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L-Valine functionalized ionic liquid catalyzed esterification reaction under approach



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Abstract Environmental eco-friendly condensation of carboxylic acids with alcohols proceeded smoothly to afford esters, by using the combination of a novel L-valine amido ethyl methyl imidazolium bromide [L-Vaemim]Br and DBU, under solvent free condition. This method features reusability of catalyst and reduced waste discharge.

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1. Introduction

In the last decades, important concerns about environmental protection for modern chemistry are the development of new methods and technologies that induced mainly (Otera, 2003; Larock, 1999), chemists to design eco-friendly processes whenever possible in the reaction. The significant strategies are performing reactions without the use of a solvent (Clark and Macquarrie, 2002; Lancaster, 2002; Afonso and Crespo, 2005; Mikami, 2005). However, the organic solvents rank high on the list of harmful chemicals for two simple reasons: they

are used in large amount, and their vapors are usually difficult to control, making them responsible for the emission of non-negligible percentage of volatile organic compounds (VOC's) (Metzger, 1998; Tanaka and Toda, 2000; Rothenberg et al., 2001; Sheldon, 2005; Kaupp, 2008). Even though, transformation under solvent free reaction condition (SFRC) can undergo a different scenario, while heat exchange is very important particularly in exothermic reactions (Correa et al., 2003). Chemists have met the environmental challenge by a new way of thinking their own work, dubbed "Green Chemistry or click chemistry", developing four main tools for the task (Clark, 2006). Novel uses of water and of supercritical fluids have been explored, and both have shown a promising "green potential". Nevertheless, water can hardly replace more green solvents/catalyst (i.e.) ionic liquids because of the poor solubility and low stability of many organic compounds in aqueous media (Anastas and Kirchoff, 2002).

In the past few years, ionic liquids have emerged as a set of green solvents with unique properties such as tunable polarity, high thermal stability, and immiscibility with a number of

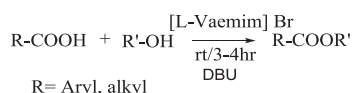
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Scheme 1 Esterification of acid using [L-Vaemim]Br/DBU under solvent free condition.

organic solvents, negligible vapor pressure and recyclability (Welton, 1999; Sheldon, 2001; Zhao et al., 2002; Dupont et al., 2002; Rajgopal et al., 2003; Jarikote et al., 2003). Their non-volatile character and thermal stability make them potentially attractive alternatives to environmentally unfavorable organic solvents, notably chlorinated hydrocarbons. They are particularly promising as solvents for the immobilization of transition metal catalysts, Lewis acids and enzymes. As a result of their green credentials and potential to enhance reaction rates and selectivities, ionic liquids are finding increasing applications in organic synthesis (Gholap et al., 2004; Zhu et al., 2010; Liu et al., 2010; Guillen et al., 2006).

Esterification is among the oldest and most often used an important transformation in organic chemistry (Salome and Kohn, 2009), and numerous/diverse methods have been advanced for this, assuring that most esters can be prepared (Paquette, 1995). Nonetheless, a simpler, general method would facilitate future synthetic studies. We sought a readily available esterification reagent that could convert carboxylic acids into their alkyl esters. From the literature survey there was no report of using [L-Vaemim]Br as catalyst for the synthesis of ester. In view of the emerging importance of amino acid based ionic liquid as novel catalyst, we wish to explore the use of novel L-valine amido ethyl methyl imidazolium bromide [L-Vaemim]Br as a recyclable catalytic system for the synthesis of ester with excellent yield (Scheme 1).

2. Experimental

All reagents purchased from Aldrich, Hi Media and Qualigens were used without further purification. Infrared (IR) spectra were recorded at room temperature from 4000 to 400 cm^{-1} with KBr pellets at a resolution of 3–4 cm^{-1} , using Avatar 330 equipped with DTGS detector. Most of the obtained vibrational bands of the IR spectrum were identified and compared with those values available in the literature. The ^1H NMR was recorded on a Bruker AMX-400 (500 MHz) instrument at room temperature using the X-WIN NMR version X-WIN NMR 1.3 cn drx software. Approximately 0.03 M solutions in DMSO-d_6 using TMS as internal reference were used for recording ^1H NMR spectra. Mass spectra were obtained using JEOL GC MATE II HRMS (EI) mass spectrometry. Column chromatography was performed on silica gel (200–300 mesh). Analytical thin-layer chromatography (TLC) was carried out on precoated silica gel GF-254 plates. Melting points were determined in open capillaries and are uncorrected.

2.1. Typical procedure for the conversion of benzoic acid into benzyl benzoate

In a 100 mL round bottomed flask, benzoic acid (1.2 mmol) and benzyl alcohol (1 mmol) were mixed and stirred at

ambient temperature. To this, [L-Vaemim]Br (0.03 mmol) and DBU (1 mmol) were added. The resulting solution was stirred for 3 h. The progress of reaction was monitored by HPLC. After completion of the reaction, the product was extracted with ether (3 \times 5 mL). The combined ether extracts were concentrated on a rotary evaporator and the crude product was purified by column chromatography over silica gel by using *n*-hexane/ethyl acetate (4:1) as eluent to give the desired product.

2.1.1. Spectral data for benzyl benzoate (3a)

^1H -NMR (CDCl_3 , 500 MHz): 5.2 (s, 2H), 7.3 (d, 2H), 7.6 (d, 2H), 8.0–8.2 (m, 4H) ^{13}C -NMR (CDCl_3 , 125 MHz): 65.43, 119.22, 120.72, 128.19, 130.77, 135.70, 149.00, and 165.43.

2.1.2. Spectral data for benzyl 4-methylbenzoate (3d)

^1H -NMR (CDCl_3 , 500 MHz): 2.3 (s, 3H), 5.2 (s, 2H), 7.5 (d, 2H), 7.6 (d, 2H), 7.8 (m, 4H) ^{13}C -NMR (CDCl_3 , 125 MHz): 21.55, 65.43, 115.25, 120.72, 127.88, 130.77, 135.70, 145.00, and 165.43.

2.1.3. Spectral data for benzyl 4-chlorobenzoate (3e)

^1H -NMR (CDCl_3 , 500 MHz): 5.2 (s, 2H), 7.2 (d, 2H), 7.5 (d, 2H), 8.0 (m, 4H) ^{13}C -NMR (CDCl_3 , 125 MHz): 65.43, 110.25, 120.72, 127.88, 130.77, 135.70, 145.00, and 165.43.

2.1.4. Spectral data for benzyl 4-nitrobenzoate (3f)

^1H -NMR (CDCl_3 , 500 MHz): 5.2 (s, 2H), 7.6 (d, 2H), 7.9 (d, 2H), 8.0 (m, 4H) ^{13}C -NMR (CDCl_3 , 125 MHz): 65.43, 104.25, 120.72, 127.88, 136.77, 140.70, 145.00, and 170.43.

3. Results and discussion

Our initial efforts in the development of this methodology began with screening various solvents as well as investigating the effect of temperature as noted in Table 1. For the coupling of benzoic acid with benzyl alcohol as a standard reaction, it was found that most of the commonly utilized solvents such as toluene, dichloromethane, and acetonitrile for the esterification reaction fared poorly in terms of reaction yield. According to the results, when the reaction was carried out in CH_3CN (entry 1) or toluene (entry 3) resulted in modulator conversion into the desired coupled product. Furthermore, use of DCM (entry 5) as a solvent gave only a small amount of benzyl benzoate formation. Moreover, there was no much difference in the conversion when the reaction was carried out at reflux condition (entries 2, 4, 6). Furthermore, esterification reaction was

Table 1 Effect of solvent and temperature on benzylation of benzoic acid using [L-Vaemim]Br and DBU system.

Entry	Solvent	Condition	Time (h)	Conversion %
1	CH_3CN	rt	10	69
2	CH_3CN	reflux	5	73
3	Toluene	rt	7	70
4	Toluene	reflux	5	75
5	DCM	rt	20	55
6	DCM	reflux	14	58
7	–	rt	3	91
8	–	reflux	1.5	91

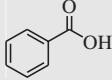
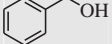
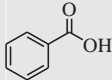
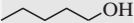
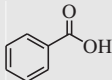
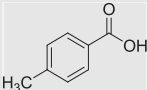
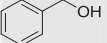
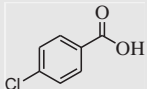
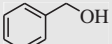
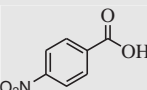
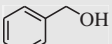
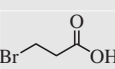
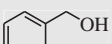
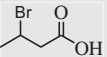
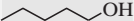
carried out in the presence of [L-Vaemim]Br under ambient and reflux condition (Table 1). These results clearly showed that this protocol was absolutely suitable for the preparation of esters with excellent yield in short duration (entries 7 and 8). After securing the optimal reaction conditions, we turned our attention to a thorough exploration of the different bases, such as NaOH, KOH, K₂CO₃, Imidazole, triethylamine, pyridine and 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) in the presence of [L-Vaemim]Br. Moreover, this reaction was unsuccessful in the absence of base (Table 2, entry 1). Furthermore, esterification reaction was carried out using NaOH and KOH, the formation of ester increases from zero level to 55% and 56% (entries 2 and 3). However, there was no ester transformation between benzoic acid and benzyl alcohol in the presence of K₂CO₃, triethylamine and pyridine (entries 4–6) even at 48 h. Moreover, the esterification reaction was carried out in the presence of imidazole for 24 h, 67% of benzyl benzoate was

Table 2 Effect of base on benzylation of benzoic acid using [L-Vaemim]Br and DBU system.

Entry	Base	Time (h)	Conversion %
1	–	48	–
2	NaOH	48	55
3	KOH	48	56
4	K ₂ CO ₃	48	–
5	Et ₃ N	48	–
6	Py	48	–
7	Imidazole	24	67
8	DBU	3	91

obtained (entry 7). Performing this transformation using DBU instead of other base, required a shorter reaction time (entry 8). This result showed the higher efficiency of DBU for

Table 3 Condensation of carboxylic acids with alcohols in the presence of [L-Vaemim]Br.^a

Entry	Acid	Alcohol	Product	Time (h)	Yield (%) ^b
1			3a	3	91
2			3b	3.5	89
3		<i>i</i> -PrOH	3c	4	85
4			3d	4.5	82
5			3e	2.5	88
6			3f	2.5	90
7			3g	3	90
8			3h	3	89

^a Reaction conditions: alcohol (1 mmol) and acid (1.2 mmol), [L-Vaemim]Br (0.03 mmol) and DBU (1 mmol), stirred at appropriate temperature.

^b Isolated yields. All products are known compounds and were identified by comparison of their physical and spectral data with those of the authentic samples (Nowrouzi et al., 2010).

Table 4 Recycling of [L-Vaemim]Br: benzoic acid to benzyl benzoate under solvent free condition.^a

Entry	Cycles	Yield ^b (%)
1	0	91
2	1	91
3	2	89
4	3	88
5	4	86
6	5	86
7	6	84
8	7	84

^a Reaction conditions: alcohol (1 mmol) and acid (1.2 mmol), [L-Vaemim]Br (0.03 mmol) and DBU (1 mmol), stirred at appropriate temperature.

^b Isolated yields.

ester transformation. After optimization, we examined primary, secondary and benzylic alcohols and aliphatic, aromatic carboxylic acids carrying electron-donating and electron-withdrawing groups and the optimized reaction conditions were applied to these substrates (Table 3). Carboxylic acids having activated and deactivated aromatic rings (Table 3, entries 1, 2 and 4) afforded the corresponding esters in high yield after 3–4.5 h, whereas carboxylic acid having electron-withdrawing substituent (entries 5–8) reacted in a shorter time. As indicated in Table 3, this catalytic system is suitable for the conversion of primary, secondary aliphatic and also benzylic alcohols into their corresponding esters. This reaction with primary alcohols was somewhat faster in comparison with the reaction when more bulky secondary ones were used (entry 3).

Subsequently, the recyclability of the [L-Vaemim]Br catalyst was confirmed for the coupling of benzoic acid with benzyl alcohol. The catalytic system could be reused directly for a new cycle, after full extraction of the product three times with 5 mL ether per extraction. The results shown in Table 4 demonstrated that this esterification system was readily recyclable for eight runs without any significant loss of catalytic activity.

4. Conclusion

In conclusion, a simple, efficient and green protocol was established using [L-Vaemim]Br/DBU for the preparation of carboxylic acid alkyl esters at ambient temperature under solvent free condition. The reaction was tolerant of varying substitution patterns on the benzoic acid components. Moreover, the reaction progresses well with either electron donating or electron-withdrawing functional groups. It is noteworthy to mention that the ionic liquid could easily be recycled and reused without the loss of activity. We believe this methodology will find a wide use within the realm of natural products synthesis and our own applications in this context will be presented in due course.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.arabjc.2012.04.032>.

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