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Enhancing nucleophilicity in ionic liquid [bmim]HSO₄: A recyclable media and catalyst for the halogenation of alcohols

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1. Introduction

Sustainable industrial development must employ less polluting neoteric solvents and this quest for new reaction media leads to the exploration of different ionic liquids [1–4]. Interest to explore various inorganic and organic reactions in ionic liquids, particularly, those based on 1,3-dialkylimidazolium cations [4–7] has flourished in recent time. Because of tremendous useful properties of ionic liquids such as vanishingly low vapour pressure, low co-ordinating ability and thermal/chemical stability, these have been used as an attractive alternative to traditional volatile organic solvents in various chemical processes, and in liquid–liquid extractions as documented by recent literature [1–7]. On the other hand, immiscibility of ionic liquid in different organic solvents paves the way for biphasic [8,9] separation of desirable products.

There is a controversy [10,11] whether ionic liquids accelerate or decelerate the nucleophilic substitution reactions. Although many types of reactions have been investigated in ionic liquid, but very few examples of nucleophilic substitution reactions [12–18] are present in the literature. These reactions are traditionally often been carried out using phase transfer catalyst [19,20] and because of the fact that IL are comprised of bulky organic cation, they seem to be an excellent substitute for phase transfer catalysis along with quarternary ammonium salts, crown ether derivatives and phosphonium salts. Alkali metal salts containing different halide anions

ABSTRACT

Bronsted acidic ionic liquid 1-butyl-3-methylimidazolium hydrogen sulphate [bmim]HSO₄ has been demonstrated as an efficient reusable catalyst and solvent, for halogenation of aromatic and aliphatic alcohols in conjunction with microwave and thermal heating. Use of microwave energy not only accelerates the reaction rate, but also provides enhanced yields. Moreover, anhydrous ionic liquid facilitates nucleophilic attack of halide ions on alcohols, thus indicating the enhancement in their nucleophilic character. Easy work up, good yields and facile regeneration of the ionic liquid further increases the scope of the developed methodology.

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viz., chloride, bromide and iodide are economical and can serve as nucleophile [21] in substitution reactions.

Halogenation of alcohols is one of the most important functional group transformation in organic chemistry. Halogen containing compounds are very useful intermediates in organic synthesis [22]. They are useful substrates or intermediates in elimination [23,24], rearrangement [25], lithiation [26,27] and carbon–carbon coupling [28,29] reactions and appropriate for the attack by numerous nucle-ophiles [17,21,30]. Because of our ongoing efforts to explore acidic ionic liquid [9,31,32] [bmim]HSO₄ in different organic reactions, we report herein, its use in nucleophilic substitution reaction for the first time and utilizing it for the transformation of alcohols into halides, using metal halides.

2. Experimental

Ionic liquid [bmim]HSO₄ was prepared by the reported method [31]. Improved version of the process is also reported using microwave reactor Plazmatronika (RM 2001 PC) (see Section 2.1). Microwave assisted reactions were also carried out in domestic microwave oven [LGMS194A (800 W)]. Ultrasound assisted reaction was carried out using Branson [B-2200 EI (60 W, 47 kHz)] ultrasonic cleaning bath.

2.1. Synthesis of [bmim]HSO₄

In a flame-dried assembly, 1-bromobutane (2 mmol) and 1methyl imidazole (2 mmol) were stirred together under microwave irradiation at 60–80 °C for 6 min (three cycles each having heating

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period 2 min, cooling period 2 min and power of magnetron 80%). NaHSO₄ (2.5 mmol) was added to the resulting light yellow viscous liquid [(bmim)Br] and irradiated with microwaves for 40 s at 50–70 °C (two cycles each having heating period 20 s, cooling period 30 s and power of magnetron 80%) or exposed to ultrasonic waves for 1 h. Resulting mixture was extracted with dichloromethane $(2 \times 20 \text{ mL})$ and evaporation of solvent under reduced pressure afforded orange coloured viscous liquid [bmim]HSO₄. Alternatively, in a dry assembly H₂SO₄ (2 mmol) was added dropwise to the light pale yellow liquid [bmim]Br prepared earlier, and stirred at 50 °C for 15 h to ensure complete ion exchange. The resulting orange viscous liquid was extracted with diethylether (2 × 20 mL) to ensure the removal of any organic impurity and the ionic liquid prepared was dried under vacuum for 6 h.

2.2. Synthesis of aryl or alkyl halides using thermal heating

In a flame-dried assembly [bmim] HSO_4 (6 mmol) and NaX [X = Br, I] (7.5 mmol) were stirred at 80 °C for half an hour, followed by addition of alcohol (5 mmol) and stirring continued at the same

temperature for the time specified (Table 1). After the completion of the reaction (monitored by TLC) the product was extracted with diethyl ether (3×20 mL). Combined organic layer was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure afforded the crude product that was purified by column chromatography using ethyl acetate and *n*-hexane (1:9) to obtain product.

2.3. Synthesis of aryl and alkyl halides using microwave energy

Ionic liquid [bmim]HSO₄ (1.2 mmol) and MX (NaI, NaBr, CsCl) (1.5 mmol) were stirred together in a vial (10 mL) under microwave irradiation in microwave reactor [Plazmatronika (RM 2001 PC)] at 60–80 °C for 1 min, followed by cooling period of 1 min. Alcohol (1 mmol) was added to vial, sealed properly and irradiated for 10 min in microwave reactor at 80–90 °C (five cycles each having heating period 2 min, cooling period 1 min and power of magnetron 80%). Alternatively, the reaction mixture can also be irradiated in domestic microwave oven [LGMS194A (800W)] at 160 W for the time specified (Table 1) with the mechanical shaking after each 30 s

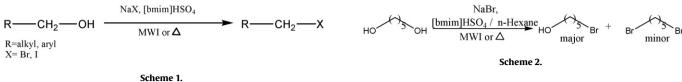
Table 1

Halogenation of different aromatic and aliphatic alcohols using [bmim]HSO4 and metal salts at 80 °C and under microwave irradiation.

S. no.	R ^a	Alkali metal salt used	Reaction time		Yield (%) ^b	
			MWI (160 W) (min)	Conventional (h)	MWI	Conventional
1.	\bigcirc	Nal	7	15	90	75
	Ш.СО	NaBr	8	16	88	72
2.	H ₃ CO H ₃ CO OCH ₃	Nal	8	16	87	78
		NaBr	10	18	85	75
3.	$\langle \mathcal{I} \rangle$	NaI	7	15	85	77
	<u> </u>	NaBr	9	16	84	74
4.		NaI	7	15	90	74
		NaBr	8	16	89	73
5.	H ₃ CO	NaI	8	16	82	70
		NaBr	9	17	80	70
6.		NaI	7	15	85	71
		NaBr	8	16	81	71
7.	ССН	NaI	7	15	75	64
		NaBr	9	18	74	62
8.		NaI	9	20	68	59
		NaBr	10	20	64	55
9.	$H_3C-[CH_2]_8-$	NaI NaBr	8 10	18 20	72 70	62 61
10	H ₃ C-[CH ₂] ₄ -	NaI NaBr	8 10	18 20	71 71	60 59

^a All the compounds were characterised on the basis of ¹H NMR and IR spectral data.

^b Isolated and unoptimised yields.



irradiation time. Resulting mixture was allowed to cool, followed by extraction with diethyl ether ($3 \times 10 \text{ mL}$). Combined organic layer was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure afforded the crude product that was purified by column chromatography using ethyl acetate and *n*-hexane (1:9) to obtain product in good yield.

2.4. Recycling of the ionic liquid

Residual ionic liquid (obtained in Section 2.2) was mixed thoroughly with NaHSO₄ (10 mmol) and irradiated with microwaves [160 W in LGMS-194A (800 W)] for 30 s. Resulting mixture was extracted with DCM (3×10 mL). Evaporation of the solvent under reduced pressure afforded the ionic liquid [bmim]HSO₄ (40%).

3. Results and discussion

Our first task was to analyze the behaviour of alkali metal salt, such as sodium bromide, towards halogenation reaction in acidic ionic liquid [bmim]HSO4. The general methodology involved addition of substrate to preheated mixture of ionic liquid [bmim]HSO₄ and sodium bromide, for 15-20 h (Scheme 1). Aromatic and aliphatic alcohols are converted to their respective bromides in moderate to good yields (Table 1) when the substrate is refluxed with a preheated mixture of sodium bromide and [bmim]HSO₄. In continuation of our work involving use of non-conventional techniques and media in organic synthesis [9,21], we explored the use of microwave energy for this specific task. It was observed that microwave energy increases the rate as well as overall yield of the reaction. Encouraged by these results, we next set out to investigate the use of sodium iodide and sodium chloride for iodination and chlorination respectively. During chlorination very poor results were obtained and results of iodination were found to be compatible with the previous one (Table 1).

To determine the accelerating effect of microwaves during the conversion, we determined the percentage of benzyl bromide formed from benzyl alcohol at various stages of reaction from NMR data. Approximately 90% conversion of alcohol to bromide (Fig. 1) was observed after 10 min irradiation period (five cycles each having heating period 2 min, cooling period 1 min, power of magnetron 80%, temperature range 80–90 °C). Yield of benzyl bromide did not increase further by increasing the irradiation time.

Moreover, alkali metal salt (NaBr/NaI) on treatment with allylic alcohols (Table 1, S. nos. 7 and 8) in ionic liquid [bmim]HSO₄ afforded the substituted product without the formation of any ring substituted or addition product. Cinnamyl alcohol (Table 1, S. no. 7)

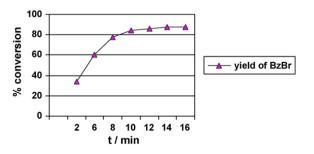


Fig. 1. %Age conversion of BzOH to BzBr under microwave irradiation.

when treated with sodium bromide afforded corresponding bromide that exhibited doublet at δ 6.61 (*J* = 12.4 Hz) indicating the presence of double bond [33] and upfield shift in the signal of saturated methylene protons containing alcoholic group.

Monohalogenation of diols [34] is often a stubborn problem in different synthetic endeavoures, as there is considerable formation of disubstituted product. Immiscibility of ionic liquid with different organic solvents, and their tendency to form biphasic media, could offer an excellent solution for this specific task. Keeping in mind good yields of monotetrahydropyranyl ethers obtained in our previous work [9], we decided to perform the monobromination of pentan-1,5-diol (4 mmol) using NaBr (4 mmol) in biphasic media of ionic liquid [bmim]HSO₄ (4.8 mmol) and hexane (5 mL).

Diol, when subjected to same reaction conditions as alcohols, provided moderate selectivity (disubstituted, monosubstituted and unreacted alcohol in the ratio 2.8:3.5:3.7 as indicated by gas chromatography), but when the reaction was carried out in biphasic media using *n*-hexane and [bmim]HSO₄, increase in selectivity was observed (Scheme 2) (ratio of disubstituted, monosubstituted and unreacted alcohol obtained is 1.8:4.7:3.5). However, the formation of dibromides could not be prevented completely. {*Caution*: Monohalogenation or the related biphasic reactions should never be tried in any closed vessel in domestic microwave oven, like other microwave-assisted reactions. Though hexane is microwave inactive, but in presence of ionic substances it can undergo heating^{*}, that can result in explosion [35]}.

After the completion of the reaction ionic liquid used can be regenerated (see Section 2.4) using NaHSO₄, which eliminates the use of corrosive and toxic substances in the regeneration process. Residual ionic liquid is believed to contain [bmim]₂SO₄, [bmim]OH and ion exchange by NaHSO₄ regenerates the acidic ionic liquid [bmim]HSO₄. The ionic liquid, thus prepared can also be used for other organic transformations and we have used it for the formation of tetrahydropyranyl ethers [9].

To study the role of ionic liquid in the nucleophilic substitution reactions, we decided to perform the aforementioned conversion in different solvents (Table 2). Keeping the time and energy source constant for the conversion of benzyl alcohol to benzyl bromide (Scheme 1, S. no. 1., Table 1) using NaBr, it was observed that the formation of bromide takes place only in case of anhydrous [bmim]HSO₄. However, when equimolar amount of water was added to the ionic liquid no formation of product was observed. So we concluded that anhydrous [bmim]HSO₄ accelerates the nucleophilic substitution reaction by its ionic character, whereas presence of water decelerate the reaction probably due to its solvation effect. Reaction does not proceed at all in other solvents like water, methanol and dimethyl sulfoxide, therefore indicating the need of protonation of alcohols by the ionic liquid and facilitating the attack of halide ion to form the corresponding substituted product, thus manifesting the catalytic role of [bmim]HSO₄.

Table 2
Reaction of benzyl alcohol with NaBr in different solvents.

S. no.	Solvent used	Yield (%) of benzyl bromide
1.	[bmim]HSO ₄	90
2.	[bmim]HSO ₄ /H ₂ O	0
3.	H ₂ O	0
4.	CH ₃ OH	0
5.	DMSO	0

4. Conclusion

In conclusion, we have found that metal salts behave as good source of nucleophiles in anhydrous ionic liquid [bmim]HSO₄, and can be used to synthesize aryl and alkyl halides from the corresponding alcohols, using microwave and thermal energy. Simple experimental and product isolation procedures, combined with ease of regeneration and reuse of ionic liquid, are expected to contribute towards the development of green methodologies.

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References

- [1] J.S. Wilkes, J. Mol. Catal. A: Chem. 214 (2004) 11.
- [2] P. Wasserscheid, T. Welton (Eds.), Ionic Liquids in Synthesis, Wiley-VCH, Weinheim, 2002.
- [3] K. Fukumoto, H. Ohno, Chem. Commun. 29 (2006) 3081.
- [4] J. Mo, J. Xiao, Angew. Chem. Int. Ed. 45 (2006) 4152.
- [5] Q.W. Yao, Y.L. Zhang, Angew. Chem. Int. Ed. 42 (2003) 3395.
- [6] S.T. Handy, J. Org. Chem. 71 (2006) 4659.
- [7] W.-H. Ou, HuangF Z.-Z., Green Chem. 8 (2006) 731.
- [8] A.M. Scurto, W. Leitner, Chem. Commun. 35 (2006) 3681.
- [9] J. Singh, N. Gupta, G.L. Kad, J. Kaur, Synth. Commun. 36 (2006) 2893.

- [10] D.W. Kim, C.E. Song, D.Y. Chi, J. Org. Chem. 68 (2003) 4281.
- [11] L. Crowhurst, N.L. Lancaster, M. Juan, P. Arlandis, T. Welton, J. Am. Chem. Soc. 126 (2004) 11549.
- [12] M. Cavazza, F. Pietra, Tetrahedron Lett. 45 (2004) 3633.
- [13] Z.M.A. Judeh, H.-Y. Shen, Chi S B.C., L.-C. Feng, S. Selvasothi, Tetrahedron Lett. 43 (2002) 9381.
- [14] C. Chiappe, D. Pieraccini, P. Saullo, J. Org. Chem. 68 (2003) 6710.
- [15] R.X. Ren, J.X. Wu, Org. Lett. 3 (2001) 3727.
- [16] N.L. Lancaster, T. Welton, J. Org. Chem. 69 (2004) 5986.
- [17] C. Wheeler, K.N. West, C.L. Liotta, C.A. Eckert, Chem. Commun. (2001) 887.
- [18] D.W. Kim, C.E. Song, D.Y. Chi, J. Am. Chem. Soc. 124 (2002) 10278.
 [19] M. Makosza, Pure Appl. Chem. 72 (2000) 1399.
- [20] J. Dockx, Synthesis (1973) 441.
- [21] G.L. Kad, V. Singh, K.P. Kaur, J. Singh, Tetrahedron. Lett. 38 (1997) 1079.
- [22] E. Yue, W.J.M. Gerdes, C.A. Mathis, J. Org. Chem. 56 (1991) 5451.
- [23] R.C. Larock, Comprehensive Organic Transformations, VCH, New York, 1989, 151.
- [24] R. Schwesinger, H. Schlemper, Angew. Chem. Int. Ed. 26 (1987) 1167.
- [25] M. Kunishima, K. Hioki, K. Kono, A. Kato, S. Tani, J. Org. Chem. 62 (1997) 7542.
- [26] J. San Filippo Jr., J. Silbermann, J. Am. Chem. Soc. 104 (1982) 2831.
- [27] H.G. Kuivila, J. Am. Chem. Soc. 107 (1985) 416.
- [28] F. Diederich, P.J. Stang, Metal Catalysed Cross-coupling Reactions, Wiley-VCH, Weinheim, 1998.
- [29] J.J. Li, Name Reactions: A Collection of Detailed Reaction Mechanisms, second edition, Springer-Verlag, Berlin, Heidelberg, New York, 2003.
- [30] D.W. Kim, D.J. Hong, J.W. Seo, H.S. Kim, H.K. Kim, C.E. Song, D.Y. Chi, J. Org. Chem. 69 (2004) 3186.
- [31] V. Singh, S. Kaur, V. Sapehiyia, J. Singh, G.L. Kad, Catal. Commun. 6 (2005) 57.
- [32] N. Gupta, Sonu, G.L. Kad, J. Singh, Catal. Commun. (2007) 1323.
- [33] Cinnamyl bromide: IR (neat)/v_{max} cm⁻¹: 3022, 2922, 1660, 1200, 640. ¹H
 NMR (CDCl₃, 300 MHz) δ: 7.42–7.34 (m, 5H, ArH), 6.61 (d, 1H, *J* = 12.4 Hz, Ar–CH=CH–), 4.58–4.49 (m, 1H, Ar–CH=CH–), 3.42 (d, 2H, *J* = 6.3 Hz, –CH₂Br). Cinnamyl iodide: IR (neat)/v_{max} cm⁻¹: 3010, 2928, 1650, 1190, 510. ¹H
 NMR (CDCl₃, 300 MHz) δ: 7.41–7.30 (m, 5H, ArH), 6.58 (d, 1H, *J* = 12.2 Hz, Ar–CH=CH–), 4.50–4.41 (m, 1H, Ar–CH=CH–), 3.34 (d, 2H, *J* = 6.1 Hz, –CH₂Br).
- [34] S.K. Kang, W.S. Kim, B.H. Moon, Synthesis (1985) 1161.
- [35] N.E. Leadbeater, H.M. Torenius, J. Org. Chem. 67 (2002) 3145.