SYNTHESIS AND CHARACTERIZATION OF 1,2-DIMETHYL IMIDAZOLIUM IONIC LIQUIDS AND THEIR CATALYTIC ACTIVITIES

Pandurangan Ganapathi and Kilivelu Ganesan
PG and Research Department of Chemistry, Presidency College (Autonomous), Chennai, India

GRAPHICAL ABSTRACT

Abstract The synthesis of substituted imidazolium-type ionic liquids via a simple method is described. Our synthesized ionic liquids are more useful in the catalytic behavior of the Mannich reaction.

Keywords Ionic liquids; Mannich reaction; metathesis; recyclable

INTRODUCTION

Salts in their liquid state at room temperature are called room-temperature ionic liquids (RTILs); they have a variety of applications including as energy storage devices[1] and solvents for nanoparticle stabilization[2] and electrode position.[3] By combining a larger organic segment with charge diffuse anion[4] it is possible to prepare ILs at room temperature. ILs are safer than other solvents because of nontoxic ions and insignificant vapor pressure. The significant properties of ILs are heat capacity and viscosity, which are easily controllable by selection of cation and anion segments.[5] An equal molar ratio of H2SO4 and IL is used as an effective chlorinating agent,[6] compared with powerful, environmentally damaging solvents and more toxic chlorinating reagents such as COCl2, PCl3, and SOCl2.[7] ILs act as product controllers to improve the stereoselectivity for the Diels–Alder reaction.[8,9] Some ILs act as
both solvent and catalyst for the Friedel–Craft reaction with effective response.\textsuperscript{[10,11]} Essawy and coworkers reported that Michael adducts of \( \alpha \)-phenyl chalcone with various ketones show a variety of medicinal activities.\textsuperscript{[12]} ILs are more suitable solvents for oxidation reactions because of their stability even under oxidizing conditions and their inertness.\textsuperscript{[13–19]} Most of the ILs have dual functions,\textsuperscript{[20]} and some of the imidazolium salts act as mild antioxidative and reducing species.\textsuperscript{[21]} The solubility property of ILs with hydrophobic (or) hydrophilic solvent can be tuned by altering the cations and anions.\textsuperscript{[22–24]} Ionic liquids act as electrolytes with a number of advantages when compared to conventional materials because of their high ionic conductivity and nonvolatile nature.\textsuperscript{[25–27]} Room-temperature ionic liquids are considered as environmentally friendly solvents for industrial actinide extraction.\textsuperscript{[28]} Convenient synthesis of bulky groups containing imidazolium/pyridinium types of ionic liquids has been reported.\textsuperscript{[29]} Herein, we report the synthesis and catalytic activity of the dimethyl imidazolium type of ionic liquids.

RESULTS AND DISCUSSION

1,2-Dimethylimidazole (1.0 equiv; 1.04 \( \times \) \( 10^{-2} \)) is treated with benzylbromide/4-nitrobenzylbromide (1.05 equiv; 1.092 \( \times \) \( 10^{-2} \)) in the presence of dry CH\(_3\)CN under refluxing conditions for 2 to 2.5 h to give \( 1a,b \) in 95–97\% yield. After \( N \)-alkylation, the anion exchange reaction is carried out with various inorganic salts in the presence of a minimum amount of deionized water, which is used as a solvent, for about 1 h to give anion-exchanged products.

The anion-exchanged product undergoes Soxhlet extraction in the presence of dry tetrahydrofuran (THF) for about 1 h to remove the metal bromide to give a pure form of imidazolium salts (\( 2a-f \)) in 90–93\% yield. The reaction between 1,2-dimethylimidazole with 4-nitrobenzylbromide is much faster than with benzyl bromide due to the nitro benzyl C-Br bond, which is weaker than simple benzyl bromide. The same reaction is repeated with dimethylsulfoxide (DMSO) and we observed that the reaction is much faster than with CH\(_3\)CN, but workup is not easier due to the water-soluble nature of both solvent and imidazolium bromide, and therefore CH\(_3\)CN is the more suitable solvent for \( N \)-alkylation.

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\begin{align*}
\text{NCH}_3 + \text{R-} \text{Br} & \xrightarrow{i)} \text{NCH}_3 \text{Br} \quad 95-97\% \\
1a: & \text{R} = \text{H}; \quad 1b: \text{R} = \text{NO}_2 \\
& \text{CH}_3 \\
\text{NCH}_3 (1a,b) & \xrightarrow{ii)} \text{NCH}_3 (2a-f) \\
2a: & \text{R} = \text{H}; \quad \text{X} = \text{BF}_4 \\
2b: & \text{R} = \text{H}; \quad \text{X} = \text{PF}_6 \\
2c: & \text{R} = \text{H}; \quad \text{X} = \text{CF}_3\text{SO}_3 \\
2d: & \text{R} = \text{NO}_2; \quad \text{X} = \text{BF}_4 \\
2e: & \text{R} = \text{NO}_2; \quad \text{X} = \text{PF}_6 \\
2f: & \text{R} = \text{NO}_2; \quad \text{X} = \text{CF}_3\text{SO}_3
\end{align*}
\]

\textit{Reagent and conditions:} i) MeCN, reflux, 2 - 2.5 hr.; ii) MX / H\(_2\)O; 1 hr.

\textbf{Scheme 1.} Synthesis of substituted imidazolium type of ionic liquids.
CATALYTIC ACTIVITIES

One-pot multicomponent organic reactions are gaining more importance because of greater diversity and efficiency.\textsuperscript{[30]} Mannich product (substituted oxazine) has more features in the area of biologically important natural residues.\textsuperscript{[31,32]} Some of the substituted oxazine and its derivatives are reported in the literature.\textsuperscript{[33–35]} Multicomponent preparation of some of the naphthol heterocyclic substituted compounds in the presence of ionic liquids needs more reaction time to complete with insignificant yield.\textsuperscript{[36]} Deepak and coworkers reported that a one-pot, three-component condensation reaction of aldehyde, ketone, and aromatic amine in the presence of mixed oxides MgO/ZrO\textsubscript{2} in the ratio of 1:3 needs 16 h to complete, with poor yield.\textsuperscript{[37]} Our synthesized ionic liquids for the Mannich reaction afforded appreciable products (Tables 1 and 2). We have tried with different concentrations of ionic liquids such as 7.299 × 10\textsuperscript{−5}, 1.497 × 10\textsuperscript{−4}, 2.245 × 10\textsuperscript{−4}, and 2.994 × 10\textsuperscript{−4} concentrations. Among these concentrations, we have observed that 2.245 × 10\textsuperscript{−4} concentration is the optimum concentration to complete the reaction with less reaction time and greater conversion. In the Mannich reaction, we have used two types of aromatic amines (\textit{m}/\textit{p}-nitro aniline). From that we observed that \textit{m}-nitro aniline is two times faster than \textit{p}-nitro aniline with greater yields (Table 1). \textit{m}-Nitroaniline shows better nucleophilic activity than the \textit{para} isomer. Mannich products are thoroughly characterized by spectral and analytical data, which are closely matching with the literature.\textsuperscript{[38]}

Table 1. One-pot synthesis of \textit{m}-nitrooxazine derivatives

| No. | IL                          | Time   | Yield (%) |
|-----|-----------------------------|--------|-----------|
| 1   | Absence of catalyst         | 8 h    | 40        |
| 2   | 1a                          | 1.5 min| 90        |
| 3   | 2a                          | 1.5 min| 85        |
| 4   | 2b                          | 1.5 min| 90        |
| 5   | 2c                          | 1.5 min| 88        |
| 6   | 1b                          | 1.5 min| 87        |
| 7   | 2d                          | 1.5 min| 80        |
| 8   | 2e                          | 1.5 min| 87        |
| 9   | 2f                          | 1.5 min| 84        |

Notes. Reagents and conditions: \textit{z}-naphthol (200 mg; 1.387 × 10\textsuperscript{−3} mol/L); paraformaldehyde (85 mg; 2.843 × 10\textsuperscript{−3} mol/L); \textit{m}-nitroaniline (0.148 g; 1.387 × 10\textsuperscript{−3} mol/L); CH\textsubscript{3}CN (10 mL); IL (2.245 × 10\textsuperscript{−4} mol/L); rt.
Our synthesized ionic liquids are potential candidates to accelerate the Mannich reaction with better yield. Our synthesized ionic liquids are recycled up to four cycles and used for the Mannich reaction with the same reaction condition. Even after the fourth recycle, the product obtained was same as we observed in the fresh use shown in Table 3.

**CONCLUSION**

We used a simple synthetic methodology to prepare the imidazolium type of ionic liquids. Our synthesized ionic liquids are more useful for catalytic behavior in the Mannich reaction to reduce the reaction time and improve the percentage of yield. We examined the catalytic activity of synthesized ionic liquids. Among the eight ionic liquids, 1a and 1b showed better catalytic activity than the others because of better Lewis character. We have tried the catalytic activities with different concentrations (7.299 x 10^{-5} mol/L, 1.497 x 10^{-4} mol/L, 2.245 x 10^{-4} mol/L, and 2.994 x 10^{-4} mol/L) of our synthesized ionic liquids. From the result, we have concluded that 2.245 x 10^{-4} concentration is the optimum concentration to complete the Mannich reaction with greater yield and lesser reaction time. The same reaction is repeated with our recycled ILs, which showed good catalytic activity with good yields.

| No. | IL   | Time | Yield (%) |
|-----|------|------|-----------|
| 1   | Absence of catalyst | 10 h | 30        |
| 2   | 1a   | 2 min| 82        |
| 3   | 2a   | 2 min| 78        |
| 4   | 2b   | 2 min| 81        |
| 5   | 2c   | 2 min| 81        |
| 6   | 1b   | 2 min| 77        |
| 7   | 2d   | 2 min| 72        |
| 8   | 2e   | 2 min| 75        |
| 9   | 2f   | 2 min| 75        |

Notes. Reagents and conditions: x-naphthol (200 mg; 1.387 x 10^{-3} mol/L); paraformaldehyde (85 mg; 2.843 x 10^{-3} mol/L); p-nitroaniline (0.148 g; 1.387 x 10^{-3} mol/L); CH_3CN (10 mL); IL (2.245 x 10^{-4} mol/L); rt.

### Table 2. One-pot synthesis of p-nitrooxazine derivatives

| No. | IL   | Time | Yield (%) |
|-----|------|------|-----------|
| 1   | Absence of catalyst | 10 h | 30        |
| 2   | 1a   | 2 min| 82        |
| 3   | 2a   | 2 min| 78        |
| 4   | 2b   | 2 min| 81        |
| 5   | 2c   | 2 min| 81        |
| 6   | 1b   | 2 min| 77        |
| 7   | 2d   | 2 min| 72        |
| 8   | 2e   | 2 min| 75        |
| 9   | 2f   | 2 min| 75        |

**Table 3. One-pot synthesis of oxazine by using recycled ILs, fourth run**

| No. | IL | Yield (%) |
|-----|----|-----------|
| 1   | 1a | 72-85     |
| 2   | 2a | 70-80     |
| 3   | 2b | 74-82     |
| 4   | 2c | 70-75     |
| 5   | 1b | 70-76     |
| 6   | 2d | 66-70     |
| 7   | 2e | 68-73     |
| 8   | 2f | 65-70     |
EXPERIMENTAL

Procedure for N-Alkylation

1,2-Dimethylimidazole (1.040 × 10⁻² mol/L; 1.0 equiv) is treated with benzylbromide (1.092 × 10⁻² mol/L; 1.05 equiv) in the presence of 30 mL of dry CH₃CN under refluxing condition for about 2 h, and afforded the N-alkylated quaternary ammonium bromide 1a in 95% yield after purification.

1,2-Dimethyl(3-methylene benzene)-imidazolium Bromide 1a

Yield 2.75 g; 95% semisolid; ¹H NMR (D₂O): δ: 2.45 (s, 3H); 3.66 (s, 3H); 5.22 (s, 2H); 7.20 (d, J=1.8 Hz, 2H); 7.24 (s, 2H); 7.33 (t, J=7.2 Hz, 2H). ¹³C NMR δ: 9.19, 34.75, 51.42, 121.10, 122.37, 127.76, 129.26, 133.73, 144.58. MS: 267. Elemental analysis: Molecular formula (C₁₂H₁₅N₂Br); calculated: C: 53.93; H: 5.61; N: 10.48; found C: 53.86; H: 5.52; N: 10.40.

Procedure for Anion Exchange Reaction

N-Alkylated quaternary ammonium bromide (1.0 equiv) is treated with NaBF₄ (1.05 equiv) in the presence of 10 mL deionized water at room temperature with stirring for about 1 h to afford the anion exchanged ionic liquid. After the anion exchange reaction, we used Soxhlet extraction for separation using dry tetrahydrofuran (THF) for about 1 h followed by concentration, which gives ionic liquid 2a in 93% yield.

1,2-Dimethyl(3-methylene benzene)-imidazolium Tetrafluoroborate 2a

Yield 0.67 g; 93%; semisolid; ¹H NMR (D₂O): δ: 2.43 (s, 3H); 3.68 (s, 3H); 5.26 (s, 2H); 7.18 (d, J=1.9 Hz, 2H); 7.21 (s, 2H); 7.4 (t, J=7.4 Hz, 3H). ¹³C NMR δ: 9.17, 34.78, 51.44, 121.08, 122.35, 127.74, 129.27, 133.71, 144.55. MS: 274. Elemental analysis: Molecular formula (C₁₂H₁₅BF₄N₂); calculated: C, 52.55; H, 5.47; N, 10.22; found C, 52.48; H, 5.32; N, 10.14.

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SUPPLEMENTAL MATERIAL

Experimental procedure and ¹H and C¹³ NMR spectra of new compounds for this article can be accessed on the publisher’s website.

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