Synthetic Communications®, 36: 2887–2892, 2006

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910600770821

Mild Oxidation of Alcohols with *o*-Iodoxybenzoic Acid (IBX) in a Water/CH_2Cl_2 Mixture in the Presence of Phase-Transfer Catalyst

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Abstract: A mild oxidation of alcohols to the respective carbonyl compounds with *o*-iodoxybenzoic acid (IBX) catalyzed by *n*-Bu_4NBr in a water/dichloromethane (1:1) mixture is described. The method offers the advantage of a simple, inexpensive catalyst and the diminution of organic solvent employed in the reaction.

Keywords: Alcohols, IBX, oxidation, phase-transfer catalyst

INTRODUCTION

Hypervalent iodine reagents have gained much attention because of their mild, selective, and environmentally friendly properties as oxidizing agents in organic synthesis.[1] Among this class of compounds, the Dess–Martin periodinane (DMP) and its precursor, *o*-iodoxybenzoic acid (IBX), have gained popularity as the reagents of choice for conversion of alcohols to aldehydes or ketones and other synthetically useful oxidative transformations.[2–4] Reported since 1893,[5] IBX has been rarely used because of its virtual insolubility in most common organic solvents. The first practical applications of IBX have been conducted in DMSO.[3] Even though not entirely inconvenient,

Received in India February 28, 2006

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the limitations of using the high-boiling dimethyl sulfoxide (DMSO) as a solvent are apparent and have led to many variations.

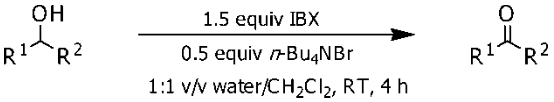
In recent years, there are several syntheses of solid-supported IBX.[6] In each work, the authors demonstrated that these solid-supported analogues of IBX have found use as oxidant particularly suitable for converting alcohols to the respective carbonyl compounds, in good to excellent yields. Efforts toward the synthesis of modified IBX reagents that allow better solubility in other solvents besides DMSO have also been reported.[7] Recently, it was demonstrated that IBX is an effective heterogeneous oxidant in most organic solvents at elevated temperature[8] or in the presence of a suitable catalyst.[9] Most recently, the oxidation of a diverse collection of alcohols using IBX was carried out in a mixture of an ionic liquid and water as the solvent.[10] The authors noted that this methodology represents mild and homogeneous reaction conditions, simplifies separation of oxidation by-products, and facilitates the recovery and reuse of the oxidant. Quite remarkably, IBX has recently been demonstrated to be employed as an oxidant under solvent-free conditions,[11] as well as a catalytic oxidant in the presence of a co-oxidizing reagent.[12]

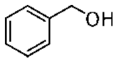
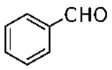
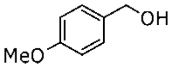
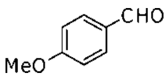
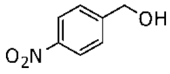
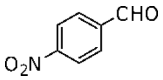
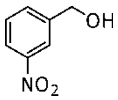
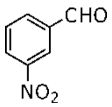
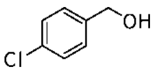
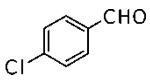
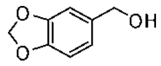
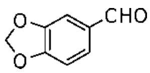
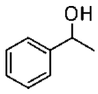
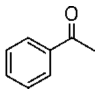
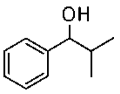
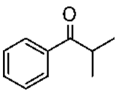
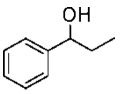
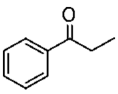
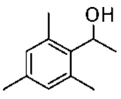
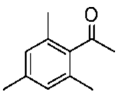
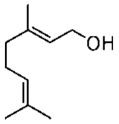
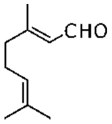
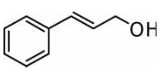
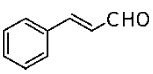
RESULTS AND DISCUSSION

As a part of our research program to develop IBX oxidation under various conditions and novel applications of IBX, we have previously reported a selective oxidation of secondary alcohols by IBX.[13] We now describe a simple and mild method for the oxidation of benzylic, allylic, and aliphatic alcohols with IBX catalyzed by *n*-Bu_4NBr in a water/CH_2Cl_2 mixture as the solvent. This allows the oxidation reaction to proceed at room temperature in an aqueous/organic medium.

Typical reaction conditions employed 1.5 equivalents of IBX and 0.5 equivalent of *n*-Bu_4NBr in 1:1 v/v mixture of water/CH_2Cl_2 as a solvent. The reaction was maintained at room temperature for 4 h. A variety of alcohols underwent oxidation to give the corresponding carbonyl compounds in variable yields. Among the alcohols investigated, benzylic alcohols gave moderate to excellent yields of the corresponding carbonyl compounds. The oxidation efficiency is seemingly dependent on the electronic environment on the phenyl ring. Initially, the study began with the oxidation of benyl alcohol and substituted benzyl alcohols containing substituents on phenyl ring (entries 1–6, Table 1). Benzyl alcohol was oxidized to benzaldehyde in good yield (81%, entry 1). The reactions show a dramatic substituent effect on the oxidative process. Electron-releasing substituents such as the methoxy group improved the yield (92%, entry 2). In contrast, the presence of the electron-withdrawing groups resulted in low yields of the aldehyde products as a function of electron-attracting power. The reaction of *p*-nitro- and *m*-nitrobenzyl alcohols sluggishly proceeded to give the corresponding aldehydes in low yields (entries 3 and 4). *p*-Chlorobenzyl alcohol gave *p*-chlorobenzaldehyde in

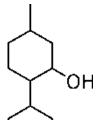
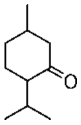
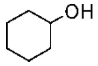
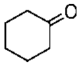
Table 1. Oxidation of alcohols with IBX using catalytic *n*-Bu_4NBr in 1:1 v/v water/CH_2Cl_2 mixture



Entry	Substrate	Product	Yield (%)[a]
1			81
2			92
3			12
4			19
5			72
6			37
7			71
8			62
9			66
10			94
11			72
12			52

(*continued*)

Table 1. Continued

Entry	Substrate	Product	Yield (%)[a]
13	$H_3C(H_2C)_4{-}CH_2OH$	$H_3C(H_2C)_4{-}CHO$	—[b]
14	$H_3C(H_2C)_6{-}CH_2OH$	$H_3C(H_2C)_6{-}CHO$	—[b]
15			19
16			80

[a]Yield of product isolated after column chromatography.
[b]Less than 1% conversion to aldehyde was observed by ^{1}H NMR (300 MHz).

moderate yield (72%, entry 5). To our surprise, 3,4-(methylenedioxy)benzyl alcohol afforded piperonal in low yield (37%, entry 6). Secondary benzylic oxidation also gave satisfactory results. 1-Phenylethanol smoothly underwent the oxidation to afford acetophenone in moderate yield (71%, entry 7). The yields were decreased when steric demanding of the alkyl groups increased (entries 8 and 9). Interestingly, when highly hindered mesityl methyl carbinol was employed as a substrate (entry 10), the corresponding ketone was obtained in excellent yield (94%). Oxidation of primary allylic alcohols was also investigated to result in the formation of α,β-unsaturated aldehydes in moderate to good yields (entries 11 and 12). It should be noted that primary aliphatic alcohol was sluggish to undergo oxidation under the reaction conditions (entries 13 and 14). On the contrary, even though menthol was not a good substrate under the reaction conditions employed, a simple aliphatic secondary alcohol (i.e., cyclohexanol) was oxidized to cyclohexanone in good yield (entries 15 and 16). All of the carbonyl compounds were characterized by ^{1}H NMR, IR, and comparison with the known compounds.

In conclusion, we have demonstrated a mild, convenient, and easy procedure for the oxidation of alcohols to carbonyl compounds using IBX at ambient temperature in the presence of a phase-transfer catalyst (n-Bu_4NBr) under a biphasic system (aqueous/dichloromethane mixture).

EXPERIMENTAL

General Procedure for the Oxidation of Alcohols with IBX Catalyzed by n-Bu_4NBr

To a suspension of IBX (1.5 equiv) in 1:1 v/v mixture of water/CH_2Cl_2 (0.25 M based on starting alcohol), n-Bu_4NBr (0.5 equiv) was added followed by alcohol (1.0 mmol). The resulting mixture was stirred at room temperature for an additional 4 h. The residual solids were filtered through filter paper and washed thoroughly with diethyl ether. The filtrate was washed successively with 8% aqueous sodium thiosulfate (15 mL), water (2 × 15 mL) and brine (1 × 15 mL). The organic layer was dried (anh. Na_2SO_4), filtered, and evaporated (aspirator) to give a crude product, which was purified by column chromatography on silica gel. All products were identified by ^1H NMR spectroscopy.

ACKNOWLEDGMENT

We acknowledge the financial support by the Thailand Research Fund (TRF) for the post doctoral research fellowship awarded to C. K. The support provided by the Postgraduate Education and Research Program in Chemistry (PERCH) and the facilities at the Department of Chemistry, Mahidol University, are also gratefully acknowledged.

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