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Mild Oxidation of Alcohols with *O*-Iodoxybenzoic Acid (IBX) in Ionic Liquid 1-Butyl-3-methyl-imidazolium Chloride and Water

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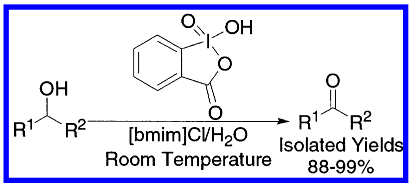
ABSTRACT



A mild, efficient, and eco-friendly procedure for the oxidation of alcohols with IBX in ionic liquid [bmim]Cl and water has been developed. Simply stirring of a solution of the alcohol and IBX in [bmim]Cl/water at room temperature followed by extraction with ether or ethyl acetate and removal of the solvent gives excellent yields of the corresponding carbonyl compounds. Recycling and reuse of the oxidant and ionic liquid have also been reported.

Hypervalent iodine reagents have attracted increasing interest during the past decade because of their selective, mild, and environmentally friendly properties as oxidizing agents in organic synthesis.[1] IBX (*o*-iodoxybenzoic acid) has gained great popularity as a mild oxidant for the conversion of alcohols to aldehydes or ketones.[2,3] IBX is virtually insoluble in most organic solvents, which accounts for the great length of time between the discovery of IBX and the first practical applications of it in DMSO (the only solvent in which it does dissolve).[1,5] While not entirely inconvenient, the limitations of DMSO as a solvent are apparent and sufficient to have motivated two independent syntheses of solid-phase analogues of IBX (polystyrene- and silica-bound).[6] In each case, the authors correctly note that these solid-phase reagents expand the range of viable solvents, simplify separation of oxidation byproducts, and facilitate recovery and reuse of the oxidant. However, it is obvious that the synthesis of these solid-phase reagents is laborious and time-consuming. Most recently, researchers have turned their attention to carrying out the oxidation in common, low boiling point molecular solvents by elevating the reaction temperature or using a suitable catalyst.[7] These two improvements are effective

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(1) (a) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis;* Academic Press: London, 1997. (b) Stang, P. J. *J. Org. Chem.* **2003**, *68*, 2997. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (d) Wirth, T.; Hirt, U. H. *Synthesis* **1999**, 1271.

(2) (a) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019. (b) Frigerio, M.; Santagostino, M.; Sputore, S.; Palmisano, G. *J. Org. Chem.* **1995**, *60*, 7272. (c) De Munari, S.; Frigerio, M.; Santagastino, M. *J. Org. Chem.* **1996**, *61*, 9272. See also ref 3a.

(3) IBX has also found use in several other oxidative transformations. For an overview, see: (a) Wirth, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 2812. For more recent developments, see: (b) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Barluenga, S.; Hunt, W. K.; Kranich, R.; Vega, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 2233. (c) Nicolaou, K. C.; Montagnon, T.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2002**, *124*, 2245.

(4) IBX was first prepared over 100 years ago: Hartman, C.; Mayer, V. *Chem. Ber.* **1893**, *26*, 1727.

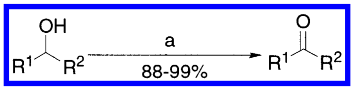
(5) Prior to its use as a terminal oxidant in its own right, IBX was identified as a valuable precursor to Dess−Martin Periodinate: Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277 and references therein.

(6) (a) Mülbaier, M.; Giannis, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4393. (b) Sorg, G.; Mengel, A.; Jung, G.; Rademan, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4395.

(7) (a) More, J. D.; Finney, N. S. *Org. Lett.* **2002**, *4*, 3001. (b) Surendra, K.; Krishnaveni, N. S.; Reddy, M. A.; Nageswar, Y. V. D.; Rao, K. R. *J. Org. Chem.* **2003**, *68*, 2058.

10.1021/ol0351549 CCC: $25.00

Scheme 1[a]



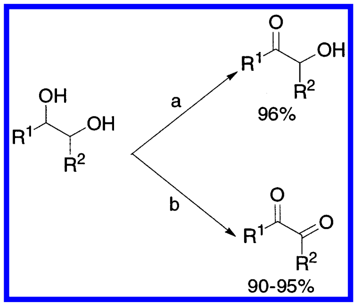
[a] Reagents and conditions: (a) IBX (1.1 equiv), [bmim]Cl/H$_2$O, 20 °C.

alternatives to classical procedure by avoiding the use of the high boiling point, difficultly removed solvent DMSO.[2a] However, the elevation of reaction temperature may cause decomposition of starting materials and bring about side reactions.

Ambient-temperature ionic liquids have been emerging as promising green solvents for the past decade.[8] Their nonvolatile nature gives them significant advantage in minimizing solvent consumption. Their polarity renders them good solvents for various organic, inorganic, and polymeric compounds and therefore good media for homogeneous reactions.[8c] Because of their unique solubility properties, i.e., miscibility gap between water and organic solvents, they have become interesting candidates for separation processes by simple liquid−liquid extraction with either aqueous or conventional organic solvents.[9]

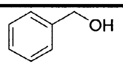
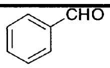
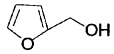
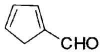
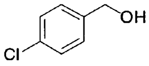
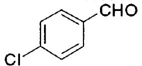
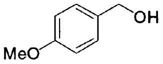
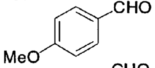
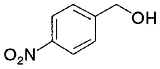
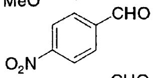
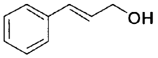
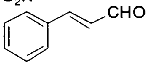
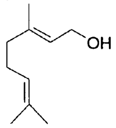
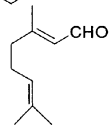
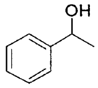
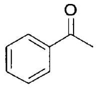
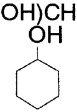
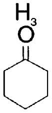
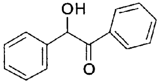
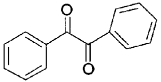
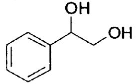
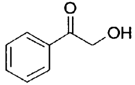
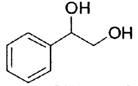
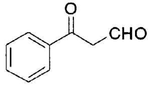
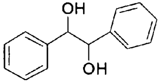
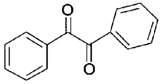
In our efforts to investigate the range of organic reactions possible in ionic liquids,[10] we report herein a simple, mild, efficient, and practical method for the oxidation of alcohols and diols with IBX using 1-butyl-3-methylimidazolium chloride ([bmim]Cl) as the solvent (Schemes 1 and 2).

Scheme 2[a]



[a] Reagents and conditions: (a) IBX (1.1 equiv), [bmim]Cl/H$_2$O, 20 °C; (b) IBX (2.5 equiv), [bmim]Cl/H$_2$O, 20 °C.

Table 1. Oxidation of Alcohols with IBX in [bmim]Cl/Water

entry[a]	alcohol	product[c]	yield (%)[e]
1			99
2			90
3			99
4			98
5			91
6			91
7			94
8	CH$_3$(CH$_2$)$_5$CH$_2$OH	CH$_3$(CH$_2$)$_5$CHO	90
9			98
10	CH$_3$(CH$_2$)$_2$CH(OH)CH$_3$	CH$_3$(CH$_2$)$_2$COCH$_3$	93
11			88
12			96
13			96[d]
14[b]			90[d]
15[b]			95

We examined the reaction in six ambient-temperature ionic liquids, butylpyridinium tetrafluoroborate (bpyBF$_4$), butylpyridinium hexafluorophosphorate (bpyPF$_6$), butylpyridinium chloride (bpyCl), 1-butyl-3-methylimidazolium chloride ([bmim]Cl), 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF$_4$]), and 1-butyl-3-methylimidazolium hexafluorophosphorate [bmim][PF$_6$]. None of these ionic liquids can dissolve IBX even when heated to 80 °C except [bmim]Cl, which can readily dissolve IBX in the presence of a small amount of water at room temperature to form a homogeneous solution.

The reactions were carried out by dissolving IBX in [bmim]Cl and water at room temperature followed by the addition of corresponding alcohol. All the alcohols investigated gave excellent yields ranging from 88 to 99%, and the products were substantially pure as indicated by ^{1}H NMR and HPLC analysis (Table 1, purities as assessed by HPLC >95%).[11] No overoxidation to acids was observed in the case of aldehyde products (entries 1−8, Table 1). Both aryl-

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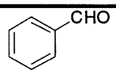
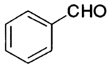
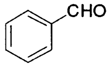
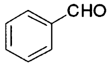
[8] (a) Zhao, H.; Malhotra, S. V. *Aldrichimica Acta* **2002**, *35*, 75. (b) Dupont, J.; De Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667. (c) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772. (d) Welton, T. *Chem. Rev.* **1999**, *99*, 2071.

[9] Huddleston, J. G.; Willauer, H. D.; Swatloski, R. P.; Visser, A. E.; Rogers, R. D. *Chem. Commun.* **1998**, 1765.

[10] (a) Xie, Y.-Y.; Chen, Z.-C.; Zheng, Q.-G. *Synthesis* **2002**, 1505. (b) Xie, Y.-Y.; Chen, Z.-C.; Zheng, Q.-G. *J. Chem. Res., Synop.* **2002**, 618. (c) Su, C.; Chen, Z.-C.; Zheng, Q.-G. *Synthesis* **2003**, 555.

[11] Alcohols in Table 1 are commercially available and were used as received.

Table 2. Results Obtained Using Recycled Ionic Liquid

entry	product	cycle	yield (%)[a]
1		1	99
2		2	99
3		3	98
4		4	98

[a] Isolated yields based on benzyl alcohol.

carbinols and aliphatic alcohols gave good to excellent yields. Various functionalities such as methoxy and nitro groups, alkene double bonds, and a furan ring can tolerate the oxidation. 1,2-Diols were cleanly oxidized, with a stoichiometric amount of IBX, to α-dicarbonyls (entries 14−15, Table 1) or α-ketol (entry 13, Table 1) without cleavage of the 1,2-diol bond. All of the compounds were characterized by mass, ^{1}H NMR, and IR and by comparison with the known compounds.[7b,12]

In these reactions, iodosobenzoic acid (IBA), obtained from the reduction of IBX, can be reoxidized to active IBX using standard procedures.[13] The regenerated IBX is indistinguishable from IBX freshly prepared from *o*-iodobenzoic acid. Ionic liquid [bmim]Cl has also been recovered and reused without decreasing the yields of products (Table 2).[13]

As a final point, we have presented an elegant and simple methodology for the oxidation of a variety of alcohols using IBX at room temperature with [bmim]Cl and water as a solvent. Compared with the classical procedure in DMSO, this procedure in ambient-temperature ionic liquid [bmim]Cl and water shares the advantage of mild reaction conditions, homogeneous solution, facile recovery of the oxidant, and excellent yields of products and is, to some extent, superior in terms of the ready separation of products, small degree of consumption of the solvent, and recycling of the ionic liquid without decreasing the yields of products. We anticipate that this protocol will be of broad interest and use to the chemical community.[14]

Acknowledgment. We thank the analytical center of chemistry department, Zhejiang University for providing the spectra data.

Supporting Information Available: Experimental procedure and spectral data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[12] Most of the spectral data for the products can be obtained from Sigma-Aldrich via the Internet at http://www.Sigmaaldrich.com. Data for the rest of the products are available in ref 7b.

[13] In a representative (and unoptimized) case, IBA was recovered essentially quantitatively by first extracting out benzaldehyde with ether (3 × 10 mL) from the reaction mixture and then adding 10 mL of water to the remaining solution to precipitate IBA followed by filtration. Oxidation of IBA to IBX was carried out in deionized water at 70 °C using Oxone as the oxidant. For details, see: Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537. About 55% yield of IBX was recovered, which is identical to authentic IBX as indicated by ^{1}H NMR (DMSO-d_6) and elemental analysis (>99% purity by HPLC). Ionic liquid [bmim]Cl was recovered by evaporating the filtrate under vacuum to remove water, and more than 95% yield of recovered [bmim]Cl was obtained and reused (containing trace IBX, which did not affect the oxidation at all).

[14] **Representative Experimental Procedure.** To a mixture of [bmim]Cl (3 mL) and water (0.6 mL) was added IBX (0.31 g, 1.1 mmol). The resulting mixture was stirred at room temperature for 5−10 min, and benzyl alcohol (0.11 g, 1 mmol) was added. The reaction mixture was stirred at room temperature for 5 min, and then the product was extracted with ether (3 × 10 mL). The organic phase was dried over anhydrous sodium sulfate and concentrated under vacuum to yield 0.11 g (99% yield, >98% pure by HPLC) of benzaldehyde as a pale yellow liquid.