light weight and nonporous skin starch foams with excellent water resistance which would be desirable properties for their utilization as a biodegradable material. The synthesis of silver nanostructures has been reported using SC-CO_2 in the presence of polyvinylpyrrolidone and ethylene glycol [162].