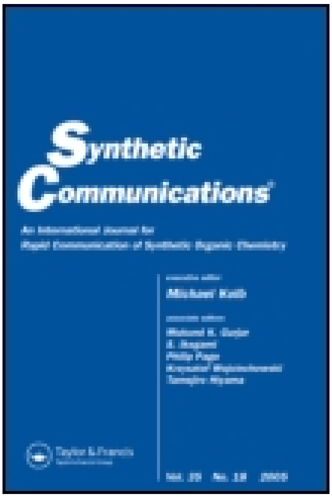
This article was downloaded by: [Temple University Libraries]
On: 05 December 2014, At: 06:20
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Mild, Efficient, and Regioselective Monobromination of Arylamines and Phenols Using [BBIm]Br_3 as a New Reagent

Sanjay P. Borikar [a] , Thomas Daniel [a] & Vincent Paul [a]

[a] Division of Organic Chemistry , National Chemical Laboratory , Pune, India

Published online: 04 Feb 2010.

To cite this article: Sanjay P. Borikar , Thomas Daniel & Vincent Paul (2010) Mild, Efficient, and Regioselective Monobromination of Arylamines and Phenols Using [BBIm]Br_3 as a New Reagent, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 40:5, 647-653, DOI: 10.1080/00397910903009430

To link to this article: http://dx.doi.org/10.1080/00397910903009430

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the “Content”) contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms &

Synthetic Communications®, 40: 647–653, 2010
Copyright © Taylor & Francis Group, LLC
ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910903009430

MILD, EFFICIENT, AND REGIOSELECTIVE MONOBROMINATION OF ARYLAMINES AND PHENOLS USING [BBIm]Br_3 AS A NEW REAGENT

Sanjay P. Borikar, Thomas Daniel, and Vincent Paul
Division of Organic Chemistry, National Chemical Laboratory, Pune, India

We report here an efficient method for the synthesis and characterization of the room-temperature ionic liquid 1,3-di-n-butylimidazolium tribromide ([BBIm]Br_3) (2) and its application as an efficient reagent and solvent for regioselective bromination of arylamines and phenols under mild conditions. The bromination was carried out in the absence of organic solvents, and in most cases, the only extraction solvent needed was water. The spent 1,3-di-n-butylimidazolium bromide (1) was easily recycled.

Keywords: [BBIm]Br_3; ionic liquid; monobromination; regioselective; solvent-free

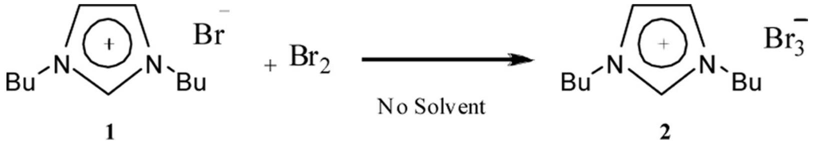
INTRODUCTION

Haloarylamines and halophenols are important versatile synthetic intermediates that can be used as products.[1,2] A variety of methods using molecular bromine,[3] transition-metal catalysts,[4] and alkali metal halides[5] have been reported in the literature. However, bromine is a hazardous chemical that is difficult to manipulate because of its toxicity and high vapor pressure. Many brominating reagents, such as N-bromosuccinimide (NBS),[6] tetrabutylammonium tribromide,[7] 1,8-diazabicyclo[5.4.0]undec-7-ene hydrobromide perbromide (DBUH) · Br_3,[8] cetyltrimethylammonium tribromide,[9] pyridinium tribromide,[10] LiBr/ceric ammononium nitrate,[11] and HBr/dimethylsulfoxide (DMSO),[12] are available. Bromination in classical room-temperature ionic liquid (RTIL) media, such as [BMIm]PF_6, which replace environmentally problematic chlorinated solvents, have been demonstrated.[13] There are some disadvantages in these methods, such as harsh reaction conditions, relatively poor selectivity and yields, or the need for large amount of reagents, oxidants, and catalysts. Therefore, the development of an efficient, selective monobromination reaction of arylamines and phenols is still a major challenge in organic synthesis.

Ionic liquids (ILs) were introduced as alternative green reaction media because of their unique chemical and physical properties of nonvolatility, nonflammability, thermal stability, and ease of recyclability. In recent years, there has been considerable interest in developing green chemistry[14] for organic synthesis because of

Received February 5, 2009.

Address correspondence to Vincent Paul, Division of Organic Chemistry, National Chemical Laboratory, Pune 411 008, India. E-mail: vp.swamy@ncl.res.in



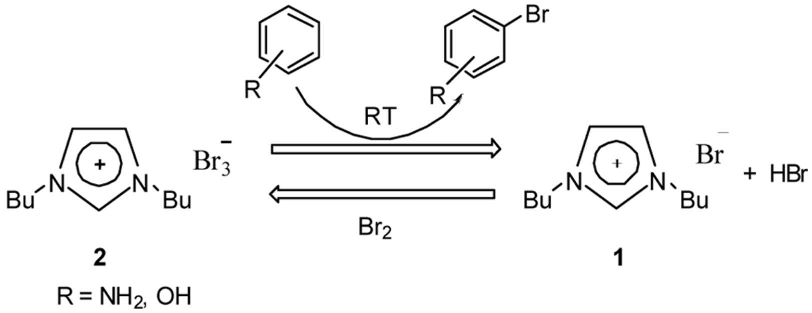
Scheme 1. Synthesis of 1,3-di-*n*-butylimidazolium tribromide.

environmental demand and sustainability. Today, ILs have marched far beyond this border, showing their significant roles in controlling the reactions as new reagents.[15] For example, tribromide ILs based on imidazolium or pyridinium, as nonvolatile and regioselective bromination reagents, have been developed by different groups.[16] There are some disadvantages such as temperature conditions, poor conversion, poor selectivity, and need for more reagent. In continuation of our ongoing program to develop environmentally benign and new synthetic methods using ionic liquids as novel promoters and selective reagents,[17] we report here a new and efficient method for the regioselective monobromination of arylamines and phenols using 1,3-di-*n*-butylimidazolium tribromide ($[BBIm]Br_3$).

RESULTS AND DISCUSSION

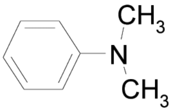
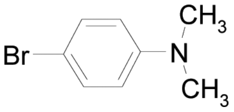
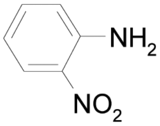
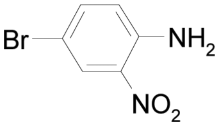
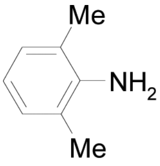
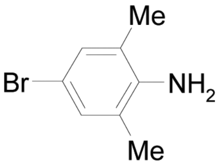
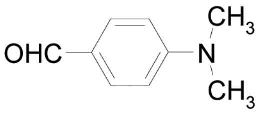
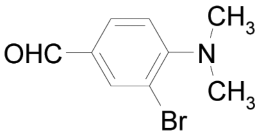
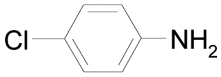
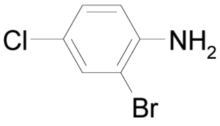
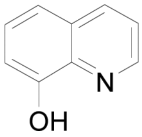
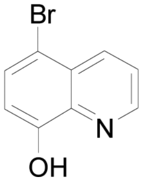
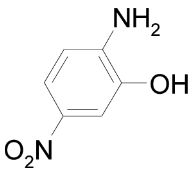
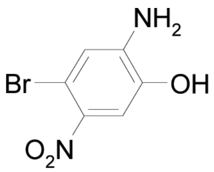
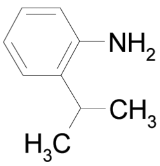
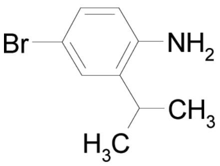
We hereby disclose the synthesis, full characterization, and reactivity of $[BBIm]Br_3$, a proton-free RTIL bromine analog. This does not have any measurable vapor pressure and has been demonstrated for regioselective nuclear monobromination reactions.

This tribromide is a stable liquid, readily prepared by the addition of molecular bromine to [BBIm]Br dropwise under stirring, that forms exothermally the red liquid $[BBIm]Br_3$ (density 1.55 g cm^{-3} and viscosity 59.5 cP) (Scheme 1). Excess bromine absorbed by **2** was removed completely under a high vacuum. RTIL **2** is hydrophobic, forming two phases with water, whereas the IL **1** is highly hydrophilic and hygroscopic. IL **2** can be stored for several months without change of structure and loss of activity. Even after prolonged heating at 60°C under vacuum (<5 mm Hg), IL **2** was recovered unaltered without loss of bromine. IL **2** was miscible with



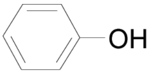
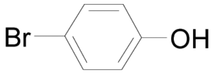
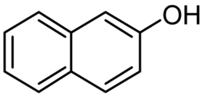
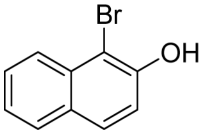
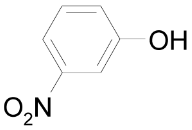
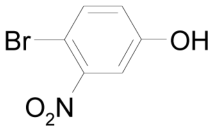
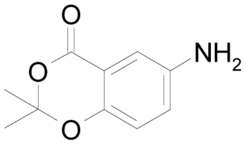
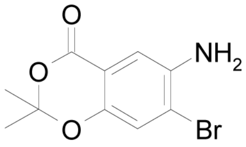
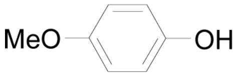
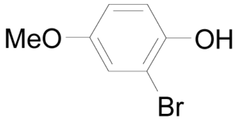
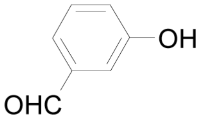
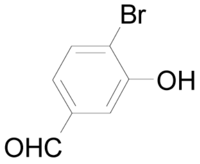
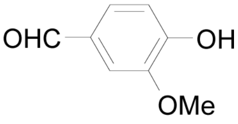
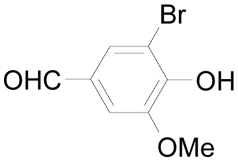
Scheme 2. Regioselective monobromination of arylamines and phenols with $[BBIm]Br_3$ under solvent-free conditions.

Table 1. Solvent-free bromination using $[BBIm]Br_3$ at room temperature[a]

Entry	Substrate	Product	Time	Yield (%)[b]
1			5 min	98
2			15 min	95
3			Immediately	97
4			8 min	92
5			Immediately	98
6			2 min	97
7			35 min	89
8			Immediately	94

(*Continued*)

Table 1. Continued

Entry	Substrate	Product	Time	Yield (%)[b]
9			Immediately	97
10			3 min	98
11			8 min	95
12			13 min	97
13			15 min	91
14			8 min	95
15			Immediately	98

[a] All reactions were carried out with 1.0 equivalent of [BBIm]Br_3 at room temperature.

[b] All compounds showed satisfactory ^1H NMR and spectral data.

MeOH/EtOH, acetone, DMSO, and other strong polar organic solvents and immiscible with water, ether, $CHCl_3$, and other weakly polar organic solvents.

1,3-Di-*n*-butylimidazolium tribromide ([BBIm]Br_3) is an efficient and novel reagent for the regioselective monobromination of various arylamines and phenols with complete selectivity and excellent yields (Scheme 2), and the results are summarized in Table 1.

Phenol was cleanly monobrominated in the absence of any solvent at room temperature by [BBIm]Br_3, affording exclusively p-bromophenol (Table 1, entry 11). *m*-Nitrophenol was monobrominated in 8 min (entry 11). β-Naphthol, a bulky molecule, took only 3 min for monobromination (entry 10). Similarly, a variety of substituted arylamines and phenols underwent regioselective monobromination (Table 1, entries 1–15).

All the reactions were quenched by adding water. This caused precipitation of the products as solids or oils, which were readily separated, washed with fresh portions of water, and then dried (either with sodium sulfate or in vacuo). The aqueous phase containing highly water-soluble IL **1** was easily concentrated in vacuo to recycle **1**, which then could be used to regenerate RTIL **2** with bromine (Scheme 2).

All the reactions were carried out in air at room temperature, adding 1.0 equiv of [BBIm]Br_3 to an equimolar amount of substrate without any solvent. Although the reactions were slightly exothermic, no special precautions were taken for cooling. They were monitored by thin-layer chromatography (TLC) and stopped after the disappearance of the substrate.

CONCLUSION

In conclusion, a new RTIL bromine analog, which is safer and easier to use, was synthesized and characterized. It displayed improved selectivity and better reaction conditions than current monobromination techniques. This new functional [BBIm]Br_3 may be classified as "green" for the following reasons: (1) it eliminates toxic bromine vapors, (2) the bromine carrier [BBIm]Br can be easily recovered and recycled, and (3) it avoids the use of organic solvents. Furthermore, [BBIm]Br_3 afforded good to excellent yields for a wide variety of arylamines and phenols at room temperature.

EXPERIMENTAL

General

The NMR spectra were recorded on a Bruker system (200 MHz for ^1H and 75 MHz for ^{13}C) using tetramethylsilane (TMS) as an internal standard. The reactions were monitored by TLC using 0.25-mm Merck silica-gel plates (60F-254), and the products were purified by column chromatography on silica gel (60–120 mesh) obtained from M/s Spectrochem India Ltd. Infrared (IR) spectra were recorded on Perkin-Elmer Fourier transform (FT)–IR 16 PC spectrometer.

Preparation of [BBIm]Br_3 Ionic Liquid

In a fume cupboard, molecular bromine (1.956 mL, 0.038 mol) was added dropwise over 15 min to [BBIm]Br (10.0 g, 0.038 mol) with stirring and cooling in a ice bath, affording the deep red liquid IL **2**, and stirring was continued for 2 h. Under reduced pressure over 5 h at 60°C, the pure IL **2** was obtained 15.5 g (96.1%) as a red oil. ^1H NMR ($CDCl_3$, 200 MHz): δ 0.98 (t, 6H, $J = 7.31$ Hz), 1.36 (m, 4H), 1.90 (m, 4H), 4.31 (t, 4H, $J = 7.52$ Hz), 7.44 (d, 2H, $J = 8.11$ Hz), 8.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 12.86, 18.82, 31.60, 49.11, 121.92, 135.99; MS (ESI): 181 (M-X_3). Anal. calcd. for $C_{11}H_{21}Br_3N_2$: C, 31.38; H, 5.03; N, 6.65. Found: C, 31.31; H, 4.93; N, 6.50.

Typical Experimental Procedure for Monobromination of Arylamines and Phenols

1,3-Di-*n*-butylimidazolium tribromide (3.3 mmol) was added to a stirred mixture of arylamines or phenols (3.3 mmol) at room temperature. After completion of the reaction as indicated by TLC, water was added into the reaction mixture to quench the IL. The resulting reaction mixture was extracted with diethyl ether, and the organic layer was separated, dried over sodium sulfate, and concentrated to afford pure monobromo arylamines or monobromo phenols.

ACKNOWLEDGMENTS

This work was carried out under Indo-Mexican Inter-Governmental joint project (GAP 264126) and is greatly acknowledged. We are grateful to Dr. Ganesh Pandey for his support and encouragement.

REFERENCES

1. (a) Kuroboshi, M.; Waki, Y.; Tanaka, H. Palladium-catalyzed tetrakis(dimethylamino)ethylene-promoted reductive coupling of aryl halides. *J. Org. Chem.* **2003**, *68*, 3938; (b) Qingwei, Y.; Elizabeth, P. K.; Zhi, Y. Ligand-free Heck reaction: $Pd(OAc)_2$ as an active catalyst revisited. *J. Org. Chem.* **2003**, *68*, 7528.
2. (a) Gao, C.; Tao, X.; Qian, Y.; Huang, J. A highly efficient catalytic system for cross-coupling of aryl chlorides and bromides with malononitrile anion by palladium carbene complexes. *Chem. Commun.* **2003**, *12*, 1444; (b) Euzenat, L.; Horhant, D.; Ribourdouille, Y.; Duriez, C.; Alcaraz, G.; Vaultier, M. Monomeric (dialkylamino)-boranes: A new and efficient boron source in palladium-catalyzed C-B bond formation with aryl halides. *Chem. Commun.* **2003**, *18*, 2280.
3. Onaka, M.; Izumi, Y. Selective monobromination of aniline derivatives by use of bromine adsorbed on zeolite 5A. *Chem. Lett.* **1984**, *13*, 2007.
4. Larock, R. C. *Comprehensive Organic Transformation*; VCH: New York, 1989; p. 315.
5. Dewkar, G. K.; Narina, S. V.; Sudalai, A. $NaIO_4$-mediated selective oxidative halogenation of alkenes and aromatics using alkali metal halides. *Org. Lett.* **2003**, *5*, 4501.
6. Paul, V.; Sudalai, A.; Daniel, T.; Srinivasan, K. V. Regioselective bromination of activated aromatic substrates with N-bromosuccinimide over HZSM-5. *Tetrahedron Lett.* **1994**, *35*, 7055.
7. Buckles, R. E.; Popov, A. I.; Zelezny, W. F.; Smith, R. J. Spectrophotometric study of tetrabutylammonium tribromide. *J. Am. Chem. Soc.* **1951**, *73*, 4525.
8. Muathen, H. A. 1,8-Diazabicyclo[5.4.0]undec-7-ene hydrobromide perbromide: A new, mild, stable, brominating agent for aromatic compounds. *J. Org. Chem.* **1992**, *57*, 2740.
9. Cerichelli, G.; Luchetti, L.; Mancini, G. Surfactant control of the *ortho*/*para* ratio in the bromination of anilines. *Tetrahedron Lett.* **1989**, *30*, 6209.
10. Reeves, W. P.; King, R. M. A convenient method for bromination of aromatic amines. *Synth. Commun.* **1993**, *23*, 855.

11. Roy, S. C.; Guin, C.; Rana, K. K.; Maiti, G. An efficient chemo- and regioselective oxidative nuclear bromination of activated aromatic compounds using lithium bromide and ceric ammonium nitrate. *Tetrahedron Lett.* **2001**, *42*, 6941.
12. Srivastava, S. K.; Chauhan, P. M. S.; Bhaduri, A. P. Novel site-specific one–step bromination of substituted benzenes. *Chem. Commun.* **1996**, *23*, 2679.
13. Chiappe, C.; Capraro, D.; Conte, V.; Pieraccini, D. Stereoselective halogenations of alkenes and alkynes in ionic liquids. *Org. Lett.* **2001**, *3*, 1061.
14. Horvath, I. T.; Anastas, P. T. Innovations and green chemistry. *Chem. Rev.* **2007**, *107*, 2169.
15. (a) Ranu, B. C.; Banerjee, S. J. Ionic liquid as reagent: A green procedure for the regioselective conversion of epoxides to *vicinal*-halohydrins using [AcMIm]X under catalyst and solvent-free conditions. *J. Org. Chem.* **2005**, *70*, 4517; (b) Davis, J. H. Task-specific ionic liquids. *Chem. Lett.* **2004**, *33*, 1072; (c) Earle, M. J.; Katdare, S. P.; Seddon, K. R. Paradigm confirmed: The first use of ionic liquids to dramatically influence the outcome of chemical reactions. *Org. Lett.* **2004**, *6*, 707.
16. (a) Iranpoor, N.; Firouzabadi, H.; Azadi, R. A new diphenylphosphinite ionic liquid (IL-$OPPh_2$) as reagent and solvent for highly selective bromination, thiocyanation, or isothiocyanation of alcohols and trimethylsilyl and tetrahydropyranyl ethers. *Tetrahedron Lett.* **2006**, *47*, 5531; (b) Le, Z. G.; Chen, Z. C.; Hu, Y.; Zheng, Q. G. [Bmim]Br_3 as a new reagent for regioselective monobromination of arylamines under solvent-free conditions. *Synthesis* **2004**, *17*, 2809; (c) Salazar, J.; Dorta, R. Pentylpyridinium tribromide: A vapor pressure free room temperature ionic liquid analogue of bromine. *Synlett* **2004**, *7*, 1318; (d) Chiappe, C.; Leandri, E.; Pieraccini, D. Highly efficient bromination of aromatic compounds using 3-methylimidazolium tribromide as reagent/solvent. *Chem. Commun.* **2004**, *22*, 2536.
17. Borikar, S. P.; Daniel, T.; Paul, V. An efficient, rapid, and regioselective bromination of anilines and phenols with 1-butyl-3-methylpyridinium tribromide as a new reagent/solvent under mild conditions. *Tetrahedron Lett.* **2009**, *50*, 1007.