An Efficient Synthesis of Pyrrolidinone Derivatives in the Presence of 1,1'-Butylenebis(3-sulfo-3H-imidazol-1-ium) Chloride

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The catalytic efficiency of 1,1'-butylenebis(3-sulfo-3H-imidazol-1-ium) chloride as a sulfonic acid-functionalized ionic liquid was demonstrated for the synthesis of pyrrolidinone derivatives under mild conditions. The electronic effect of substituents on aniline derivatives was investigated. Further, a study on the structure-activity relationship of ionic liquids containing sulfonic groups for the synthesis of ethyl-2-(4-chlorophenyl)-4-hydroxy-5-oxo-1-(p-tolyl)-2,5-dihydro-1H-pyrrrole-3-carboxylate was performed under optimal conditions. The results showed that the catalytic properties of ionic liquids containing two sulfonic or imidazole moieties with carbon spacers was superior to ionic liquids having one sulfonic or imidazole moiety with no carbon spacer.

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Introduction

Ionic liquids (ILs) have become alternative solvents, catalysts, and extracting agents owing to environmental considerations including low vapour pressure, thermal and chemical stability, high ionic conductivity, tunable polarity, and potential reusability. 1-3 Immiscibility of ILs with some organic solvents is another valuable property for organic synthesis. This property allows the simple separation of the desired products and catalysts in different phases, which avoids tedious and expensive work-up procedures along with the consumption of high volumes of toxic and volatile organic solvents. 4-5

2-Pyrrolidinones are found in many pharmaceuticals and in active natural products. They have achieved much attention owing to their wide spectrum of biological and pharmacological activities and their applications in medicinal chemistry and drug designing. 6-14 Therefore, a variety of synthetic protocols have been reported for the preparation of substituted pyrrolidinones. 15-23

The ILs containing the SO3H functional group on the imidazole ring are well known to exhibit catalytic activity for multicomponent reactions. 24-28 Very recently, 1,1'-butylenebis(3-sulfo-3H-imidazol-1-ium) chloride ([BBSI]Cl) was synthesized and its dual solvent-catalytic activity was studied for the synthesis of xanthenes under mild conditions. 29 Herein, we describe the synthesis of 2-pyrrolidinone derivatives in the presence of [BBSI]Cl as an efficient catalyst under mild conditions. Also, in continuing our investigation on the influence of IL structure on catalytic efficiency, 30 the cation effect of some mono- and di-cationic ionic liquids was investigated for the synthesis of ethyl-2-(4-chlorophenyl)-4-hydroxy-5-oxo-1-(p-tolyl)-2,5-dihydro-1H-pyrrrole-3-carboxylate (21).

Results and Discussion

Synthesis of Pyrrolidine Derivatives in the Presence of [BBSI]Cl

Initially, the reaction of 4-chlorobenzaldehyde (1a), aniline, and diethyl acetylenedicarboxylate as the model reaction was studied in the absence of catalyst and solvent at room temperature. The model reactions were carried out using a planetary ball mill to afford the desired product in trace yield after 4 h at room temperature, confirming the need for solvent and/or catalyst for this reaction (Table 1, entry 1). Then, the model reaction was performed in green solvents such as H2O and C2H5OH in the absence of a catalyst at room temperature for 4 h, which afforded 2a in 20 and 26% yield respectively (Table 1, entries 2 and 3). A higher yield was observed in ethanol because the model reactants were considerably more soluble in ethanol than in water. 2a was obtained in 79% yield when 0.5 mol-% of [BBSI]Cl was added to the model reactants in ethanol and the mixture was stirred for 1 h at room temperature (Table 1, entry 4). A significant