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SHORT COMMUNICATION

A GREEN AND EFFICIENT SYNTHESIS OF QUINOXALINE DERIVATIVES CATALYZED BY 1-*n*-BUTYL-3-METHYLIMMIDAZOLIUM TETRAFLUOROBORATE

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ABSTRACT. The room temperature ionic liquid 1-*n*-butyl-3-methylimmidazolium tetrafluoroborate ([bmim]BF_4) was used to promote the synthesis of quinoxaline derivatives under grinding condition. The yields were ranged in 86.0-95.1%. It was shown that the proposed method is fast, efficient and environmentally benign.

KEY WORDS: Ionic liquid, Quinoxaline derivatives, Synthesis

INTRODUCTION

Quinoxaline derivatives are an important class of benzoheterocycles [1], which have a wide range of biological and pharmacological activity [2]. They have been widely used as anticarcinogen [3], antimicrobial [4], antihelmintic [5], HIV-1 reverse transcriptase inhibitor [6], and pesticide [7]. Moreover, they also serve as building blocks in the synthesis of organic semiconductors [8], rigid subunits in macrocyclic receptors or for molecular recognition [9], dyes [10], and electroluminescent materials [11].

In recent years, the synthesis of quinoxalines has attracted considerable attention [12] and a wide range of synthetic methods has been developed for the synthesis of quinoxaline derivatives [13]. The conventional synthetic methods of quinoxaline derivatives were carried out in organic solvent via the condensation of arene-1,2-diamines with 1,2-dicarbonyl compounds for 2-12 hours under refluxing conditions with the yields of 34-85% [14], or in high boiling point solvent such as dimethylsulfoxide (DMSO) using the molecular iodine as the catalyst [15].

A number of catalysts have been developed for the preparation of quinoxalines, including Bi^{3+} [16], MnO_2 [17], $POCl_3$ [18], $Ga(OTf)_3$ [19], cerium ammonium nitrate [20], $CuSO_4.5H_2O$ [21], AcOH [22] or $RuCl_2$-$(PPh_3)_3$ [23] as well as SA/MeOH [24]. Very recently, other catalysts, such as metal hydrogen sulfates [25], $CuCl_2$ combined with molecular sieve [26], molybdophosphoric acid exchanged by iron [27], and supported-sulfonic acid [12] have also been used for the synthesis of quinoxalines. However, most of the existing methodologies suffer from one or more limitations such as complicated reaction process, expensive and detrimental metal catalysts, using of volatile organic solvents, low product yields, and harsh reaction conditions, which come into collision with both economical and environmental requirements. Due to these disadvantages, the search for new catalysts which are green and cheaper remains an existing challenge.

Room temperature ionic liquids (RTILs) are deemed to potential "greener" alternatives to volatile organic solvent, which have been investigated extensively as solvents or catalysts for many important organic synthesis, such as 5-arylmethylidene-2-thio-4-thiazolidinone

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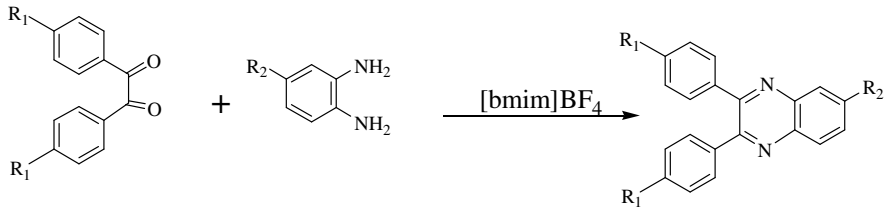
derivatives, 5-arylidene barbituric acid, xanthenedione derivatives, etc. [28]. Because RTILs have special properties such as their negligible vapor pressure, tunable polarity, high thermal stability, good solvating ability, ease of recycle-ability and their potential to enhance reaction rates and selectivity [29].

In continuing our endeavor in green synthesis and using ILs as recyclable reaction media to enhance rates and selectivity [28], we reported here a new method for the synthesis of quinoxalines catalyzed by RTILs under solid-state grinding (Scheme 1).



Scheme 1

EXPERIMENTAL

Melting points were recorded on an electrothermal apparatus and are uncorrected. ^{1}H-NMR (400 MHz) spectra were determined with a JEOL-JNM-GSX 400 spectrometer (DMSO-d_6) using TMS as internal standard. IR spectra (cm^{-1}) were measured with a Jasco FT/IR-800 spectrometer. [bmim]BF_4 was synthesized according to the literature [30].

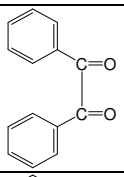
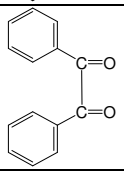
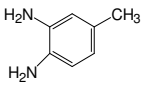
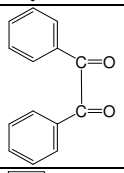
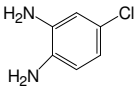
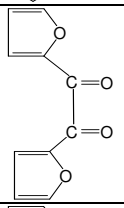
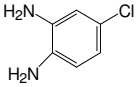
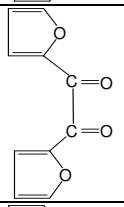
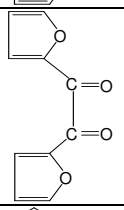
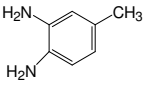
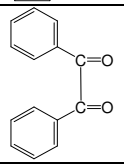
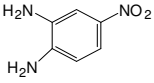
General procedure. A mixture of 5 mmol 1,2-dicarbonyl compounds **1**, 5 mmol arene-1,2-diamines **2**, 0.2 mL [bmim]BF_4 were ground with agate mortar and pestled for 5 min and kept standing at room temperture for 10-60 min (monitored by TLC), then the products was washed with 5 mL water and the filtrate containing [bmim]BF_4 was concentrated under reduced pressure to recover the ionic liquid. The obtained solid was recrystallized from 95% ethanol. Then the products **3a-m** were obtained. All the products were fully characterized by IR and ^{1}H NMR. The products are given in Table 1.

RESULTS AND DISCUSSION

Since the recovery and reuse of catalyst and solvent are highly preferable for a green process, so we investigated the reusability and recycling of the ionic liquid. After completion of the reaction, water was added into the reaction mixture, and the solid was collected by filtration to give the product. The filtrate containing [bmim]BF_4 was concentrated under reduced pressure to recover the ionic liquid. The recycled [bmim]BF_4 was reused in the model reaction of **1a** and **2**. The catalytic activity of [bmim]BF_4 did not show any significant decrease even after five runs. The results were shown in Table 2. The results also indicated that the ionic liquid employed was stable under the reaction temperature.

In conclusion, we have reported a reliable, rapid and environmentally benign method for the preparation of quinoxalines under solvent-free conditions at room temperature. The advantages of this method are high yields, short reaction time, low catalyst loading and solvent-free. Further investigation on the application of RTILs for other reactions is ongoing in our laboratory.

Table 1. Quinoxaline derivatives from the reaction of 1,2-diamines and 1,2-diketones catalyzed by [bmim]BF_4.

Entry	**1**	**2**	Time (min)	M.p. (lit) (^oC)	Yield (%)
3a			25	127-129 (128-129) [19]	93.0
3b			10	114-115 (112-114) [19]	95.1
3c			15	124-126 (124-126) [19]	93.6
3d			15	123-124 (124-126) [19]	86.0
3e			10	133-135 (134-136) [19]	94.0
3f			20	115-116 (116-118) [19]	91.0
3g			25	192-194 (188-190) [19]	90.1

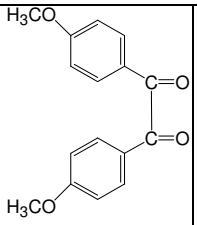
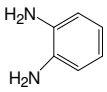
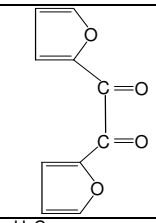
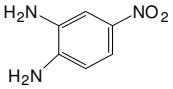
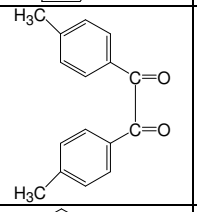
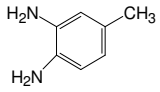
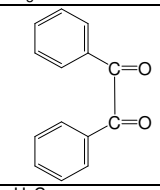
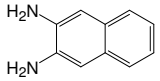
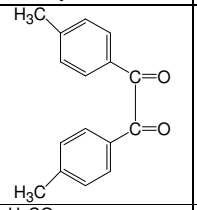
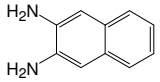
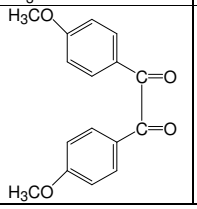
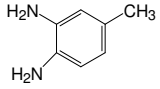
3h			30	152-154 (148-150) [31]	86.9
3i			15	172-174 (174-176) [19]	93.2
3j			20	137-138 (138-139) [31]	90.7
3k			60	190-192 (186-188) [31]	88.5
3l			60	195-196 (196-198) [31]	86.3
3m			15	127-128 (129-131) [31]	92.3

Table 2. Studies on the reuse of the [bmim]BF_4 for the preparation of **3a**.

Round	1	2	3	4	5
Yield (%)	93	91	92	90	88

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