A Mild and Versatile Method for the Oxidative Cleavage of Oximes and Tosylhydrazones to Carbonyl Compounds

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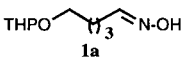
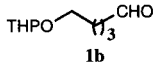
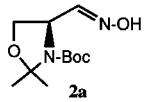
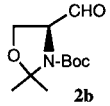
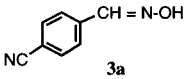
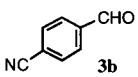
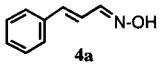
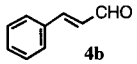
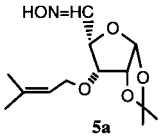
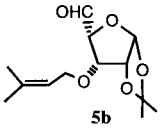
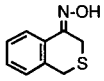
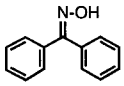
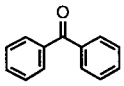
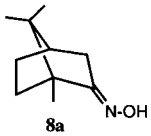
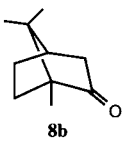
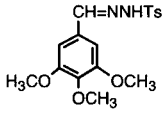
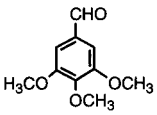
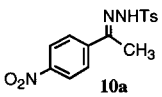
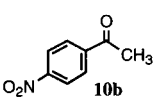
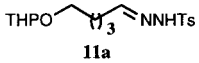
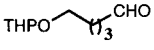
Abstract : 1-Hydroxy-1,2-benziodoxol-3(1H)-one 1-oxide (IBX) was found to be an efficient and selective reagent for the mild oxidative cleavage of the C=N of oximes and tosylhydrazones to yield their corresponding carbonyl compounds rapidly at room temperature in high yields.

Oximes of aldehydes and ketones not only served as protecting[1], selective α-activating[2] groups and intermediates for many reactions such as the preparation of amides by Beckmann rearrangement[3] but also represents a series of derivatives for classical identification of carbonyl compounds[4] as exemplified in the synthesis of erythromycin derivatives[5]. Since many valuable reactions have been developed to prepare oximes from other than carbonyl compounds (such as Barton reaction[6]), an efficient deoximation reaction assumes great importance leading to new methods of preparing carbonyl compounds[7]. Although several methods are available for oxime cleavage, acid catalyzed hydrolysis of oximes to carbonyl compounds and hydroxylamines was proved unsatisfactory, especially when acid-sensitive functional groups are present[8]. Therefore, oxidative[9] or reductive[10], clay-supported ferric nitrite[11], trimethylsilyl chlorochromate[12], titanium silicalite-1[13], zirconium sulfophenyl phosphonate[14], N-haloamides[15] manganese triacetate[16] and microwave-assisted[17] deoximation reactions have been developed.

However, many of the conventional procedures for the preparation of carbonyl compounds from their nitrogen derivatives have several limitations; i.e. the reagents used are often hazardous and expensive transition metals etc. along with reactions requiring long reaction times or reflux temperatures. Moreover, many of the methods cited in the literature do not describe the deoximation of aldoximes[9a,b,18], give low yields of aldehydes[19], or the liberated aldehydes are overoxidised. Benzaldoxime, for example, was deoximated in poor yield by pyridinium chlorochromate (PCC)[20], in 35% yield by PCC-H_2O_2[21], in 56% yield by trimethylammonium chlorochromate[22] and in 72% yield by chromium trioxide-chlorotrimethylsilane[23]. In order to circumvent some of the problems highlighted above, a mild and efficient method is still warranted for the regeneration of carbonyl compounds. Herein, we wish to report a new and practical method for the cleavage of oximes and tosylhydrazones with inexpensive *o*-iodoxybenzoic acid (IBX)[24], as an oxidising agent, that overcomes many of the disadvantages associated with oxidative methods developed so far. The salient features of our method are, the reaction proceeds efficiently in high yields at room temperature within a few minutes[25], mild nature of IBX, easy work-up procedure.

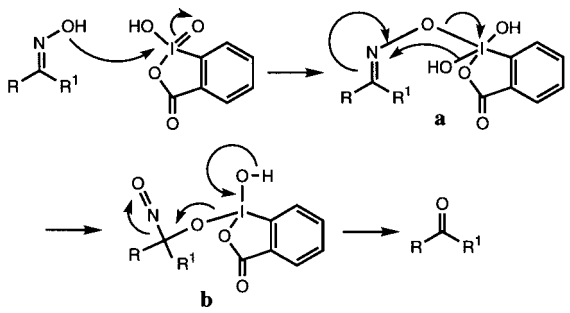
Several examples illustrating this procedure for the conversion of oximes and tosylhydrazones to parent carbonyl compounds are summarized in Table-1. It is noteworthy that, unlike other oxidative hydrolytic methods, the major drawback of over-oxidation of the resulting aldehydes, is not encountered under the reaction conditions (entries 1-5). Even the sterically hindered camphor oxime has been successfully converted to camphor in good yields (entry 8). Interestingly, the α,β-unsaturated oximes underwent deoximation very efficiently without affecting the C=C bond and the reaction is essentially chemoselective (entry 4). Similarly, acid-sensitive as well as base-sensitive protecting groups, and ester and ether linkages can survive under the present conditions. In addition to that, stereochemical integrity at the aldehyde-bearing carbon was retained (entries 2[26] and 5).

Table 1. Oxidative cleavage of oximes and tosylhydrazones with IBX

entry	substrate	time, min.	product[27]	isolated Yield (%)
1	 **1a**	22	 **1b**	88
2	 **2a**	25	 **2b**	91
3	 **3a**	20	 **3b**	95
4	 **4a**	24	 **4b**	86
5	 **5a**	22	 **5b**	90
6	 **6a**	18	 **6b**	87
7	 **7a**	20	 **7b**	92
8	 **8a**	27	 **8b**	85
9	 **9a**	25	 **9b**	92
10	 **10a**	28	 **10b**	89
11	 **11a**	38	 **1b**	83

A proposed reaction mechanism is shown in scheme 1. An intermediate **b** is formed through nucleophilic addition of the hydroxyl group of oxime to IBX, followed by the sigmatropic rearrangement of **a**. The

intermediate **b** undergoes decomposition to give the carbonyl compound.



Scheme 1

In conclusion, we have developed a facile method for the regeneration of carbonyl compounds from both aldoximes, ketoximes and tosylhydrazones which has wide scope, a simple procedure, high yields, reduced reaction times and mild conditions. Further applications of this reagent to many other types of organic functional group transformation reactions are in progress.

General procedure: To a stirred solution of oxime or tosylhydrazone (3.0 mmol) in DMSO-THF (1:3, 3 mL) was added solid IBX (4.5 mmol) in portions during 2-3 minutes. The suspension was vigorously stirred at room temperature for specified time (Table 1). The reaction was monitored by TLC. After completion, it was diluted with water (2x5 mL), the white precipitate was filtered off, and the reaction mixture was extracted with ether (2x25 mL). The combined organic phase was washed with brine, dried (Na_2SO_4) and the solvent was removed *in vacuo* to afford the crude product which was purified by column chromatography on silica gel (E-Merck 60-120 mesh).

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25. For a most recent report using expensive 70% tert-butyl hydroperoxide (TBHP), which required 8-18 hr for the completion of the deoximation and constitutes a serious limitation to this procedure, see Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Sudalai, A. *Tetrahedron Lett*. **1997**, *38*, 653.
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27. All the products were characterized by IR, ^{1}H NMR and mass spectral data. The products **3b,4b,6b-10b** melting points were compared with authentic samples obtained from Aldrich and Lancaster Chemical Co. L-oxazolidine Oxime **2a** : $[\alpha]_D$-25.3° (c, 2.5, $CHCl_3$) : ^{1}H NMR ($CDCl_3$) : δ 1.32 (s, 9 H), 1.38 (brs, 3 H), 1.55 (brs, 3 H), 3.72 (dd, 1 H, J = 8.7 and 8.3 Hz), 3.85 (dd, 1 H, J = 8.7 and 2.9 Hz), 4.05-4.12 (m, 1 H), 6.71-6.83 (bs, 1 H), 7.29-7.42 (m, 1 H). L-oxazolidine aldehyde **2b** : $[\alpha]_D$ -88.5° (c, 0.5, $CHCl_3$) : lit^{26} -91.7° ($CHCl_3$, c 1.34), ^{1}H NMR ($CDCl_3$) : δ 1.35 (s, 9 H), 1.41 (bs, 3 H), 1.54 (bs, 3 H), 3.75 (dd, 1 H, J = 8.7 and 8.3 Hz), 3.92 (dd, 1 H, J = 8.7 and 2.9 Hz), 3.97-4.01 (m, 1 H), 9.54 (brs, 1 H). IR(neat) cm^{-1} : 1735, 1700. Oxime **5a** : ^{1}H NMR ($CDCl_3$) : δ 1.32 (s, 3 H), 1.50 (s, 3 H), 1.65 (s, 3 H), 1.72 (s, 3 H), 3.92-4.12 (m, 2 H), 4.23-4.25 (m, 1 H), 4.52-4.55 (m, 1 H), 5.18-5.31 (m, 2 H), 5.95 (d, 1 H), 6.92 (d, 1 H), 8.45-8.61 (bs, 1 H). MS (CI) m/z (relative intensity) : 271 (M^+, 100%), 203 (42), 128 (21), 116 (55). $[\alpha]_D$ -135° (c, 1.2, $CHCl_3$). IR (neat) cm^{-1} : 3200, 1650. Oxime **6a** : ^{1}H NMR ($CDCl_3$) : δ 3.65 (s, 2 H), 3.78 (s, 2 H), 7.03-7.35 (m, 3 H), 7.81 (m, 1 H). m.p. 132-135°C. lit. 134-135. Price, C.C.; Hori, M.; Parasaran, T.; Polk, *J. Am. Chem. Soc.* **1963**, *85*, 2278.