

## APPLICATION OF IONIC LIQUIDS IN ORGANIC SYNTHESIS

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Our research is aimed at development of reactive and non-reactive ionic liquids for new synthetic organic methodologies. These activities may provide more information on the understanding of mechanisms of organic reactions using ionic liquids as reaction media, which have been traditionally conducted in molecular solvents. It may also provide improved methodologies for product separations, particularly in industrial and pharmaceutical chemistry.

Conventional organic solvents are used in a range of pharmaceutical and industrial applications. Ionic liquids have been gaining growing attention from synthetic organic chemists and practitioners in chemical industries in general. Ionic liquids are defined as containing organic cations and inorganic or organic anions (non-aqueous salt-like character) but are liquid at or close to ambient temperature. An important class of non-aqueous ionic liquids belongs to the imidazolium-based salts. In contrast to conventional organic solvents that are composed of molecular entities such as DMSO, DMF, methylene chloride, ionic liquids have no significant vapor pressure. Moreover, the low solubility of organic compounds and water in some types of ionic liquids will make it possible that separation of products can be achieved using extraction and/or decantation. It should be noted that the tendency of ionic liquids to suppress conventional solvation phenomena should be dramatically different from those occurred in molecular solvents.

So far, several classes of ionic liquids have been tested as novel reaction solvents in organic synthesis and transition metal catalysis.<sup>1</sup> They have shown great potential to replace hazardous organic solvents as reaction media while maintaining similar and sometimes enhanced chemical selectivity and reactivity. However, there are a number of barriers in the realization of ionic liquids as new media/reagents. For examples, the conditions for reactions as well as the ensuing separation of products need to be tested. The recycling and reuse of ionic liquids also need to be addressed.

Our research interests in the area of ionic liquids focus on the utilization of various ionic liquids as the sources of reaction media and reagents for organic reactions. We have devised a method for one-pot synthesis of water-immiscible ionic liquids, such as 1-*n*-butyl-3-*n*-butylimidazolium hexafluorophosphate (bbiPF<sub>6</sub>)<sup>2</sup> (Scheme 1).

We have demonstrated that halide-based ionic liquids ILX (IL represents cations such as 1,3-dialkyl-imidazolium, 1-alkylpyridinium and tetraalkyl-ammonium; X represents halide anions) can be used as reagents in nucleophilic substitution for the conversion of alcohols to alkyl halides. This reaction provides an alternative way of preparing other types of ionic liquids (ILA) based on the conjugate bases of acids (HA) used<sup>3</sup> (Scheme 2).

These halide-based ionic liquids (ILX) can also be used as reaction media for copper-catalyzed nucleophilic aromatic substitution reaction for formation of aryl nitriles (ArCN)<sup>4</sup> (Scheme 3).

We are currently working on the development of trihalide-based ionic liquids (ILX<sub>3</sub>) that can be used as reagents as well as reaction media in halogenation reactions<sup>5</sup> (Scheme 4).

*Scheme 1: One-pot synthesis of ionic liquids:*

*Scheme 2: Non-metathetic synthesis of ionic liquids:*



ILX: halide-based ionic liquids, X=Cl, Br, I.

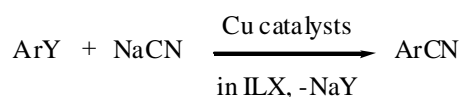
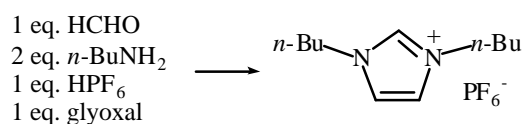
HA: acids.

ROH: alcohols.

ILA: new ionic liquids with conjugate bases of HA.

*Scheme 3: Rosenmund-von Braun Reaction:*

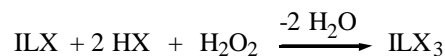
*Scheme 4: Synthesis of trihalide ionic liquids:*



ArY: Aryl halides, Y=I or Br.

ILX: halide-based ionic liquids, X=Cl, Br, I.

Cu catalysts: CuX, X=Cl, Br, I, CN.



ILX: halide-based ionic liquids, X=Cl, Br, I.

HX: hydrogen halides.

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