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In situ NMR Methods in Catalysis

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Volume Editors: Joachim Bargon · Lars T. Kuhn

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Preface

A chemist, faced with the problem of determining the mechanism of a chemical reaction, tries to identify a set of reactions that will account for the observed behavior: Ideally, a small set of known reactions should describe in great detail exactly what takes place at each stage of a chemical transformation. The fact that many reactions proceed in a stepwise fashion can most convincingly be demonstrated if intermediate species can be isolated and shown to proceed to the same products under otherwise identical reaction conditions. An intermediate is the reaction product of each of these steps, except for the last one that forms the final **product**. Some intermediates are stable compounds in their own right; some others, however, are so reactive that their isolation is not possible.

Occasionally, evidence for the existence of short-lived intermediates may be obtained, in particular by spectroscopic observation. The latter may allow a direct observation or an indirect inference from unusual phenomena occurring in the reaction products during in situ investigations of their corresponding chemical reactions. In NMR spectroscopy, for example, transient emission and enhanced absorption lines may be observed, and one is inclined to believe that there is a universal and unambiguous reason for their appearance. This is not necessarily the case, however, since this seemingly identical phenomenon may have a strikingly different origin: During free radical reactions, a phenomenon called chemically induced dynamic nuclear polarization (CIDNP) may give rise to virtually the same effect as occasionally observed during homogeneous (and possibly even heterogeneous) hydrogenations: The latter phenomenon, called parahydrogen-induced polarization (PHIP), has a completely different physical basis. It was first noticed twenty years later than CIDNP and occurs if there is an imbalance of the two spin isomers of symmetric molecules such as dihydrogen when hydrogenating unsaturated compounds using appropriate catalysts. These two effects, if not differentiated properly, can cause misinterpretations of reaction mechanisms, as occurred initially when their different origins had not yet been understood appropriately.

In this volume, both phenomena, CIDNP and PHIP, will be described and typical applications outlined. Apart from providing interesting insights into catalytic and free radical reaction mechanisms, these examples of chemical reaction-assisted nuclear polarization together with their associated signal and sensitivity enhancement of nuclear magnetic resonance are not only of interest in chemistry, but are also rapidly gaining significance in medicine and biochemistry as a potential means to boost the sensitivity of magnetic resonance imaging (MRI). "Hyperpolarizing" ^{13}C-nuclei for example, has been demonstrated to provide access to fast angiography. Likewise, following the distribution and metabolism of ^{13}C-hyperpolarized compounds might provide an alternative approach to radioactively labeled targets, augmenting or replacing imaging methods of nuclear medicine, such as positron emission tomography (PET). When superimposed with ^{1}H-MRI data, for example, the corresponding resolution of this approach may exceed that of conventional PET studies, even though at present the sensitivity of PET still substantially outshines that of MRI.

Additional chapters dealing with special boundary conditions such as ionic liquids, supercritical solvents, and biocatalysis are also highlighted and augment this account of in situ NMR methods in catalysis. The authors of these chapters were associated with the University of Bonn in one form or another early on in their careers.

University of Bonn
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Joachim Bargon
Lars T. Kuhn

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Homogeneous Catalysis in Ionic Liquids

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Abstract In the past 15 years, ionic liquids have become an alternative reaction medium for organic transformations, especially for transition metal catalysis. Their unique properties make them ideal solvents for “green” industrial processes: they are polar, thus exhibiting high solubility for a large variety of substrates and catalysts, they are immiscible with many organic solvents, and they do not evaporate in high vacuum. Many of their physicochemical properties are changed substantially by variation of the cation and the anion; thus, they are "tunable" to the desired reaction. This review focuses on the general concepts that are applicable to ionic liquids as reaction media. This knowledge is intended to enable the reader to use ionic liquids advantageously for their chemistry. In the second part, some recent examples of successful ionic liquid solvent chemistry are pointed out and discussed in more detail.

Keywords Biphasic catalysis · Green chemistry · Ionic liquids · Transition metal catalysis

Abbreviations

bdmim	1-Butyl-2,3-dimethylimidazolium
bmim	1-Butyl-3-methylimidazolium
bmpy	1-Butyl-4-methylpyridinium
BTA	Bis(trifluromethylsulfonyl)amide
C_{10}mim	1-Decyl-3-methylimidazolium
emim	1-Ethyl-3-methylimidazolium
IL	Ionic liquid
RTIL	Room-temperature ionic liquid
scCO_2	Supercritical carbon dioxide

1
Introduction

Since the beginning of the 1990s, chemistry has rapidly started to evolve towards more and more environmentally benign processes for synthetic applications. Nowadays, "green chemistry" [1] is an important keyword in chemical research. Analysis of the factors that have the strongest influence on environmental issues in a chemical process frequently comes down to the influence of the solvents: heating and cooling of the reaction mixture consume energy, solubility problems reduce the choice of solvents and the efficiency of processes, the toxicity of solvent vapours are of concern, recycling of toxic or expensive catalysts is often difficult, etc. Therefore, many attempts have been made to substitute classical organic solvents with novel reaction media, tailor-made for the specific task they are needed for. Among the more frequent examples are perfluorinated solvents [2], supercritical carbon dioxide (scCO_2) [3], and, of course, ionic liquids (ILs).

The field of ILs as reaction media in organic synthesis has evolved rapidly in the last 15 years—Fig. 1 shows the number of publications with the keyword "ionic liquids" as a function of the publication year. Consequently, there are numerous reviews in the literature already, giving a comprehensive overview about the topic as well as focusing on certain specialities [4–11]. In 2003, the first comprehensive book, *Ionic liquids in synthesis* [12], was published, which

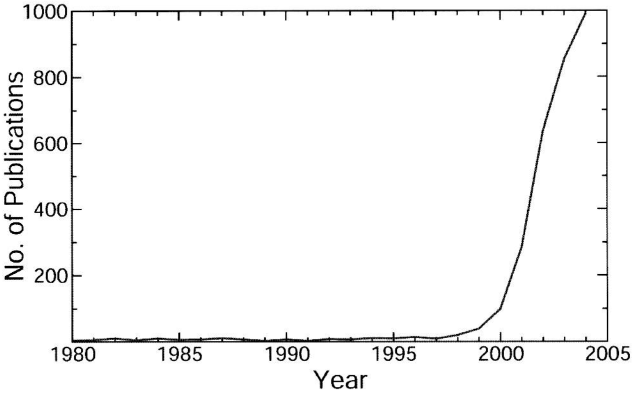


Fig. 1 Numbers of publications with ionic liquids as the topic (Source: SciFinder Scolar)

contains the state of the art when it comes down to ILs. Therefore, there is no urgent need for another comprehensive review at the present date. This article will, although giving a general overview about the topic, focus on recent developments of the last 5 years and on certain specific issues in transition metal catalysis that the author perceives as especially important and interesting to the public. The goal is to give the reader a "feeling" for what is possible and what we can expect from IL chemistry in the near future.

2
A Short History of Ionic Liquids

The "modern history" of ILs as reaction media for homogeneous transition metal catalysis really started in 1990, when Chauvin et al. [13] developed weakly acidic chloroaluminate melts for dimerisation and polymerisation reactions. Shortly afterwards, in 1992, Wilkes and Zaworotko [14] developed a totally new class of IL solvents with tetrafluoroborate and hexafluorophosphate anions. These melts were stable towards hydrolysis and showed a high tolerance towards molecules with reactive functional groups. From that time on, room-temperature ILs (RTILs) were available as general reaction media for synthetic chemistry.

Of course, organic salts that were liquid at room temperature were no invention of the 1990s. In fact, the very first IL (although this term was introduced much later) was described in 1914 [15]: ethylammonium nitrate $[EtNH_3]NO_3$, exhibiting a melting point of just 12 °C. In the years starting from 1948, RTILs were mainly used as a medium for electrochemical applications, until in the mid-1980s Seddon and Hussey started using chloroaluminate melts as media for organic synthesis [16].

3
Classification of Ionic Liquids

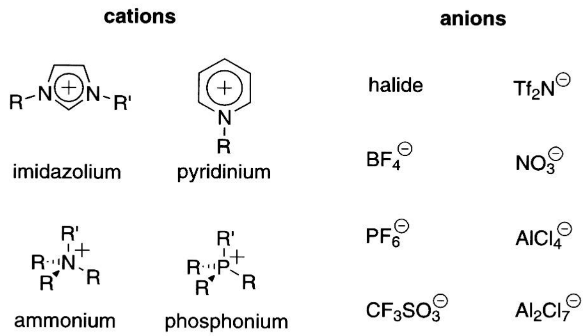
What is an IL? If we want to classify these novel reaction media, we first have to define what is to be called an IL.

An IL is a (partially) organic salt that is liquid at room temperature or reaction temperature (RTILs versus ILs). As Welton [9] has pointed out, there is nothing special about room temperature apart from the fact that this is the temperature that rooms happen to be at, so this definition is only of limited use—especially since many reactions are run at elevated temperatures. Wasserscheid and Keim [8] have proposed calling an organic salt "IL" if it is liquid below 100 °C, and this is indeed now one of the most widely accepted definitions. Where liquidity at room temperature is the key feature, the term RTIL has found widespread use in the chemical community.

In contrast to what we would call "molten salts", a term that is always associated with high melting points and a quite corrosive medium, ILs are low-melting, quite unreactive, non-corrosive, and therefore suitable as reaction media (i.e., solvents).

The classification of ILs can, of course, be based on any of their physicochemical properties, such as melting point, liquidus range, viscosity, acidity/basidity, and density. These properties will be the topic of the next section. In practical terms, the classification of ILs is normally based on their chemical structure, i.e., on the composition of their cations in combination with their anions.

Most ILs consist of a cation that bears a quarternary ammonium or phosphonium centre (Scheme 1), although systems based on arsonium, antimonium, sulfonium, etc. have also been described. This quarternary centre is normally substituted in an unsymmetric fashion, i.e., at least one of the substituents differs from all the others. This reduction of symmetry is necessary to prevent the salt from crystallising easily, widening the liquidus



Scheme 1 Commonly used cations and anions that combine to form ionic liquids

range. In the case of simple ammonium and phosphonium salts, for example, this can be achieved by having three identical and one different substituent on the quarternary centre. Nowadays, even more common are cations based on unsymmetrically substituted imidazolium, pyridinium or pyrrolidinium moieties.

Virtually every imaginable anion can be used as the counterion—every one of these showing various advantages and disadvantages. In the beginning of IL solvent chemistry, mixed anions of the chloroaluminate type, i.e., mixtures of Cl^- and $AlCl_3$, were very common, but since their properties change with composition [8, 9] and since they are not stable towards hydrolysis, these are only of limited use for transition metal catalysis and therefore beyond the scope of this review. Among the most common anions that are covered here are the halides, triflate, PF_6^-, BF_4^-, and Tf_2N^- (sometimes also called bistriflamide or bis(trifluoromethylsulfonyl)imide (BTA).[1]

Since the names of commonly used ILs can be quite long and very unhandy, a shortened nomenclature has become widely accepted in the IL community. Thus, 1-ethyl-3-methylimidazolium bromide becomes [emim]Br, 1-decyl-3-methylimidazolium tetrafluoroborate becomes $[C_{10}mim]BF_4$, 1-butyl-4-methylpyridinium bis-(trifluromethylsulfonyl)amide becomes [bmpy] Tf_2N or [bmpy]BTA and so on. If unsure, please refer to the list of abbreviations at the beginning of this review.

4
Properties of Ionic Liquids

4.1
General Properties

The most prominent property of all ILs is the fact that they do not have any measurable vapour pressure—obviously so, since they are salts and therefore are completely composed of cations and anions. (Recently, various reports of distillable ILs have appeared in the literature, e.g., [17]. At the present state, I leave it to the reader to make up his or her own mind about this topic.) This fact gives rise to one of the major advantages of using ILs in synthesis and their label of being "green": no vapour pressure means no volatile solvent and no toxic solvent vapours. Additionally, the product of a reaction run in an IL can be obtained by simply distilling it off the solvent while the catalyst stays "immobilised" in the ionic phase—the same holds

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[1] There is an ongoing disagreement in the chemical literature about the question whether the Tf_2N^- anion is to be called an imide or an amide. From an inorganic point of view (and this anion is surely inorganic), salts of the general formula M^+NR_2 are amides, $M_2{}^+NR$ salts are imides and $M_3{}^+N$ salts are nitrides. It seems therefore quite obvious to the author that Tf_2N^- has got to be bis(trifluoromethylsulfonyl)amide