



Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Short Communication

OCAIJ, 3(4), 2007 [163-165]

An improved protocol for the synthesis of alkyl or acyl azides by using [bmim]BF₄ or [bmim]PF₆ at ambient temperature under solvent free and neutral condition

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Received: 26th July, 2007 ; Accepted: 31st July, 2007

ABSTRACT

The present investigation deals with the synthesis of alkyl or acyl azides from the corresponding halo congeners employing room temperature ionic liquids 1-butyl-3-methylimidazolium tetrafluoroborate [Bmim]BF₄ or 1-Butyl-3-methylimidazolium hexafluorophosphate [Bmim]PF₆ as solvents at ambient temperature. Moreover, [Bmim]BF₄ or [Bmim]PF₆ can be recycled up to three runs without remarkable yield loss.

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KEYWORDS

Alkyl or acyl azides;
Ionic liquids;
Ambient temperature;
Solvent free condition.

INTRODUCTION

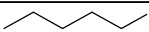
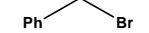

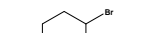
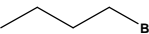
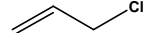
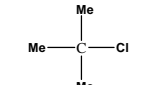
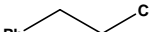
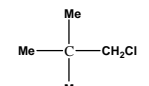
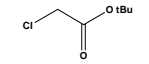
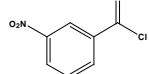
The development of benign synthetic methodology for fine and speciality chemicals comprises the replacement of Volatile Organic Compounds (VOCs) by water, room temperature ionic liquids (RTILs), supercritical fluids, immobilized solvents, fluoruous solvents and solventless conditions^[1] because organic solvents are often harmful to environment which may lead frequently to government restrictions and high waste disposal costs^[2]. The versatile reactivity and the synthetic applications of the azido group is well documented^[3]. For example, they can be used for the synthesis of variety of heterocycles^[4], natural products^[5], and pharmacologically active substances^[6]. Azide derivatives have also been used in rubber vulcanization, polymer cross-linking, dyes, tire coated adhesives, foaming of plastics,

pesticides and herbicides^[7]. Moreover, they also found for wide utility as photoaffinity probes/labels due to their ability to be made radioactive with high specific activities^[8]. There are several methods reported for the synthesis of alkyl or acyl azides from corresponding halo congeners^[3,9] many of these still suffer some serious drawbacks such as long reaction rate, irregular temperature condition, tedious work-up procedure, unsatisfactory yields, difficulties in azide isolation, formation of troublesome azeotropes, economically non-viable, threat of explosion of azides, removal of surfactants and phase-transfer catalyst from the reaction mixture, harmful to environment due to the use of volatile organic solvents and/or acidic or basic promoters etc. Among all, none of the methodology provides the recyclability of the solvent.

In order to resolve the problems associated with all

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TABLE 1 : Synthesis of alkyl or acyl azides from respective halides and lithium azide using [Bmim]BF₄ or [Bmim]PF₆ as reaction media at ambient temperature

Entry	Substrates	[Bmim]BF ₄		[Bmim]PF ₆		Azides Bp/mm in °C	Bp/mm in °C(lit.)
		Time/min	Yield (%)	Time/min	Yield (%)		
1		15	89	25	90	64-65/ 95	63.5/95 ^[10a]
2		120	87	100	89	190-191/689	190/690 ^[10b]
3		25	87	35	84	71-72 / 77	72/77 ^[10a]
4	2 nd run	25	86	35	83	-	-
5	3 rd run	25	85	35	82	-	-
6		30	82	25	88	72-74 / 30	72/30 ^[10a]
7		25	86	45	89	71-73 /224	71/225 ^[10a]
8		45	79	35	78	61-62/ 690	62/690 ^[10b]
9		20	87	25	85	75-76/ 691	74/690 ^[10b]
10	2 nd run	20	86	25	84	-	-
11	3 rd run	20	85	25	83	-	-
12		50	86	45	89	201-203/690	203/690 ^[10b]
13		40	81	30	84	105-106/690	104/690 ^[10b]
14		30	90	40	87	71-72 / 14	72-73/13 ^[10d]
15		15	90	25	91	§70	§68-69 ^[10c]
16	2 nd run	15	88	25	90	-	-
17	3 rd run	15	89	25	89	-	-

§Denotes the mp/°C of the compound

these methodologies, herein we disclose our findings through environment friendly methodology by employing room temperature ionic liquids [Bmim]BF₄ or [Bmim]PF₆ as solvents for the nucleophilic displacement of alkyl or acyl halides to respective azides at ambient temperature under solvent free and neutral conditions. To our best knowledge this is the sole protocol reported to date, which provides the recyclability of the solvents for the synthesis of alkyl or acyl azides. All synthesized compounds were characterized by comparison of their boiling points or melting point with those of authentic samples^[10]. Since, all alkyl or acyl halides are efficiently transform into azides within short time and gives high reaction yields (TABLE 1).

RESULTS AND DISCUSSION

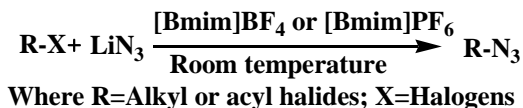
The displacement of iodide in pentyl iodide (Entry 1) is faster than other alkyl halides it might be due to good leaving group characteristic of iodide ion. The reaction

rate of benzyl bromide(Entry 2) is slowest than other alkyl halides eventhough, we get better reaction yields i.e. 87% and 89% with [Bmim]BF₄ and [Bmim]PF₆ respectively. 3-Nitrobenzoyl chloride(Entry 15) an acyl halide is also smoothly converted in to respective azide with highest yields, i.e 90% and 91% with [Bmim]BF₄ and [Bmim]PF₆ respectively. While in case of allyl chloride (Entry 8) we get 79% and 78% yields with [Bmim]BF₄ and [Bimm]PF₆ respectively.

Recyclability study

In order to evaluate the recyclability of [Bmim]BF₄ or [Bmim]PF₆, three different experiments were carried out with different substrates up to three runs. After the initial experimentation with cyclo pentylbromide (Entry 3), the reaction mixture was taken in to diethyl ether and collected. Substrates for the next run were charged into the resulting mother liquor and follow the same reaction condition, 86% with [Bmim] BF₄ and 83% with [Bmim]PF₆ yields were obtained for second

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SCHEME 1

run. By employing the recycling procedure as mentioned above, 85% and 82% yields were observed with [Bmim]BF₄ and [Bmim]PF₆ respectively for the third run. Similar procedure for recyclability was followed for t-butyl chloride (Entry 9), where 86%, 84% and 85%, 83% yields for the second and third runs with [Bmim]BF₄ and [Bmim]PF₆ respectively. In order to further broaden the scope of this protocol, the recyclability study was also carried out for acyl chloride (Entry 15), almost same yield were obtained for second and third runs (TABLE 1). The recyclability of [Bmim]BF₄ and [Bmim]PF₆ were checked up to three runs. The findings revealed that [Bmim]BF₄ or [Bmim]PF₆ can be reusable up to three cycles without any remarkable yield loss. Diethyl ether is used for the work-up procedure offering future scope for improvement.

EXPERIMENTAL

To a stirred solution of lithium azide (0.008mole, 1.5eq.) in [Bmim]BF₄ or [Bmim]PF₆ (1ml), alkyl or acyl halide (0.005mole, 1eq.) was added. The reaction mixture was stirred at room temperature (27°C) for appropriate time (TABLE 1). After completion of reaction as indicated by TLC, the reaction mixture was taken up into diethyl ether (30ml). The combined ether extracts were dried and evaporated under reduce pressure to leave crude azides, which was purified by column chromatography on silica gel (200-400 mesh) using n-pentane as eluents to give pure azides.

CONCLUSION

In conclusion, current protocol describes an efficient process for the azidation of alkyl or acyl halides using imidazolium based ionic liquids as novel and potential reaction media. The notable features of this method are mild reaction condition, simplicity in operation, economically viable, improved yields and reaction rates, cleaner reaction profiles, recyclability of ionic liquids, avoidance

of VOCs as solvent and costly phase-transfer catalysts and eco-friendly process which make it convenient for the synthesis of alkyl or acyl azides having multiple applications.

ACKNOWLEDGEMENT

The authors are grateful to Department of Chemistry, Saurashtra University, Rajkot for providing necessary infrastructural facilities.

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