A Mini-Review on Greenness of Ionic Liquids

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Review
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Ionic liquids (ILs) have been considered as "green solvents" in many published works. However, recent research on their eco-toxicity and degradability has proven that some ILs are not as "green" as expected. In this review, the greenness of ILs was discussed in terms of their synthesis, eco-toxicity and degradability and their applications. Greenness of ILs depends not only on themselves but also on their synthesis and specific applications. For a chemical process where the IL is employed, its greenness should be assessed using the life cycle analysis method and compared with other alternative processes. The green process is much more important than the IL itself with respect to green chemistry, and more research should be made to improve the greenness of process employing ILs.

Key words:
Ionic liquid, green solvent, green process

Introduction

Ionic liquids (ILs) are room temperature fluids composed entirely of ions, typically large organic cations and small inorganic anions. Interests in ILs have steadily grown in recent years because their non-detectable vapor pressures and unique solvent properties provide the possibility for clean manufacturing in chemical industry.[1–3] Novel applications of ILs appear regularly in various publications and patents, such as catalytic synthesis,[4–7] separation,[8–11] polymerization,[12] nanotechnology,[13] bio-catalysis,[14–15] composite preparation[16] and renewable resource utilization.[17–19] To date, there have been over a dozen commercial applications[20] since BASF's first successful use of the IL in 2003.[21] Research on ILs has become one of the most active areas in green chemistry[1–20] and in some literature,[1–19,21–24] the ILs have been considered as green solvents, which are superior to the conventional molecular solvents in the context of greenness. The reason behind that consideration is that ILs have non-detectable vapor pressures and do not emit volatile organic compounds to pollute air.[25] However, in most cases, some conventional volatile organic solvents are used to synthesize and recover ILs.[26] To some extent, air pollution is transferred to synthesis and recovery of ILs. Even if applications of ILs indeed helps to reduce air pollution, it is possible to release them into environment by accidental spills or effluents, which might cause water or soil pollution, and especially cause aquatic contamination.[27–29] Recent research on their eco-toxicity and degradability has shown that some ILs are not as eco-friendly as we expected.[27–29] Therefore, the greenness of ILs should be assessed for their specific applications on entire basis including their synthesis and recovery using the life cycle analysis method.[30] Life cycle analysis is a useful tool to systematically study the broad environmental implications of ILs according to their resource use, emissions and impacts throughout their life cycle.[30–34] Zhang *et al.*[34] systematically analyzed the greenness of the use of [Bmim]BF_4 for the production of cyclohexane and in a Diels-Alder reaction employing the life cycle analysis method. It is noteworthy that greenness for a specific process is a relative concept and application of ILs provides a potential alternative for green process, but greenness for a specific process depends on its environmental impact, and use of ILs cannot guarantee a green process. In this paper, the greenness of ILs is discussed in terms of their synthesis, eco-toxicity and degradability, and their application. Emphasis was put on how to make full use of ILs for green chemistry with a balanced view on ILs themselves and their applications.

Synthesis of ILs

Extensive literature [26,35,36] deals with synthesis of ILs and many new ILs are synthesized almost

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every-day. More and more functionalized ILs are prepared for their specific applications.[37–39] However, little attention has been taken for their green syntheses, especially for preparation of some functionalized ILs.[35] In fact, synthesis of ILs, like preparation of other chemicals can cause severe environmental pollution. Even for the most widely used imidazolium-based ILs, their synthesis causes air and water pollution because the volatile organic solvents are used and wastewater is formed.[26] Take the synthesis of [Bmim]BF_4 for example,[26] its typical production process requires three steps: 1) synthesis of 1-methylimidazole, 2) synthesis of [Bmim]Cl from 1-methylimidazole and butyl chloride, 3) synthesis of [Bmim]BF_4 by replacing the anion Cl^- in [Bmim]Cl with BF_4^-. During the preparation of [Bmim]BF_4, volatile organic compounds such as CH_3NH_2, CH_3OH, HCHO, CHOCHO, NH_3, acetone, toluene, ethyl acetate, methylene chloride, *n*-butanol and cholorobutane are used as reactants or solvents. Apart from the above-mentioned organic materials, HF, HCl, H_2SO_4 and NaOH are also used as reactants. Obviously, synthesis of [Bmim]BF_4 will inevitably lead to air and water pollution and is not a green process. Moreover, it will also consume large amounts of energy. Compared with preparation of most conventional molecular solvents, synthesis of [Bmim]BF_4 is more complicated and has a more adverse environmental impact.[34] Because most ILs are prepared with a series of reaction and purification steps employing various volatile organic compounds as described for [Bmim]BF_4, it is often that synthesis of ILs has a more severe environmental impact than preparation of conventional molecular solvents.[34] Especially in preparation of some functionalized ILs, the synthesis procedures are rather complicated to induce the functionalized group into the ILs and even in some special cases, the toxic chemicals, which have severe impact on the environment and human health, are used.[26] For example, the highly toxic $NaCo(CO)_4$ and $Ag[N(CN)_2]$ are used for preparation of [Bmim]$Co(CO)_4$ and [Emim]$[N(CN)_2]$ respectively.[26] In contrast to preparation of most conventional molecular solvents, synthesis of ILs is not a completely green process and has higher environmental impact.[34] To some extent, greenness for applications of ILs is achieved by transferring process pollution into their synthesis. Therefore, more effort should be made to improve synthesis of ILs in an environmentally friendly way. It is encouraging that some progress in this respect has been made in recent years. Varma and Namboodiri[40] synthesized the imidazolium-based ILs, for example, [Bmim]Br and [Bmim]BF_4 in a microwave oven without any solvents. Handy *et al.*[41] and Tao *et al.*[42] synthesized such ILs as $[HOCH_2Bmim]X$, $[(H_2N)RN(COOH)]X$ and $[(H_2N)R_1N(COOR_2)]X$ using renewable feedstock as starting material (fructose and amino acid respectively). Despite this useful research, lot of work is yet required for the green synthesis of ILs. For a green chemist, it is essential to reduce or eliminate the use and generation of hazardous substances for preparation of ILs by simplifying their synthesis procedures, using renewable raw materials and improving their atom efficiency. Green synthesis of ILs is as important as the improvement of their properties, and preparation of functionalized ILs.

Toxicity and degradability of ILs

Greenness of ILs themselves depends on two aspects: possible leakage into the environment and their bioaccumulation, toxicity and degradability.[29] Their non-detectable vapor pressures prevent emitting volatile organic compounds into air and pollute atmosphere. This is the essential reason that ILs have been considered as “green solvents” for ideal replacement of the conventional volatile organic solvents in many published works.[1–19] However, ILs can be released into the environment in other ways, such as accidental spills or effluents.[27–29] Therefore, although ILs can reduce air pollution, it is possible to cause water and soil pollution, which depends on their bioaccumulation, toxicity and degradability.[27–29] Because most ILs can dissolve in water and they have similar diffusion coefficient with the conventional organic solvents and inorganic salts, they can cause water contamination as commonly-used chemicals.[26,35] Moreover, the decomposition of ILs like [Bmim]BF_4 and [Bmim]PF_6 in the presence of water can also lead to severe water pollution when they enter the environment due to the formation of hydrofluoric and phosphoric acid.[29] Domanska *et al.*[43] and Ropel *et al.*[44] reported the octanol-water partition coefficients of some organic solvents and ILs, their results showed that some ILs, for example, [Omim]Tf_2N, [Emmim]Tf_2N and [Hmmim]Tf_2N had relatively high octanol-water partition coefficients, which indicates these ILs probably can accumulate in organisms. In recent years, the toxicity and degradability of ILs have drawn much attention and there are many reports on their toxicity to microorganisms,[45–47] cells and animals,[48–51] especially to aquatic ecosystems[27,52–55] and on their degradability.[29,35,56,57] Docherty and Kulpa[45] investigated the toxicity of imidazolium and pyridinium-based ILs to *V. fischeri* using the Microtox method. They found the toxicity of ILs rose with the increasing alkyl chain length on their cations and the octyl- and hexyl- substituted ILs were more toxic than commonly used molecular solvents such as toluene, benzene and phenol. Bornscheuer and Ganske[46] reported that [Bmim]BF_4 and [Bmim]PF_6 had similar inhibitory effects on the growth of *E. coli, P. pastoris* and *B. cereus* with dimethylsulfoxide. Matsumoto *et al.*[47] found that imidazolium-based ILs had a negative effect on the production of lactic acid by *Lactobacillus*. Ranke *et al.*[48] studied the toxicity of imidazolium-based ILs to the promyelocytic leukemia rat cell line and the rat glioma cell line. They found their toxicity was mainly determined by their cation constituents. The increased alkyl chain length led to their higher toxicity. Stepnowski *et al.[49]* investigated the toxicity of imidazolium-based ILs to Hela human tumor cell lines using WST-1 cell viability assay. They found these ILs had lower EC50 values than the commonly-used organic solvents, example.g. dichloromethane and ethanol. Swatloski *et al.*[51] studied the toxicity of [$C_x$mim]Cl to *C. elegans* and found that the longer alkyl chain imparted higher toxicity. Wells and Coombe[52] reported the results of freshwater ecotoxicity tests of some common ILs with imidazolium, ammonium, phosphonium and pyridinium cations on invertebrate *D. magna* and the green algae *P. subcapitata*. The EC50 values of the most toxic were four orders of magnitude higher than the least toxic IL. For all tested ILs, there was a relation between their toxicity and the alkyl side chain length of their cation. The increased alkyl chain length led to their higher toxicity to both organisms. Even for the least toxic IL, its toxicity was comparable with that of toluene and xylene. For the most toxic IL, its toxicity was by many magnitudes more acute than common organic solvents, such as methanol, dichloromethane, acetonitrile and *tert*-butyl methyl ester. Bernot *et al.*[53,54] tested the LC50 values of some imidazolium and pyridinium based ILs using *P. acuta* and *D. magna* as model organisms. Their results were similar with Wells and Coombe's. Although data on their toxicity are still scarce and need to be further accumulated, it is certain that ILs are as toxic as the commonly used organic solvents, that is, they are not as green as we expected.[28,29] The degradability of ILs is another problem. Some studies have indicated that ILs are difficult to biodegrade. Wells and Coombe[52] found that none of the selected ILs with imidazolium, ammonium, phosphonium and pyridinium cations showed any sign of biodegradation according to the measured BOD_5 values. Garcia *et al.*[56] tested the biodegradation of [Bmim]PF_6 using a closed bottle test, in which no biodegradation was observed. Stepnowski *et al.*[57] explored the relationship between the structure of imidazolium based ILs and their photo-chemical degradability. Their results demonstrated that the ILs with longer alkyl chains were difficult in photo-chemical degradation. In general, most ILs are more difficult in degradation than commonly used organic solvents. Hence, more effort should be made to seek out low-toxic and degradable ILs.[29,35] In principle, this can be realized using the structure-bioaccumulation, toxicity and degradability relationship strategy. Some progress has been made in increasing their degradability and reducing their toxicity by adjusting their structure and using non-toxic or renewable materials in their synthesis.[58–60] Gathergood *et al.*[59] used the concept of biodegradable surfactants and developed a series of biodegradable improved imidazolium-based ILs incorporating ester and amide groups. Vidis *et al.*[60] created the environmentally and toxicologically benign ILs using nontoxic precursors such as saccharin and acesulfame.

Applications of ILs

The growing worldwide academic and commercial interests in ILs come from their potential applications[1–19] such as catalysis with increased rates and yields,[4–7] less complex and more energy-efficient separations,[8–11] and solvents that may reduce environmental impacts for commercial processes.[20,21] In most cases, these applications are described as greener than traditional processes.[1–19] The reason is that there is no air pollution, while the ILs can be recovered in these applications. It seems true if only the application phase of ILs is examined. Take the synthesis of norfloxacin ethyl ester in [Bmim]PF_6 for example.[61] Norfloxacin ethyl ester is an important intermediate for preparation of norfloxacin, which is widely used for the clinical treatment of certain infections caused by bacteria, such as gonorrhea, prostate, and urinary tract infections. It is prepared by condensation with EMME [ethoxymethylenemalonic diethyl ester], cyclization, ethylation and condensation with anhydrous piperazine. During its conventional preparation, these four reaction steps are carried out separately and large amounts of volatile organic solvents, for example, high-temperature oils, dimethyl formamide and toluene are used in these reactions. In our laboratory, these reactions are conducted in a one-pot process by using [Bmim]PF_6 as reaction medium. The [Bmim]PF_6 can be recovered and reused 5 times. This process has simplified the preparation procedures of norfloxacin ethyl ester, increased the norfloxacin overall yield from 66.3 % to 72.7 %, and eliminated the use of volatile organic solvents. It is obvious that the process using [Bmim]PF_6 as reaction medium is superior to the conventional one if the environmental impact for preparation and recovery of [Bmim]PF_6 is ignored. However, synthesis of [Bmim]PF_6 and its recovery are not green because volatile organic solvents are used in these processes. Therefore, the greenness of preparing norfloxation ethyl ester using $[Bmim]PF_6$ as reaction medium should be assessed on an entire basis including $[Bmim]PF_6$ synthesis and its recovery using the life cycle analysis method. The life cycle analysis results indicate that the process using $[Bmim]PF_6$ has longer life cycle environmental impact than the conventional process. Zhang *et al.*[34] systematically analyzed the greenness of using $[Bmim]BF_4$ for the production of cyclohexane and in a Diels-Alder reaction employing the life cycle analysis method. These examples all demonstrate that it is possible to shift the adverse environmental impact of the ILs application phase to their synthesis and recovery phase. In most cases, the recovery of ILs is an arduous effort. Numerous recovery approaches, such as evaporation, salting-out, membrane separation and ionic exchange, have been reported in literature,[1–3,62,63] but only few can be commercially scaled up. It is often that water and volatile organic solvents are used to purify the recovered ILs. After purifying the recovered ILs, whether they can be reused is still problematic. Even if the recovered ILs can be reused, the recovery and purification process can also cause environmental pollution. Therefore, greenness of IL applications depends on their synthesis, toxicity and degradation as well as their specific applications. As discussed above, application of ILs is not an absolutely green process, whose greenness is a relative concept and needs to be evaluated using the life cycle assessment method. It is noteworthy that ILs are not always superior to the conventional molecular solvents from a green chemistry perspective. To improve the process greenness using ILs, their efficient green recovery is essential. Some progress has been made, for example, process integration[21] and supercritical carbon dioxide extraction[64] are useful methods for green recovery of ILs. Keskin *et al.*[65] recently gave a comprehensive review on the use of supercritical carbon dioxide extraction for the recovery of ILs.

Conclusions

This mini-review deals with the greenness of ILs from their synthesis to process application and to their recovery for reuse. For most cases, synthesis of ILs always includes a series of reactions and purification steps employing volatile organic solvents. In contrast to production of commonly used organic solvents, preparation of ILs often has more severe environmental impacts. ILs themselves are not instinctively green and some recent research on their bioaccumulation, toxicity and degradability has revealed that they are not as green as we expected previously. Their non-detectable vapor pressures and unique solvent properties indeed provide the possibility for green manufacturing in chemical industry, but the recovery of ILs is always an arduous effort. For a specific process, the greenness of IL application should be evaluated using the life cycle assessment method considering the entire process: from their synthesis to process application, to their recovery for reuse. As scientists and engineers, we should hold a balanced view on ILs and their applications. In order to improve their greenness, more effort should be made in green synthesis of ILs, reducing their toxicity and increasing their degradability, developing novel applications and seeking their suitable recovery and purification approaches. ILs will become one of the most useful tools to maintain sustainable development of the chemical industry.

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