Abstract

As part of an ongoing program in the area of green chemistry, we have considered the synthesis of room temperature ionic liquids and their application as reaction medium in organic transformations. The efforts and contribution towards the preparation and application of ionic liquids have been summarized in the form of this thesis. The thesis entitled “Synthesis of ionic liquids: Application to Wittig, reduction and aromatic nucleophilic substitution reactions” is divided into five chapters.

CHAPTER-I: Introduction to ionic liquids

This chapter deals with the 12 principles of green chemistry, ‘E’ factor, atom efficiency, possible alternative solvents and their applications, ionic liquids, and a few examples on the application of RTILs in organic synthesis.

CHAPTER-II: Synthesis and characterization of citronellal based chiral ionic liquids

Chapter 2 deals with the preparation and characterization of a series of chiral ionic liquids starting from the chiral pool citronnellal. Several new chiral ionic liquids were prepared starting from both the isomers of citronellal with dialkyl amine as the amine source. The Schiff base, thus obtained, was reduced and further reacted with alkyl halides to give ionic liquids. The strategy could be
generalized with several dialkyl amines to design chiral ionic liquids.

\[
\begin{align*}
(S)-19a-e & \quad (S)-18 \quad (S)-20a-e \\
(R)-19a-e & \quad (R)-18 \quad (R)-20a-e
\end{align*}
\]

Figure: 2.1 Retrosynthesis of Citronellal-based chiral ionic liquids.

Most of the ionic liquids prepared in this series were found to be liquids at room temperature.

CHAPTER-III: Application of ionic liquids in the Wittig reaction and synthesis of lacidipine using ionic liquids

Chapter 3 deals with the application of ionic liquids in the Wittig reaction. The generality of the methodology has been demonstrated with various substituted benzaldehydes and ylides. The Wittig reaction is observed to proceed faster in ionic liquid (C) as compared to traditional organic solvents.
Scheme: 3.8 Recovery and reusability of pyrrolidine-based ionic liquid (30).

Chart-3.1: Structures of ionic liquids A, B and C.

The recovery and reusability of ionic liquids in chemical transformations have been studied in details. A practical application of the methodology is demonstrated towards the synthesis of biologically active molecules, lacidipine, a calcium channel blocker.

Scheme: 3.9 Synthetic pathway of lacidipine.

CHAPTER-IV: Reduction of aryl ketones in ionic liquids

This chapter describes the study of metal hydride reduction of ketones, particularly substituted acetophenones, using ionic liquids
as reaction media. The representative acetophenones chosen for the study contain aromatic ring with electron releasing, electron withdrawing and neutral substituents.

Reaction of substituted acetophenones with sodium borohydride in both the selected ionic liquids ‘A’ and ‘B’ is found to give the corresponding benzylic alcohols in high yield as compared to the reactions using methanol as solvent.

![Scheme: 4.8 Synthetic pathway of reduction of substituted acetophenones.](image)

The recovery and reusability of ionic liquids in chemical transformations have been studied with p-chloroacetophenone using ionic liquid (C).

**CHAPTER-V: Green chemistry approach to aromatic nucleophilic substitution reactions: Formal synthesis of linezolid**

This chapter describes the application of ionic liquids in aromatic nucleophilic substitution reactions. The nucleophilic substitution study was taken up with morpholine on a variety of halogen substituted mono and dinitrobenzenes in trihexyl(tetradecyl)phosphonium tris (pentafluoroethyl)
trifluorophosphate ionic liquid (A & C) as the reaction medium, and found to be faster in ionic liquids.

Scheme: 5.4 Aromatic substitution reactions in ionic liquid.

In order to demonstrate the significance of aromatic nucleophilic substitution reaction in ionic liquids, we demonstrated a short and practical enantioselective synthesis of linezolid (2).

Scheme: 5.5 Synthetic pathway of linezolid.