IONIC LIQUIDS FOR ORGANIC SYNTHESIS

Editor:
Ravi Tomar

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Ionic Liquids for Organic Synthesis

Edited by

Ravi Tomar
Department of Chemistry
SRM Institute of Science and Technology
Delhi NCR Campus, Modinagar
Uttar Pradesh, India

SERB-TARE Fellow
Indian Institute of Technology Delhi, India

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Editor: Ravi Tomar

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CONTENTS

PREFACE

Ionic liquids have provided solutions to problems associated with increased production with sustainable green approaches over the last three decades. Gorden critically reviewed earlier developments in the field of ionic liquids in 1969. Ionic liquids have been explored in various applications such as catalysis, pharmaceuticals, drug discovery, solvents, and so on. As per our knowledge, there is no such book that has yet summarised ionic liquids for organic synthesis. Hence, in this book, ionic liquids are discussed with their applications in organic transformation such as biomass conversion, carbon dioxide fixation, carbon-carbon bond formation, and so on. Ionic liquids are widely used as heterogeneous catalysts in catalysis, as solvents, and as therapeutic agents. Ionic liquids have published over 500 articles in various fields every year. In this book, Ionic liquids are summarised along with their applications in organic synthesis. Chapter 1 of this book deals with the history, types and applications of ionic liquids. Chapter 2 deals with ionic liquids as a solvent for organic synthesis. Chapter 3 deals with the recent advances in cross-coupling reactions using ionic liquids. This chapter is very useful for researchers who are working in the field of carbon-carbon formation. Chapter 4 deals with the catalytic application of ionic liquids in organic transformations and describes the advantages of these liquids over other materials with respect to the mythology used in organic transformations. This chapter also discusses various chemical industries and organic chemists. Chapter 5 deals with carbon dioxide fixation using ionic liquids and this chapter will be helpful for those researchers who are working on carbon fixation and waste-to-wealth research. Chapter 6 summarises the catalytic transformation of biomass conversion in ionic liquids. Chapter 7 reviews the multicomponent reactions in ionic liquids for eco-compatible heterocyclic synthesis.

We sincerely hope that this book will be a great help to the researchers and we look forward to your observations.

Ravi Tomar
Department of Chemistry
SRM Institute of Science and Technology
Delhi NCR Campus, Modinagar
Uttar Pradesh, India

SERB-TARE Fellow
Indian Institute of Technology, Delhi
India

List of Contributors

Ajeet Kumar	Department of Chemistry, University of Florida, Gainesville, FL, USA
Archa Gulati	Department of Chemistry, Ramjas College, University of Delhi, Delhi-110007, India
Anjaneyulu Bendi	Department of Chemistry, Presidency University, Rajanukunte, Itgalpura, Bangalore, 560064, Karnataka, India
Chinmay	Department of Chemistry, Faculty of Science, SGT University, Gurugram-122505, Haryana, India
Debabrata Konar	Department of Chemistry, University of Florida, Gainesville, FL, USA
Debarati Chakraborty	National Institute of Technology, Silchar, Cachar, Assam, 788010, India
Kamalakanta Behera	Department of Chemistry, University of Allahabad, Prayagraj, Uttar Pradesh, India
Mohini Kalra	Amity Institute of Pharmacy, Amity University Haryana, Panchgaon, Manesar, Gurugram, Haryana 122412, India
Manoj Kumar	TLC Pharmaceutical Standards Ltd, New market, ON, Canada & Department of Chemistry & Chemical Biology, McMaster University, Hamilton, ON, Canada
Naveen Khatri	College of pharmacy, GIMS (SDPGIPS) Pt. B.D. Sharma UHS, Rohtak Haryana, India
Nidhi Kalia	Department of Chemistry, University of Florida, Gainesville, FL, USA
Preeti Kasana	Department of Chemistry, J.C. Bose University of Science and Technology, YMCA, Faridabad, Haryana, India
Priyanka Bhatt	TLC Pharmaceutical Standards Ltd, New market, ON, Canada & Department of Chemistry & Chemical Biology, McMaster University, Hamilton, ON, Canada
Saloni	Department of Chemistry, J.C. Bose University of Science and Technology, YMCA, Faridabad, Haryana, India
Shabnam Thakur	Amity Institute of Pharmacy, Amity University Haryana, Panchgaon, Manesar, Gurugram, Haryana 122412, India
Satish Sardana	Amity Institute of Pharmacy, Amity University Haryana, Panchgaon, Manesar, Gurugram, Haryana 122412, India
Siddhartha Sankar Dhar	National Institute of Technology, Silchar, Cachar, Assam, 788010, India
Vinod Kumar	Department of Chemistry, J.C. Bose University of Science and Technology, YMCA, Faridabad, Haryana, India
Vineet Jakhar	Department of Chemistry, University of Florida, Gainesville, FL, USA
Vishaka Chauhan	Department of Chemistry, Faculty of Science, SGT University, Gurugram-122505, Haryana, India

CHAPTER 1

Introduction to Ionic Liquids

Vinod Kumar[1,*], **Preeti Kasana**[1], **Saloni**[1] and **Kamalakanta Behera**[2]

[1] *Department of Chemistry, J.C. Bose University of Science and Technology, YMCA, Faridabad, Haryana, India*

[2] *Department of Chemistry, University of Allahabad, Prayagraj, Uttar Pradesh, India*

Abstract: Currently, ionic liquids (ILs) is a topic of interest to physical, organic inorganic chemists as well as biologists due to their unusual physical, chemical, and biological properties. The fine-tuning of physical, chemical, and biological properties with the help of their cations, anions as well as side chains attached to them makes these suitable for various applications. Unlike inorganic salts, these salts generally have low melting points (sometimes below room temperature), and remain liquid over a wide range of temperatures including room temperature, therefore termed as room temperature ionic liquids (RTILs). A variety of cations and anions can serve the purpose of the synthesis of ionic liquids. Cations and anions are chosen in such a way that their structures are asymmetric in nature and hence their packing in the lattice is not closed one and hence their melting points are not as pronounced as in the case of inorganic salts having symmetric cations and anions. Ionic liquids solely consist of ions only and are liquid at room temperature; therefore, these salts can serve the purpose of a unique solvent that is ionic in nature, unlike molecular solvents, which are molecular in nature. The other important characteristic features such as large electrochemical window, high thermal and chemical stability, and low vapor pressure make these salts suitable for various applications such as electro-analysis, synthesis, catalysis, separation, extraction, mass spectrometry, dye aggregation, excited state proton transfer reactions, sensing, CO_2 capture, and energy-related applications. Due to their ionic nature, these salts possess quite interesting and unusual solvent properties and many research groups have reported unusual solvation processes within these solvent media. It has been reported that the ions of ionic liquids not only interact with each other but also interact with solute species. The quantification of the interactions between ionic liquid ions and solute species is a topic of interest to many researchers. The present chapter provides an overview of various salient features associated with ionic liquids.

Keywords: Catalysis, Designer solvents, Electrochemical applications, Ionic liquids, Sensors.

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[*] **Corresponding author Vinod Kumara:** Department of Chemistry, J.C. Bose University of Science and Technology, YMCA, Faridabad, Haryana, India; E-mail: vinod@jcboseust.ac.in

Ravi Tomar (Ed.)

INTRODUCTION

Solvents are one of the integral parts of chemistry as far as the preparation of various chemical substances is concerned. Most of the chemical reactions take place in solvent media and the rate of reactions mostly depends on the type of solvent characterized on the basis of various physicochemical properties, such as density, viscosity, dielectric constant, refractive index, boiling point, *etc*.

Therefore, proper selection of solvents is the priority before approaching specific chemical reactions, and this selection procedure is of paramount importance for the success of any particular chemical reaction carried out in solution. This prospect of solvents, however, makes the solution chemistry stimulating [1 - 5].

In academic as well as industrial research, organic solvents are broadly used and play important roles in electrochemistry, catalysis, synthesis, separation, and extraction, processes. It has been reported that most of these organic solvents are volatile in nature and hence these are toxic and hazardous to human health [6]. Furthermore, these organic solvents are generally quite expensive and it is very difficult to separate them from the products, difficult to recycle/reuse, and most importantly, impractical to dispose off. Consequently, it becomes necessary to replace and/or minimize the use of these harmful solvents to prevent the environment from their damaging effects on the environment, therefore, volatile organic compounds (VOCs) used in academic and industrial research should be replaced by more suitable alternatives [7, 8]. Scientists have developed alternative solvent systems that might be environmentally benign in the sense they spread pollution in the atmosphere to a considerably lesser extent. They are proven to be a step towards ‘green chemistry’ as far as their impact on the global environment is concerned, and they, by virtue of their novelty as solvents, have added a new avenue in solution chemistry [9 - 11].

Replacement of volatile organic solvents by green solvents can save the environment from damaging effects. One way is the substitution of these harmful solvents with other solvents having better biodegradability or reduced ozone depletion potential [12 - 14] and other environmental, health and safety (EHS) properties. The second alternative to address the same problem is to promote the use of “bio-solvents” such as ethanol produced by the fermentation of sugar-containing feeds as well as starchy feed materials [15]. The third way to minimize solvents’ harmful effects on the environment is the substitution of volatile organic solvents with supercritical fluids [16 - 18].

One more way to address the issue of the environmental impact of volatile organic solvents is to use environmentally benign ionic liquids as new and alternative solvent media so as to replace traditional industrial solvents and prevent the emission of VOCs, a major source of environmental pollution. An ideal solvent has to fulfill certain conditions such as negligible vapor pressure, chemical inertness, inexpensiveness, reusability, and capacity to dissolve a wide variety of probe materials, tendency to allow more selective and quick transformations.

Greener Media in Chemistry

Supercritical Fluids

A supercritical fluid (SCF) is defined as a material that can be either liquid or gas. Supercritical fluids are used in a state above the critical temperature (T_c) and critical pressure (P_c); where gases and liquids can co-exist. The physicochemical properties of supercritical fluids can be fine-tuned. Supercritical carbon dioxide (scCO_2) is an interesting solvent and has played an important role in green chemistry and catalysis. The non-flammable nature, less toxic as compared to most of the organic solvents, high availability, interesting physical properties and chemical stability, high gas solubility, weak solvation, high diffusion rates and good mass transfer help SCFs as new solvents for organic and catalytic reactions [19, 20].The critical temperature and pressure for carbon dioxide are 31.1 ºC and 73 atm and these conditions are easily achieved in the laboratory.

Poly (Ethylene Glycol)s

Poly (ethylene glycol) (PEG) is the linear polymer formed as a result of polymerization of ethylene oxide. PEG usually indicates the polyether of molecular weight (MW) less than 20,000. PEG is considered to be an environmentally benign alternative media for organic reactions due to low vapor pressure, non-flammable nature, simple work-up procedures and recyclability, low melting point, inexpensive, thermally stable, recoverable, biologically compatible and non-toxic nature, and its commercial availability [21].

Water

On account of its environmentally benign nature, low cost, safety, and availability, water is a universally greener solvent. Water has unique properties as a solvent that can sometimes lead to surprising results. The stereoselectivities of many types of organic reactions can be dramatically enhanced in water due to solvophobic effects. It has been reported that the solubility of non-polar reactants can be improved with the help of organic solvents and surfactants, which can disrupt the hydrogen bond network of pure water [22].

CHAPTER 2

Ionic Liquid as a Solvent for Organic Synthesis

Shabnam Thakur[1,*], **Mohini Kalra**[1], **Satish Sardana**[1] and **Naveen Khatri**[2]

[1] *Amity Institute of Pharmacy, Amity University Haryana, Panchgaon, Manesar, Gurugram, Haryana 122412, India*

[2] *College of pharmacy, GIMS (SDPGIPS) Pt. B.D. Sharma UHS, Rohtak Haryana, India*

Abstract: Ionic liquids (ILs) are a class of designer solvents that have unique physical and chemical properties. They are non-volatile, thermally stable, and can be tailored to have a wide range of properties, making them attractive as solvents for various chemical reactions. This book chapter aims to provide an overview of the use of ILs as solvents in organic synthesis, with a focus on their applications in various reactions such as oxidations, reductions, and coupling reactions. The chapter also discusses the advantages and challenges of using ILs as solvents in organic synthesis. The advantages of ILs include their low toxicity, recyclability, and ability to dissolve a wide range of compounds. The challenges include the high cost of ILs, their limited availability, and their potential environmental impact. Finally, the chapter explores the future prospects of ILs in organic synthesis, including emerging trends and developments in the field. Overall, this chapter provides a comprehensive overview of the use of ILs as solvents in organic synthesis and highlights their potential as a sustainable alternative to traditional solvents.

Keywords: Coupling reactions, Catalytic reactions, Designer solvents, Ionic liquids, Low volatility, Oxidations, Organic synthesis, Physicochemical properties, Reductions, Renewable resources, Solvents, Sustainable chemistry, Tunable solvation properties, Thermal stability.

INTRODUCTION

Ionic liquids (ILs) have received a lot of interest recently as promising solvents for chemical synthesis. Because of their particular features, such as low volatility, a wide liquid temperature range, excellent thermal stability, and strong solubility for a variety of organic and inorganic chemicals, these unique liquid salts have arisen as alternatives to typical organic solvents. ILs are made up of large organic cations and small inorganic or organic anions, which gives them their non-volatile and non-flammable properties [1, 2].

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[*] **Corresponding author Shabnam Thakur:** Amity Institute of Pharmacy, Amity University Haryana, Panchgaon, Manesar, Gurugram, Haryana 122412, India; E-mail: sthakur233@gmail.com

Ravi Tomar (Ed.)

The use of ILs as organic synthesis solvents has various advantages over traditional solvents. For a wide variety of chemical reactions, ILs improve reaction selectivity, yield, and reaction speeds. Furthermore, ILs are frequently recyclable, minimizing trash output and perhaps providing environmental benefits. These qualities make ILs appealing for a variety of organic synthesis applications such as catalysis, extraction, electrochemistry, and polymerization.

This review aims to provide a comprehensive overview of the history and current status of ILs as organic synthesis solvents. The review will cover a variety of topics, such as the distinctive properties of ILs, their synthesis and characterization, and their applications in various organic reactions. Special attention will be paid to the benefits and difficulties associated with the use of ILs in organic synthesis, as well as prospective future developments in this field [3].

Overall, the purpose of this review is to emphasize the significance and applicability of ILs as solvents in organic synthesis and to provide researchers with a thorough comprehension of the current state of the art in this field. This review aims to inspire further exploration and application of ILs in the development of sustainable and efficient synthetic methodologies by examining their unique properties and applications.

BACKGROUND AND SIGNIFICANCE OF IONIC LIQUIDS IN ORGANIC SYNTHESIS

Due to their distinct characteristics and possible advantages, ILs have attracted a lot of interest as substitute solvents in chemical synthesis. Large organic cations and small inorganic or organic anions make up ILs, giving them their distinctive non-volatile and non-flammable properties. These liquid salts have excellent solubility for a variety of organic and inorganic chemicals, a broad liquid temperature range, low vapor pressure, and strong thermal stability [3].

When used as solvents in organic synthesis, ILs provide a number of benefits over conventional organic solvents. Their capacity to increase response selectivity and yield is one of their main advantages. Increased product selectivity and reaction speeds can result from the use of ILs to modify the reaction environment and encourage particular interactions between reactants, catalysts, and solutes. Reactive intermediates can be stabilized, charge transfer processes can be facilitated, and the reaction mechanism can be influenced by the special solvation properties of ILs.

In the synthesis of organic materials, ILs may potentially provide environmental advantages. ILs can decrease the release of volatile organic compounds (VOCs) into the atmosphere, which is a major concern for conventional volatile solvents due to their low volatility. Additionally, because ILs are recyclable, it is possible to reuse them in chemical processes, which reduces waste formation [4].

ILs have shown promise in a number of domains, including catalysis, extraction, electrochemistry, and polymerization, when used as solvents in organic synthesis. ILs can be used as efficient reaction media for a variety of organic processes, including the creation of carbon-carbon bonds, the modification of functional groups, and asymmetric synthesis. The adjustable nature of ILs—achieved by fusing various cations and anions—allows for the tailoring of solvent characteristics to meet certain reaction requirements. The use of ILs in organic synthesis is not without difficulties, though. It is important to address problems including the high viscosity, high price, and potential toxicity of some ILs. ILs' compatibility with catalysts and any potential effects on reaction kinetics and selectivity must also be carefully taken into account [5].

In conclusion, because of their distinct qualities and prospective advantages, ILs present interesting opportunities as solvents in organic synthesis. Utilizing ILs can increase reaction selectivity, boost yields, and aid in the creation of ecologically acceptable and sustainable synthetic processes. It is anticipated that more work will be done in this area to address the problems with ILs and realize their full potential in organic synthesis.

OBJECTIVES

The objective of this chapter is to furnish a thorough comprehension of the utilization of ILs in the domain of organic synthesis. The objective of this chapter is to examine the historical context and general outline of ILs as solvents in the realm of organic synthesis, emphasizing their distinctive characteristics and benefits in comparison to conventional organic solvents. The following are the objectives of ionic liquids as a solvent for organic synthesis [5 - 8].

1. To provide an overview of ILs as a distinct family of organic synthesis solvents. The purpose of this chapter is to introduce the notion of ILs and their unique features that make them appropriate solvents for a variety of chemical processes.

2. To discuss the advantages of using ILs as solvents in organic synthesis. The purpose of this chapter is to emphasize the distinguishing characteristics of ILs, such as their low volatility, high thermal stability, and wide liquid temperature range, which contribute to their usefulness as solvents in organic processes. It investigates how these features can improve reaction selectivity, make polar and non-polar molecules dissolve more easily, and stabilize reactive intermediates.

CHAPTER 3

Ionic Liquid Assisted Cross-Coupling Reactions: Recent Advances and Challenges

Ajeet Kumar[1], **Vineet Jakhar**[1], **Debabrata Konar**[1], **Nidhi Kalia**[1] and **Archa Gulati**[2,*]

[1] *Department of Chemistry, University of Florida, Gainesville, FL, USA*

[2] *Department of Chemistry, Ramjas College, University of Delhi, Delhi-110007, India*

Abstract: Ionic liquids (ILs) are of sustained interest in synthetic organic chemistry due to their unique properties. The unique properties involve high thermal stability and ionic conductivity, and tunable solvation properties due to tunable cationic and anionic counterparts. There are a variety of cross-coupling reactions present in organic chemistry, which facilitate new carbon-carbon and carbon-heteroatom bond formation. Ionic liquids play various crucial roles in cross-coupling reactions. First, ILs are a greener alternative to flammable and hazardous volatile organic solvents (VOCs). Second, ILs are used as co-solvent in cross-coupling reactions to enhance the solubility of organometallic reagents. Third, ILs are used as the precursors of *N*-heterocyclic carbene (NHC) ligands that find their excellent utility in homogenous catalysis. The NHCs are an excellent alternative to air-sensitive tertiary phosphine ligands and serve as ligands for several palladium-catalyzed cross-coupling reactions. Apart from this, ILs are exploited as additives to stabilize palladium nanoparticles (Pd-NPs) in many cross-coupling reactions. This chapter outlines recent progress in key metal-catalyzed cross-coupling reactions, employing ionic liquids in diverse capacities.

Keywords: Cross-coupling reactions, Green solvents, Ionic liquids, Metal-catalyzed reactions, Synthetic organic chemistry.

INTRODUCTION

Ionic Liquids (ILs) are described as compounds consisting solely of cations and anions and are poorly coordinated. They have a low melting point (less than 100 °C) and are found to be in a liquid state at room temperature with relatively low viscosity [1, 2]. The first reported IL was ethyl ammonium nitrate $[EtNH_3]^+[NO_3]^-$ by Paul Walden in 1914. However, it gained attention after the development of binary ILs by Hurley and Weir in 1951, comprised of alkylpyridinium cation with a tetrachloroaluminate(III) anion [3]. A significant breakthrough occurred in 1992

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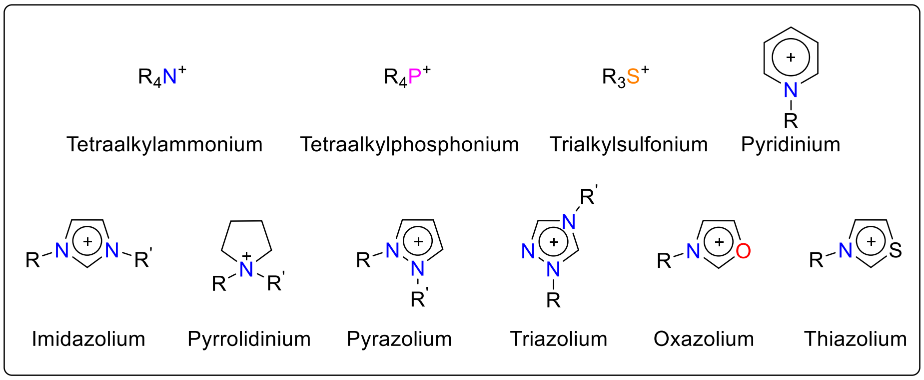
[*] **Corresponding author Archa Gulati:** Department of Chemistry, Ramjas College, University of Delhi, Delhi-110007, India; E-mails: archagulati@ramjas.du.ac.in; gulatiarcha@gmail.com

Ravi Tomar (Ed.)

when John Wilke's group reported synthesizing a series of air and moisture-stable imidazolium-based salts with anions of hexafluorophosphate and tetrafluoroborate [4]. These salts are now widely used as reaction media for various organic reactions. During the early 2000s, James Davis introduced the notion of task-specific ILs (TSILs) [5]. Different perspectives are available in the literature for the comprehensive historical overview of ILs [6 - 8]. Since then, there has been tremendous growth in the field of ILs, with many researchers reporting various combinations of cations and anions to tailor the properties of ILs to suit specific applications.

ILs are often termed "designer solvents" because they can tune and tailor the phase behavior of systems and their physio-chemical properties by the variation in constituting ions [9]. The cations in ILs are usually organic structures, often containing but not limited to nitrogen, phosphorus, or sulfur atoms with linear, branched, or functionalized side chains, and can vary from ammonium to phosphonium, pyridinium, imidazolium or pyrrolidinium (Fig. **1**, top). The anions in ILs can be either organic or inorganic, and the most commonly used organic anions include halides, alkylphosphates, alkylsulfates, bis(trifluoromethyl-sulfonyl)imide, *etc*., as shown in Fig. (**1**), bottom.



$[BF_4]^-$	$[AlCl_4]^-$	X^-	$[PF_6]^-$
Tetrafluoroborate	Tetrachloroaluminate	Halide	Hexafluorophosphate
$[NTf_2]^-$	$[OTf]^-$	$[RSO_4]^-$	$[N(CN)_2]^-$
Bis(trifluoromethylsulfonyl)imide	Trifluoromethanesulfonate triflate	Alkylsulfate	Dicyanamide

Fig. (1). Some commonly used cations (top) and anions (bottom) for ILs.

Due to their unique characteristics, ILs have gained significant attention from research groups and industry in recent decades. Unlike traditional molten salts, which have high melting points (m.p. >100 °C) and are highly corrosive, ILs have distinct properties. The structure of constituent ions in molten salts like sodium chloride (NaCl) differs from that of ILs. In NaCl, cations and anions are small, spherical, and similar in size, enabling them to pack well next to each other, contributing to extremely strong coulombic forces. However, in ILs, one or both of the ions are large, and the cation has a low degree of symmetry; this reduces lattice energy and consequently lowers the melting points. ILs also have other desirable properties, including having negligible vapor pressure, being non-flammable, having a wide electrochemical (conductivity) window, and being highly thermally stable. Moreover, ILs are recyclable and an excellent solvent and/or catalyst for several organic reactions. These properties have led to ILs finding applications in various fields such as electrochemistry, nanotechnology, extraction processes, solvents and catalysts, analytical chemistry, and several others, earning them the label "solvents of the future" [10]. In addition, ionic liquids find notable application in the precise detection of hazardous heavy metal ions [11 - 16], biologically and environmentally relevant anions [17 - 20], and organic acids [21, 22]. Their unique properties, as elucidated earlier in this section, enable sensitive and selective sensing. This versatility positions ionic liquids as valuable tools for addressing environmental and safety concerns associated with these hazardous substances.

ILs have gained attention from researchers for their potential to reduce or eliminate the use of harmful and toxic chemicals, which has led to the development of more efficient, improved, and environmentally friendly processes and products [23, 24]. Not surprisingly, ILs have also been used in cross-coupling reactions and are seen as a greener alternative over hazardous volatile organic solvents (VOCs) [25]. The unique properties of ILs mentioned above allow them to replace conventional organic solvents, which are often less efficient and more hazardous. There is a growing interest in utilizing ILs in transition metal-mediated cross-coupling reactions, which requires an examination of their task-specific roles.

ILs are also used as additives to enhance the quality and performance of different substances, including paints, lubricants, adhesives, shampoos, conditioners, and detergents [26]. Certain ILs are referred to as surface-active ionic liquids (SAIL) [27] as they exhibit surface activity by attaching long alkyl chains that possess an amphiphilic nature owing to their distinct hydrophilic head and hydrophobic tail. This surface-active nature [28], combined with other important properties of ILs, allows them to be an effective alternative to traditional surfactants.

CHAPTER 4

Catalytic Application of Ionic Liquids in Organic Transformations

Vishaka Chauhan[1], **Chinmay**[1] and **Anjaneyulu Bendi**[2,*]

[1] *Department of Chemistry, Faculty of Science, SGT University, Gurugram- 122505, Haryana, India*

[2] *Department of Chemistry, Presidency University, Rajanukunte, Itgalpura, Bangalore, 560064, Karnataka, India*

Abstract: Heterocyclic chemistry is one of the prominent areas of organic chemistry that synthesizes a variety of medicinally important drug moieties. Heterocycles make up the majority of pharmaceutical medicines that imitate biologically active natural compounds. Ionic liquids (ILs) have recently drawn more attention in relation to green organic synthesis. Ionic liquids have evolved since their first introduction as alternative green reaction media due to their distinct chemical and physical characteristics of non-volatility, non-flammability, thermal stability, and regulated miscibility. Nowadays, the scientific community has focused on using ILs as effective catalysts in different organic transformations for synthesizing biologically active heterocycles. The current work highlights the essential insights into the indisputable uses of ionic liquids as effective catalysts in different organic transformations.

Keywords: Catalyst, Green synthesis, Heterocycles, Ionic liquids (ILs), Organic transformations.

INTRODUCTION

Nowadays, heterocyclic compounds have received greater attention from the scientific community because of their utility in anti-microbial technology, medicine, and industry [1 - 3]. Numerous natural compounds, including DNA, RNA, chlorophyll, haemoglobin, vitamins, and other related compounds contain heterocyclic moiety in their ring system [4 - 8]. The three heteroatoms that are found most frequently in most of the biologically active heterocycles are nitrogen, oxygen, and sulphur [8 - 10]. Numerous heterocyclic substances, such as triazine analogues, have been used as therapeutics, urinary antiseptics, and anti-inflammatory drugs in the management of a number of diseases [11]. The anti-

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[*] **Corresponding author Anjaneyulu Bendi:** Department of Chemistry, Presidency University, Rajanukunte, Itgalpura, Bangalore, 560064, Karnataka, India; E-mail: anjaneyulu.bendi@gmail.com

Ravi Tomar (Ed.)

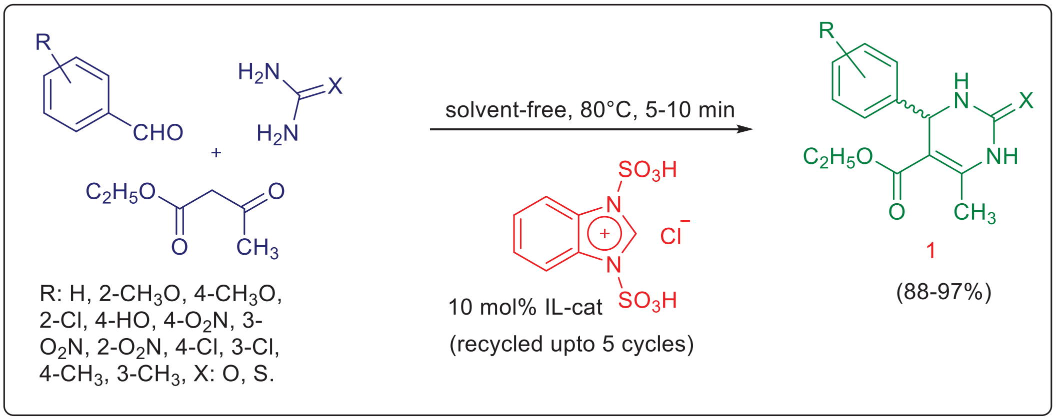
bacterial, antifungal, antiviral, and anthelmintic effects of benzimidazole derivatives have been proven [12 - 15]. Most pharmaceutical drugs are composed of heterocyclic molecules. Some of the most common organic compounds contain heterocycles, which include synthetase precursors, amino acids, and vitamins [16 - 18]. Fungicides, corrosion protection chemicals, photo stabilizers, agrochemicals, colouring agents, copolymers, kodak developers, fluorescents, flavourings, and other significant applications are only a few of the numerous synthetic heterocyclic compounds with notable applications [4, 19 - 21]. Even though, some methods are used to synthesize heterocycles, the synthesis of heterocycles using ILs as an efficient catalyst is one of the emerging areas.

ILs are versatile molten salts having melting point lower than 100°C and made up of an organic cation such as benzimidazolium, imidazolium, pyridinium, tetraalkyl ammonium, sulfonium, pyrrolidinium, or tetraalkyl phosphonium ions and anions, typically $[Cl]^-$, $[Br]^-$, $[PF_6]^-$, $[TfO]^-$, $[BF_4]^-$, $[TsO]^-$, $[HSO_4]^-$, $[NTf_2]^-$ [9]. The appealing physiochemical characteristics of ILs attracted the scientific community in recent years [10 - 13]. Interestingly, mixed ILs commonly called task-specific ILs (TSILs) can have several properties that are easily changed for a particular function [14 - 17]. As an illustration, acidic ILs (AILs) are a significant family of TSILs with numerous applications [18, 19]. In order to create biologically active heterocycles, the scientific community has recently concentrated on using ILs as efficient catalysts in a variety of organic reactions. The current study emphasizes the key understandings regarding the undeniable applications of ILs as most emerging catalysts in a variety of organic reactions [20 - 32].

CHEMISTRY OF DIHYDROPYRIMIDINONE DERIVATIVES

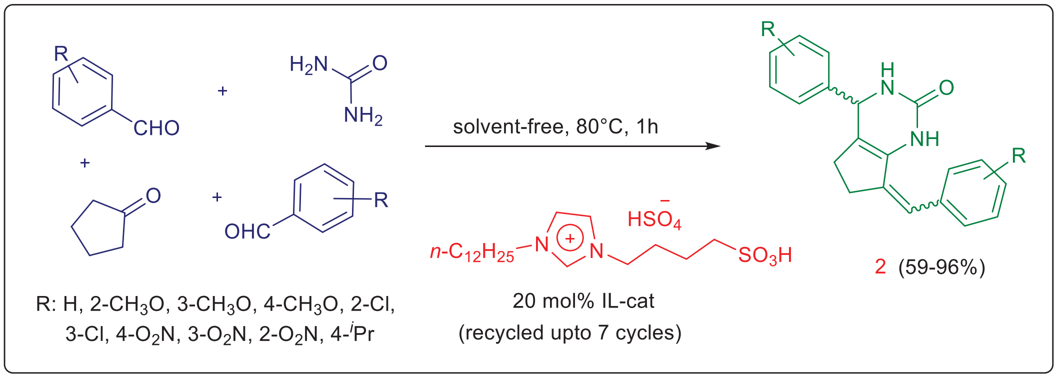
Dihydropyrimidinones (DHPMs) are an important family of *N*-heterocycles with a wide variety of bio- and pharmacological applications that have been produced *via* the popular multicomponent reaction called Biginelli. This has been regarded as the most effective approach since the XIX century [33, 34].

Abbasi *et al*. [35] (Scheme **1**) developed a high-yield method to produce the series of DHPMs **1** starting from substituted phenyl-aldehydes, ethyl acetoacetate and urea/thiourea in the presence of a small quantity of benzimidazolium chloride [BIm][Cl] 1,3-dissulfonic acid as IL-catalyst through one-pot Biginelli tricomponent cyclo-condensation. A study on the catalyst's recyclability revealed that there was no discernible loss in yields (90-95%) after using it for five consecutive cycles.



Scheme (1). Biginelli MCR catalyzed by 1,3-dissulfonic acid benzimidazolium chloride.

Similarly, Zhou *et al*. [36] (Scheme **2**) synthesized a variety of dialkyl imidazolium-based ILs with SO_3H functionalization for the synthesis of DHPM derivatives **2** by reacting substituted phenyl-aldehydes, urea, and cyclopentanone.



Scheme (2). Biginelli-type reaction catalyzed by SO3H-functionalized 1,3- dialkylimidazolium catalyst.

The optimum catalyst was $[(SO_3H)^3C_3C_{12}Im]$ $[HSO_4]$ because it has been observed that a long-*n*-C_{12} alkyl chain connected to the imidazolium cation boosts the solubility of the catalyst in the organic phase, which in turn improves the interactions between the reactants and the catalyst.

Rahman *et al*. [37] (Scheme **3**) used sulfoalkyl-based imidizolium acidic ILs to create benzoquinazoline-based DHPM derivatives **3** utilizing a modified Biginelli method.

CHAPTER 5

Catalytic Transformation of Biomass Conversion in Ionic Liquids

Debarati Chakraborty[1,*] and **Siddhartha Sankar Dhar**[1]

[1] *National Institute of Technology, Silchar, Cachar, Assam, 788010, India*

Abstract: The last few years have seen a noticeable rise in the consideration of ionic liquids as green solvents in chemical processes. These liquids, characterized by their adaptability, have found multiple applications in different fields. This review aims to provide a thorough outlook on the utilization of ionic liquids for the processing of carbohydrate biomass, while also encompassing the latest advancements in this particular realm. In the context of biomass refineries, ionic liquids (ILs) play a pivotal role in achieving greater efficiency and improved product selectivity under milder conditions when contrasted with conventional molecular solvents. The principal constituents of biomass are carbohydrates and lignin. The primary objective of this article is to present an up-to-date account of advancements in catalytic systems that employ ionic liquids for transforming lignocellulosic biomass. This account is largely based on works published within the last five years. Furthermore, attention is drawn to the potential use of functionalized ionic liquid as both a sustainable solvent and catalyst. The variables impacting the catalytic alteration of carbohydrate biomass within the ionic liquid, as well as the mechanisms behind producing 5-HMF (5-hydroxymethylfurfural) and LA (Levulinic acid), are also outlined. Additionally, the potential to recycle the ionic liquid for processing carbohydrate biomass is examined. Subsequent research endeavors concerning the transformation of biomass in ionic liquids could refer to this review to pick out suitable reaction conditions imperative for fulfilling their particular objectives. Furthermore, the merging of methods from ionic liquids and strategies for converting biomass into assorted fuels and higher-value chemicals can be comprehended for potential implementation in a lignocellulosic biorefinery.

Keywords: Cellulose, Catalytic transformation, Hemicellulose, Ionic liquids, Lignin, Lignocellulose, Mechanism.

INTRODUCTION

In contemporary times, the majority of indispensable fuels and chemicals utilized by humanity are mostly derived from non-renewable fossil resources, namely

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[*] **Corresponding author Debarati Chakraborty:** National Institute of Technology, Silchar, Cachar, Assam, 788010, India; E-mail: debaratichakraborty130@gmail.com

Ravi Tomar (Ed.)

petroleum, coal, and natural gas. Nevertheless, the availability of these fossil reserves is depleting. The persistent need for chemicals and energy remains unabated. The phenomenon is experiencing an upward trend. In the interim, the utilization of non-renewable fossil fuels. The utilization of resources results in the production of substantial quantities of greenhouse gases. Greenhouse gas (GHG) emissions are responsible for the phenomenon of global climate change, which poses a significant and complex challenge for the global community. Hence, the pursuit of eco-friendly alternatives to the diminishing fossil resources for energy and chemicals provision is a pressing imperative and a global research endeavour of significant magnitude. The effective utilization of naturally plentiful and renewable resources holds significant relevance in the endeavour to achieve a sustainable future [1 - 9].

Biomass, the exclusive organic carbon source found in the natural environment that is renewable, has garnered substantial attention as an environmentally friendly carbon source for the formation of various chemicals, functional materials, and fuel products. Additionally, biomass serves as the fourth largest energy reservoir globally for generating power and heat, ranking after coal, oil, and natural gas. The transformation of biomass into valuable fuels and chemicals has the potential to mitigate our significant reliance on fossil reservoirs. Additionally, this approach has been acknowledged as an efficient means of reducing the overall emission of CO_2 through the integration of photosynthetic and chemical processes [10 - 12].

Lignocellulosic biomass, which includes wood and other plant biomass, constitutes the majority of the weight of plant substances devoid of moisture, involving both herbaceous and woody constituents. It is considered the most prevalent kind of biomass among several feedstocks such as triglycerides, lignocellulose, chitin, and starch. Lignocellulose can be described as a composite material comprised predominantly of three oxygen-containing organic polymers with high molecular weights: hemicellulose, cellulose, and lignin (Fig. **1**) [13]. Additionally, there are small quantities of extraneous substances such as oils terpenes, and, inorganic minerals. The percentage by weight of each constituent exhibits variation and is contingent upon the wood or plant species. However, as a general trend, common wood-derived biomass comprises approximately 20-35% hemicellulose (a heteropolymer primarily composed of xylose), 30-50% cellulose (a glucose polymer), and 15-30% lignin (an amorphous aromatic macromolecule). Lignocellulose has been utilized to synthesize a range of value-enhanced chemical products and high-quality fuel products. These include organic acids such as formic acid, gluconic acid, levulinic acid, and lactic acid, as well as alcohols like ethylene glycol, sugar alcohols, and propylene glycol. Cellulose serves as a source of these chemicals. Additionally, furfural-based compounds such as 5-

hydroxymethylfurfural and furfural can be derived from hemicellulose and cellulose. Furthermore, lignin can be utilized to generate various aromatic chemicals [14 - 20].

The consideration of ecologically friendly methods for transforming feedstocks is a significant concern in relation to the advancement of green chemical processes and the establishment of facilities for biorefining. The use of environmentally friendly solvents, such as supercritical fluids, water, ionic liquids, and polyethylene glycols has gained significant attention as a viable alternative to volatile organic solvents (VOCs). Solvents are integral components in numerous chemical and chemical engineering processes, making this topic of great interest. Ionic liquids (ILs) have garnered significant interest in recent years as a promising category of environmentally friendly and efficient solvents. Ionic liquids are a category of molten salts that exhibit low-temperature characteristics, consisting of a wide range of cations and anions. Fig. (**1**) illustrates the structures of the anions and cations often found in ionic liquids (ILs) [21 - 25]. The physicochemical characteristics of ionic liquids (ILs) are typically differentiated from those of water and traditional volatile organic solvents due to their low vapor pressure, wide electrochemical range, and non-flammable nature. Some categories of ionic liquids have been discovered to possess unique solubility properties for individual or multiple constituents of lignocellulosic biomass. Additionally, these ILs exhibit remarkable capabilities as reaction media and catalysts for facilitating the transformation of lignocellulosic biomass *via* catalytic conversion. Efficient and selective catalytic transformation necessitates the breaking down and separating of lignocellulosic biomass because of the distinct catalysts and reaction conditions involved in the conversions of lignin and carbohydrates. Isomerization ligands (ILs) have been extensively employed as efficient solvents for separation and as reaction media in the second approach [26, 27].

In recent times, there have been notable advancements in the chemical and physical processes involved in the utilization of ILs (ionic liquids). These advancements have resulted in the enhancement of more efficient techniques for industrial progress for the conversion of carbohydrates and lignin obtained from sustainable biomass into chemicals and fuels of significant value. The utilization of ionic liquids (ILs) as reaction solvents has the potential to enhance the efficiency of reactions by facilitating the dissolution of lignocellulosic macromolecules. This, in turn, improves the accessibility of bonds that are targeted by catalysts. Consequently, the reaction conditions necessary are generally milder compared to those required when employing alternative solvents. In the context of lignocellulose processing, it has been observed that ILs have the ability to safeguard and stabilize active intermediates such as radicals and carbocations. Additionally, ILs possess unique properties that enable them to

CHAPTER 6

Multicomponent Reaction in Ionic Liquid for Eco-compatible Heterocyclic Synthesis

Priyanka Bhatt[1] and **Manoj Kumar**[1,*]

[1] *TLC Pharmaceutical Standards Ltd, New market, ON, Canada & Dept. of Chemistry & Chemical Biology, McMaster University, Hamilton, ON, Canada*

Abstract: Multicomponent reactions (MCRs) provide a unique way to incorporate the structural attributes of three or more reactants in a single operation. Along with their operational simplicity and synthetic convergence, MCRs are generally atom, step, and time economical than comparable multistep processes. On the other hand, ionic liquids (ILs) are salts with low melting points. Because of their low vapor pressure, recyclability, and tunability, ILs offer a task-specific alternative to commonly employed organic solvents. Thus, merging both strategies (MCRs & ILs) together opens the way to a plethora of possibilities for greener productions of heterocyclic compounds. In the proposed chapter, attempts will be made to cover the MCRs relevant to heterocyclic synthesis conducted in ionic liquids (ILs) with a special emphasis on process sustainability.

Keywords: Brønsted acid ionic liquids, Designer ionic liquid, Green chemistry, Heterocyclic synthesis, Ionic liquids, Multicomponent reactions, Polymeric ionic liquid, Room temperature ionic liquids, Task-specific ionic liquids.

INTRODUCTION

Multicomponent Reactions (MCRs) in Ionic Liquids (ILs): a Perfect Synergy for Green Heterocyclic Synthesis

Today, the success of a chemical process is not only judged by its yield or robustness but also by its compatibility with green chemistry and environmental impact. Design and development of newer more sustainable processes/protocols have now become a central theme of chemical research, which also syncs well with the twelve principles of green chemistry [1].

Chemists are now looking at multiple factors for their synthetic strategy based on available information. Some of the factors include the toxicity of the reagent/

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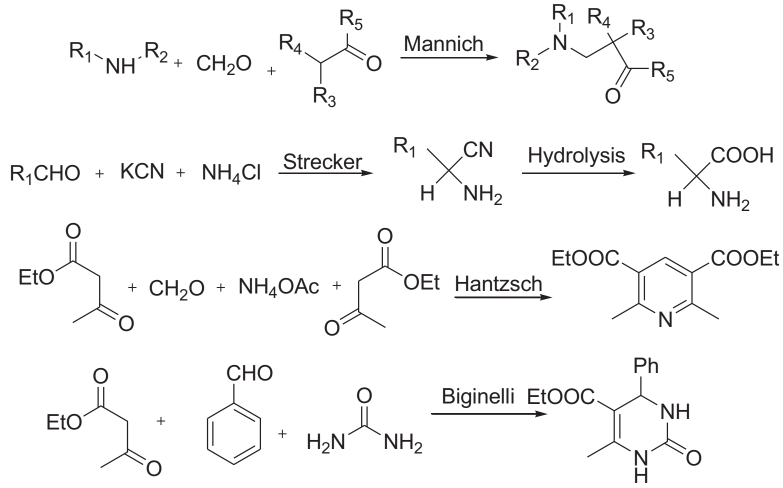
[*] **Corresponding author Manoj Kumar:** TLC Pharmaceutical Standards Ltd, New market, ON, Canada & Dept. of Chemistry & Chemical Biology, McMaster University, Hamilton, ON, Canada; E-mail: mksdcy@gmail.com

Ravi Tomar (Ed.)

chemical used, characteristics of the solvent used in the core process and subsequent purification, method/s of purification, nature of side product/s, disposal method/s for undesired products, number of steps, atom economy, *etc*. Overall, a "smart" way to carry out a chemical reaction is always needed [2, 3]. While the use of the word "smart" looks somewhat intuitive, it is not without any scientific qualification and the criteria here is to seek an optimal balance of yield, energy efficiency, and greenness.

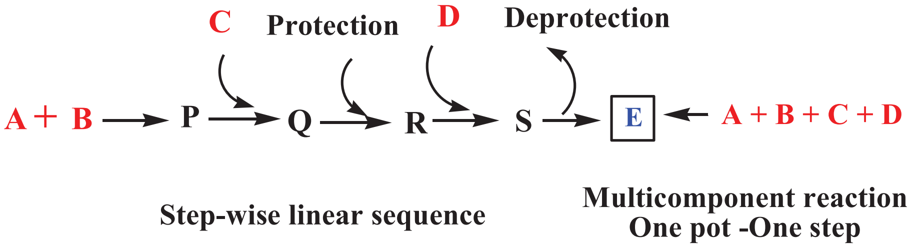
To realize the above-mentioned aims, some newer and innovative approaches have been devised such as solid phase organic synthesis, the use of polymer-supported reagents, parallel and micro reactor-based synthesis, microwave-assisted high-speed reactions, the use of ionic liquids and click and multicomponent reactions, *etc*. While the use of any of these strategies itself does not guarantee a higher eco-compatibility of a process, it definitely gives a toolkit to make a judicious and informed decision.

The focal theme of this chapter is to review the multicomponent reaction in ionic liquid for green heterocyclic synthesis. As defined by Ganem [4], multicomponent reactions (hereafter abbreviated as MCRs) are reactions where (1) more than two (at least 3 or more) starting materials/inputs are mixed in one pot (one pot – one step) (2) sequence of input addition does not affect the outcomes in term of yield or product identity and, (3) final product motif arises from the structural contribution from all the starting materials. The Biginelli, Mannich, Strecker, Ugi, Passerini, and Groebke reactions are some of the classical and well-known examples of this class (Scheme **1**).



Scheme (1). A snapshot of a few classical multicomponent reactions.

MCRs are synthetically convergent processes and hence greatly reduce the number of steps and pots required to reach a desired product. A classical example can be given by isocyanide based Groebke–Blackburn–Bienaymé (Groebke reaction) three-component reaction. In this reaction, an amino-azine, aldehyde, and isocyanide are mixed in the presence of an acidic catalyst to yield functionalized imidazole (one step and one pot). Theoretically, the same imidazoles can also be accessed by two reactions by treating amino-azine input to aldehydes first and isolating iminium (Schiff base) product, and then this intermediate is subjected to isonitrile based [2+1] cycloaddition (two steps and two pots operation) in a subsequent step. In a stepwise manner sometimes, the product has to be isolated and purified, and it will generally decrease the yield while increasing solvent, energy, and time consumption. Similarly, in some instances, protection and deprotection steps also need to be included in the sequential stepwise scheme (compared to MCRs), which only increases the chemical and economic burden (Scheme **2**) [3].



Scheme (2). Stepwise linear sequence *vs* multicomponent reaction.

In general, MCRs are step, atom, and time economical processes than the comparable two or more steps linear sequences. These reactions are simple to operate, show high convergence, and are a good source of diversity-oriented synthesis (DOS) and library design. These features make them a good candidate for the current idea of sustainable chemistry [5, 6].

On the other hand, ionic liquids (hereafter abbreviated as ILs) are salts in the molten or liquid state. In other words, Molecular frameworks of ILs are made up of ions and this feature makes them an unconventional but unique choice as solvent [7]. Although the physical state of a salt (like any other material) depends on temperature and pressure for all practical purposes, the salt that exists in the liquid phase below or near 100 ^{o}C are generally considered ILs [7, 8].

ILs have some interesting attributes that make them a good candidate for eco-compatible process development. One of the most notable features is their low vapour pressure, and hence generate none or negligible volatile organic

SUBJECT INDEX

Ravi Tomar (Ed.)

Ravi Tomar

Ravi Tomar is an assistant professor at the Department of Chemistry, SRM Institute of Science and Technology, Delhi-NCR Campus, Modinagar, Uttar Pradesh. He is also a SERB-TARE fellow at the Department of Chemical Engineering at the Indian Institute of Technology (IIT), Delhi. He received the doctorate degree from the Department of Chemistry, University of Delhi in 2019. During his Ph.D., he worked on the synthesis, characterization, and application of Cerium-based catalysts. His research interests revolve around the synthesis of various materials and ionic liquids, as well as exploring their applications across diverse fields. He has contributed significantly to the academic community, and served as a guest editor for Current Organic Chemistry and Current Organic Synthesis, in addition to his role as a reviewer for various peer-reviewed journals e.g. International Journal of Biological Macromolecules, iScience, BMC Chemistry, Current Medicinal Chemistry, Scientific Reports, Letter in Organic Chemistry, etc. He has been awarded with two research grants from ANRF (formerly SERB) and CST UP. He has an extensive publication record with more than 40 publications and 4 books in esteemed publishers.