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A mild and efficient method for preparation of azides from alcohols using acidic ionic liquid [H-NMP]HSO_4

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ABSTRACT

We report here an efficient method for the synthesis and characterization of [H-NMP]HSO_4 and its application as an efficient catalyst and solvent for preparation of azides from corresponding alcohols under mild conditions. This processor showed high chemoselectivity for conversion of various alcohols to their corresponding azides.

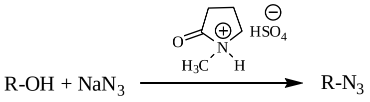
1. Introduction

Conversions of alcohols to their corresponding azides are very important and essential in functional group transformation. Alkyl azides have frequently been used for the synthesis of amino groups and for the construction of N-heterocycles.[1] There are a few reported methods for preparation of alkyl azide including using Mitsunobu reactions using hydrazoic acid as the azide source,[2] oxidation–reduction condensation using a quinone derivative and trimethylsilylazid ($TMSN_3$),[3] *N*-(*p*-toluenesulfonyl) imidazole (TsIm)/tetrabutylammonium iodide (TBAI)/triethylamine (TEA).[4] diphenylphosphorazidate (DPPA),[5] zinc azid/bis pyridine complex,[6] (DPPA)/1, 8-diaza bicyclo[5.4.0]undec-7-en,[7], $NaN_3/BF_3{\cdot}ET_2O$,[8] and other useful methods.[9,2f] Azides have been used for preparation of medicines such as azido pyrimidines and purines due to their anti HIV-1 biological activity,[10] also 5-azido-5-deoxyxylofuranose has been employed for synthesis of sugar triazole derivatives as anti tuberculosis agents.[11] Protic acidic ionic liquids (ILs) have frequently been used as green solvents and catalysts in place of conventional organic solvents and acid catalysts.[12] In continuation of our ongoing projects to develop efficient methods for organic functional groups transformation,[13–15] here we wish to report the synthesis and characterization of pyrrolidinium bisulfate [H-NMP]HSO_4, which is a new acidic ionic liquid,[16] as a highly chemoselective, inexpensive, and efficient catalyst and also as a solvent for conversion of alcohols to the corresponding azides using NaN_3 (Scheme 1).

2. Results and discussion

Initially to optimize the conversion of benzyl alcohol to benzyl azide, we tried the reaction under solvent-free conditions and in different solvents such as water, acetonitrile, and dichloromethane and under different temperatures including 60, 80, 100, and 120 °C for evaluating the acidity and applications of this Brönsted acid. Different amounts of acidic ionic liquid and sodium azide were also tried for optimization of the reaction conditions. We found that reaction at 120 °C and using 3 mmol of ionic liquid, 1 mmol of benzyl alcohol, and 1.5 mmol of sodium azide gave the best yield in shorter reaction time. We applied these conditions for synthesis of various azides from corresponding alcohols (Table 1).[17]

The procedure showed high chemoselectivity for azidation of secondary benzyl alcohols in the presence of primary, tertiary benzylic, and also aliphatic alcohols. As demonstrated in Table 1 in comparison to secondary alcohols with withdrawing groups the secondary alcohols with donor groups were reacted faster and in



Scheme 1.

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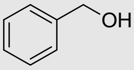
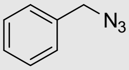
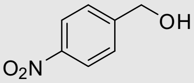
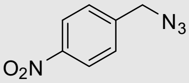
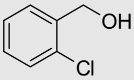
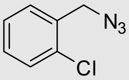
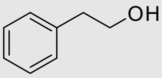
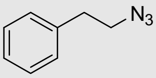
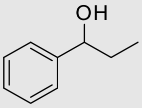
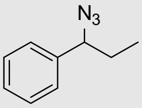
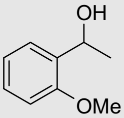
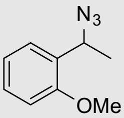
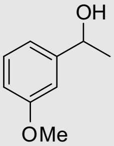
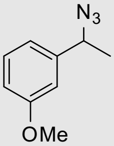
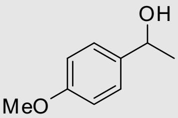
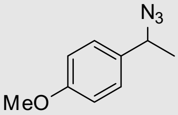
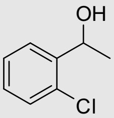
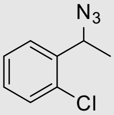
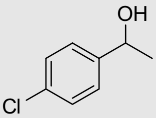
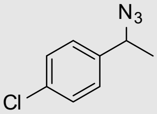
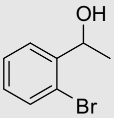
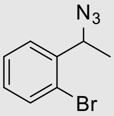
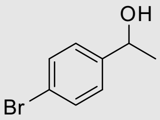
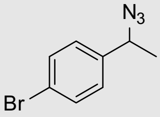
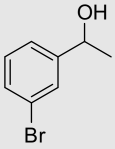
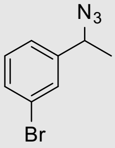
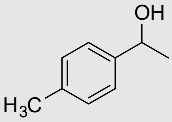
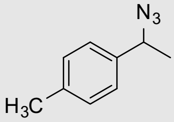
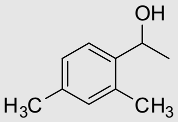
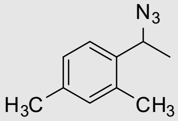
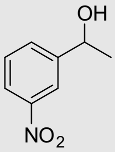
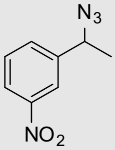
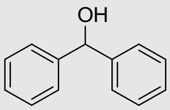
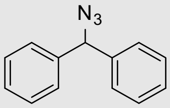
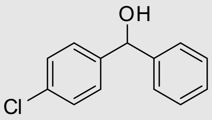
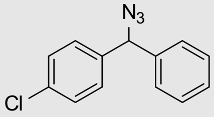
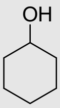
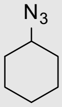
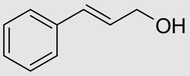
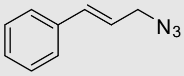
Table 1
Conversion of various alcohols to corresponding azides with optimized procedure

Entry	Substrate	Product	Time (h)	Conversion (%)[a]
1			6	80
2			12	5
3			8	40
4			24	0
5			2	100
6			2	100
7			1	100
8			1	100
9			3	80
10			2	95
11			1.5	100

(continued on next page)

Table 1 (*continued*)

Entry	Substrate	Product	Time (h)	Conversion (%)[a]
12			1	100
13			1	100
14			1	100
15			1	100
16			4	40
17			2	100
18			1	90
19			8	0
20			1	100

[a] Conversions were determined with TLC.

higher yields. Aliphatic alcohols were not converted to their azides under these conditions (entries 4 and 19) and using alcohols were recovered without any conversion even in longer reaction times. We believed that the proton of bisulfate is the proton donor due to its higher acidity.

3. Conclusion

In conclusion, this method is a novel and convenient method for conversion of various alcohols to the corresponding azides using novel and inexpensive acid ionic liquid [H-NMP]HSO_4. The high yield, green chemistry, using inexpensive and straightforward isolation of the products are the advantages of this method over reported procedures. The method is chemoselective for conversion of secondary benzylic alcohols in the presence of primary benzylic and aliphatic alcohols and also for conversion of primary benzylic alcohols in the presence of aliphatic alcohols. In this method, the halogen groups in benzene rings were intact during the reaction.

Acknowledgments

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15. Hajipour, A. R.; Kooshki, B.; Ruoho, A. E. *Tetrahedron Lett.* **2005**, *46*, 5503.
16. *Synthesis of acidic ionic liquid [H-NMP]HSO$_4$*: In a round-bottomed flask, to a cold mixture of 1-methyl-2-pyrrolidone, (0.99 g) in 15 ml of dichloromethane on an ice bath was added. One gram of concentrated sulfuric acid (98%, $d = 1.84$) was added dropwise. The reaction mixture was stirred at room temperature for 3 h, then the solvent was evaporated under reduce pressure to produce 1.97 g of [H-NMP]HSO$_4$ (100%). FT-IR (KBr, cm^{-1}) 2300–3600 (s, Br), 1660 (s), 1509 (m), 1302 (m), 1114 (w), 962 (w), 610 (w) cm^{-1}. ^{1}H NMR (500 MHz, D$_2$O): δ 1.4 (m, 2H, CH$_2$), 1.8 (t, 2H, CH$_2$), 2.2 (s, 3H, CH$_3$), 2.9 (t, 2H, CH$_2$). ^{13}C NMR (500 MHz, D$_2$O): δ 22.22 (CH$_2$), 35.09 (CH$_2$), 42.10–43.51 (CH$_2$, CH$_3$), 180 (C=O) ppm.
17. *General procedure for the one-pot conversion of alcohol to azide*: In a 25 ml round-bottomed flask, a mixture of alcohol (1 mmol), NaN$_3$ (1.5 mmol), and ionic liquid [H-NMP]HSO$_4$ (3 mmol) was stirred on an oil bath at 120 °C. The progress of the reaction was checked with TLC (cyclohexane/ethyl acetate 70:30). When the reaction was completed, the mixture was extracted with cyclohexane (2×10 ml), filtered off the solid. The organic layer was washed with NaOH 5% (10 ml). The organic phase was dried with MgSO$_4$, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using silica gel (cyclohexane/ethyl acetate 70:30).