

Room temperature ionic liquid promoted improved and rapid synthesis of 2,4,5-triaryl imidazoles from aryl aldehydes and 1,2-diketones or α -hydroxyketone

Shapi A. Siddiqui, Umesh C. Narkhede, Sanjay S. Palimkar, Thomas Daniel, Rajgopal J. Lahoti and Kumar V. Srinivasan*

Division of Organic Chemistry; Technology, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411 008, India

Received 7 October 2004; revised 4 January 2005; accepted 28 January 2005

Abstract—An improved and rapid one-pot synthesis of 2,4,5-triaryl imidazoles in a room temperature ionic liquid is described, which does not need any added catalyst. Different ionic liquids based on 1-*n*-butyl and 1,3-di-*n*-butyl imidazolium salts were screened and their efficacy in terms of acidity and polarity have been correlated with yields and reaction period. The one-pot methodology resulting in excellent isolated yields in short reaction times is characterized by simple work up procedures and efficient recovery and recycling of the ionic liquid, which acts as a promoter.

© 2005 Elsevier Ltd. All rights reserved.

1. Introduction

The development of a simple, efficient and general synthetic method for widely used organic compounds from readily available reagents is one of the major challenges in organic synthesis. In 1858 Debus¹ reported the reaction between glyoxal and ammonia, a reaction that pioneered a novel synthetic route to imidazole. Over the century, the importance of imidazoles in biological system has attracted much interest due to their chemical and biochemical properties. Even today, 147 years later, research in imidazole chemistry continues unabated. Compounds with imidazole ring system have many pharmacological properties and play important roles in biochemical process.² Many of the substituted imidazoles are known as inhibitors of P38 MAP kinase,³ fungicides and herbicides,⁴ plant growth regulators⁵ and therapeutic agents.⁶ Recent advances in green chemistry and organometallic chemistry have extended the boundary of imidazoles to the synthesis and application of a large class of imidazoles as ionic liquids and imidazole related N-heterocyclic carbenes (NHC).^{7,8}

There are several methods reported in literature for the synthesis of imidazoles such as hetero-Cope rearrangement,⁹ four-component condensation of arylglyoxals,

primary amines, carboxylic acids and isocyanides on Wang resin,¹⁰ reaction of N-(2-oxo)-amides with ammonium trifluoroacetate,¹¹ 1,2-aminoalcohols in the presence of PCl_5 ,¹² diketones, aldehyde, amine and ammonium acetate in phosphoric acid,¹³ in acetic acid,¹⁴ organo catalyst in acetic acid¹⁵ as well as H_2SO_4 ,¹⁶ DMSO.¹⁷ Several micro-wave (MW) assisted syntheses of imidazoles from 1,2-diketones and aldehydes in the presence of a variety of catalysts have been recently reported. These include MW/silica-gel,¹⁸ MW/silica-gel/H-Y,¹⁹ MW/ Al_2O_3 ,²⁰ MW/acetic acid,²¹ in DMF.²² The condensation of α -hydroxy ketones with aldehydes and ammonium acetate on solid supported silica gel or alumina in the presence of MW has been reported recently.²³

Many of the synthetic protocols for imidazoles reported so far suffer from one or more disadvantages such as harsh reaction conditions, poor yields, prolonged time period, use of hazardous and often expensive acid catalysts. Moreover, the synthesis of these heterocycles have been usually carried out in polar solvents such as ethanol, methanol, acetic acid, DMF and DMSO leading to complex isolation and recovery procedures. These processes also generate waste containing catalyst and solvent, which have to be recovered, treated and disposed off.

One of the biggest problems posed to the chemical industry is to continuously deal with the fact that all chemical plants

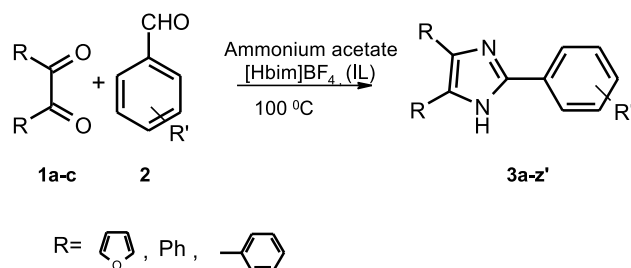
Keywords: 2,4,5-Triaryl imidazoles; Ionic liquid (IL); Ammonium acetate; Benzaldehydes; 1,2-Diketones; α -Hydroxyketone.

* Corresponding author. Tel.: +91 20 25889089; fax: +91 20 25893614; e-mail: kvsri@dalton.ncl.res.in

rely heavily on toxic, hazardous and flammable organic solvents. Organic solvents used in most of the synthetic processes in chemical industries evaporate into the atmosphere with detrimental effects on the environment as well as human health. Most of the time, these volatile organic solvents are expensive to purchase, difficult to recycle or reuse, and impractical to dispose of without incurring substantial costs and/or adversely affecting the environment and/or personnel.

Recently, room temperature ionic liquids (RTILs) have attracted much attention as promising alternative 'green' solvents to hazardous traditional organic solvents, due to their properties such as non-flammability, negligible vapour pressure, high thermal stability, solvating ability and easy recyclability.⁷ They have the potential to be highly polar yet non-coordinating. In addition to the above-mentioned salient features of ionic liquids (ILs) as reaction media, we have also recently shown that they can promote and catalyze important organic transformations under ambient conditions without the need for any added catalyst or ligand. The reactions investigated by us are Heck and Suzuki reactions,²⁴ bromination of aromatics,²⁵ Friedlander heteroannulation,²⁶ synthesis of benzodiazepines, benzimidazoles and benzthiazole,²⁷ which proceed with significantly enhanced reaction rates, high regioselectivity and excellent isolated yields.

As part of an ongoing development of efficient protocols for the preparation of biologically active heterocycles from



Scheme 1.

Table 1. Synthesis of imidazole **3k** in [bbim] X

ILs	pK _a ^a	E _T (30) (kcal mol ⁻¹) ²⁸	Yield ^b (%)
[bbim]ClO ₄	-11	76.34	21
[bbim]Br	-9	66.49	27
[bbim]Cl	-7	68.89	29
[bbim]BF ₄	0.5	75.73	43

^a The pK_a values of the parent acid of the anions.²⁹

^b Isolated yield after column chromatography.

Table 2. Synthesis of imidazole **3k** in [Hbim]X

ILs	pK _a ^a	Chemical shift -NH proton δ ppm	E _T (30) (kcal mol ⁻¹) ²⁸	Yield ^b (%)
[Hbim]ClO ₄	-11	11.83	63.82	61
[Hbim]Br	-9	12.17	73.68	81
[Hbim]Cl	-7	12.22	73.59	80
[Hbim]BF ₄	0.5	14.59	74.35	95

^a The pK_a values of the parent acid of the anions.²⁹

^b Isolated yield after column chromatography.

common intermediates using RTILs, we herein report for the first time, a one-pot condensation of 1,2-diketones or α-hydroxy ketone, aromatic aldehydes and ammonium acetate in the IL, 1-butyl imidazolium tetrafluoroborate ([Hbim]BF₄) which afforded a diverse array of 2,4,5-triaryl imidazoles in excellent isolated yields in the absence of any added catalyst.

2. Results

2.1. Synthesis of 2,4,5-triaryl imidazoles from 1,2-diketones

Ionic liquids (ILs) based on 1,3-di-*n*-butyl imidazolium salts [bbim]X and *N*-butyl imidazolium salts [Hbim]X with varying basicity of anions were tested as solvents and promoters for the typical reaction of 1,2-diphenyl-ethane-1,2-dione (**1b**) with *p*-anisaldehyde in the absence of any added catalyst to afford 2-(4-methoxy-phenyl)-4,5-diphenyl-1*H*-imidazole (**3k**) (Scheme 1). The reactions in the various ILs were carried out at 100 °C for 24 h. The yield data are recorded in Tables 1 and 2.

The polarity of different ionic liquids based on 1,3-di-*n*-butyl imidazolium salts and 1-*n*-butyl imidazolium salts were evaluated using Reichardt's dye as per the procedure reported.²⁸ The pK_a values are those of the parent acid of the anions and taken from literature.²⁹

It was observed that for a typical reaction of **1b** with *p*-anisaldehyde at the reaction temperature of 90 °C, the conversion does not go beyond 45% even after 24 h and at 130 °C the IL decomposed to give a black charry material. Hence, a reaction temperature of 100 °C was found to be optimum.

It becomes evident from these results, that the IL [Hbim]BF₄ afforded the best results. Consequently, all further studies were conducted using this IL as the reaction medium and promoter to generate a variety of imidazoles (**3a-z'**) by the reaction of 1, 2-di-furan-2-yl-ethane-1,2-dione (**1a**), 1,2-diphenyl-ethane-1,2-dione (**1b**) and 1,2-di-*p*-toluyl-ethane-1,2-dione (**1c**) with benzaldehydes (**2**), and ammonium acetate, respectively at 100 °C (Scheme 1).

The results are recorded in Table 3. All the reactions proceed to completion at the time indicated in the Table 3 and the yield data are for the isolated products after column chromatography. All the compounds were well characterized by melting point, IR, ¹H NMR and ¹³C NMR. Their elemental analyses were in conformity with their structures.

Download English Version:

<https://daneshyari.com/en/article/5233473>

Download Persian Version:

<https://daneshyari.com/article/5233473>

[Daneshyari.com](https://daneshyari.com)