IBX-TfOH mediated oxidation of alcohols to aldehydes and ketones under mild reaction conditions

Kamlesh Kumar, Prashant Kumar, Penny Joshi, Diwan S Rawat

PII: S0040-4039(20)30177-5
DOI: https://doi.org/10.1016/j.tetlet.2020.151749
Reference: TETL 151749

To appear in: *Tetrahedron Letters*

Received Date: 24 December 2019
Revised Date: 13 February 2020
Accepted Date: 15 February 2020

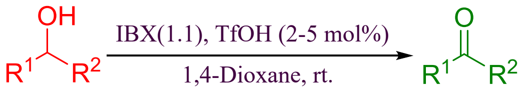
Please cite this article as: Kumar, K., Kumar, P., Joshi, P., Rawat, D.S., IBX-TfOH mediated oxidation of alcohols to aldehydes and ketones under mild reaction conditions, *Tetrahedron Letters* (2020), doi: https://doi.org/10.1016/j.tetlet.2020.151749

Graphical Abstract

IBX-TfOH mediated oxidation of alcohols to aldehydes and ketones under mild reaction conditions

Leave this area blank for abstract info.

Kamlesh Kumar, Prashant Kumar, Penny Joshi, Diwan S Rawat[*]



Tetrahedron Letters
journal homepage: www.elsevier.com

IBX-TfOH mediated oxidation of alcohols to aldehydes and ketones under mild reaction conditions

Kamlesh Kumar,[a,b] Prashant Kumar,[a] Penny Joshi,[b] Diwan S Rawat[a]*

[a] *Department of Chemistry, University of Delhi, Delhi-110007, India.*
[b] *Department of Chemistry, DSB Campus, Kumaun University, Nainital, Nainital-263601, India*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Iodoxybenzoic acid
Triflic acid
Oxidation
Carbonyls

ABSTRACT

An efficient, practical and facile procedure has been developed for the oxidation of primary and secondary alcohols using IBX-TfOH catalytic system in 1,4-dioxane at ambient temperature. The reaction affords quantitative yields of the corresponding carbonyl compounds without the formation of over oxidized products. The present synthetic protocol is compatible with a variety of substrates having arene, heteroarene and alkene functionalities. The developed synthetic protocol can be used for higher scale reactions as evident by the oxidation of alcohol at 1 gm scale in higher yields by a simple filtration process.

1. Introduction

The conversion of alcohols to aldehydes and ketones is one of the most important and challenging functional group transformations in organic synthesis. Carbonyl compounds are precursors of a wide range of agrochemicals, pharmaceuticals, fine chemicals, vitamins, and fragrances [1]. Therefore, development of a catalytic system that is selective for the oxidation of alcohols to aldehydes, or ketones while avoiding over-oxidation to carboxylic acids, esters or other by-products is of scientific interest both in academia and industry [2]. A large number of synthetic methodologies have been reported for the oxidation of alcohols, among which transition metal-catalysed approaches (Pd, Ru, Fe, Cu, Pt, Au, Ir, Rh, etc.) have been extensively studied [3]. However, several limitations and safety concerns are associated with these methods, such as the use of toxic heavy metal salts, or expensive transition metals [4-6]. Besides, the complex reaction workup makes these methods less useful. The conventional non-catalytic oxidation procedures are considered superior for the oxidation of alcohols [1,7]. Chromium or manganese-based species (e.g., MnO_2, $KMnO_4$, CrO_3) [8], hypervalent iodine reagents [9], and activated sulfoxides [10,13], have been successfully utilized for such conversions. Alcohols can also be oxidised by non-metal-based catalytic systems such as Swern oxidation [10-12], Moffatt oxidation [13,14], Corey- Kim oxidation [15] etc. Even though a plethora of procedures are available at our disposal, yet there is a necessity for the development of a better methodology that obviates the use of copious amounts of heavy metal oxidants and environmentally inauspicious halogenated solvents [16].

Recently, *o*-iodoxybenzoic acid (IBX, 1-hydroxy-1,2-benziodoxol-3(1H)-one 1-oxide) [17] has emerged as a popular oxidant as it works under mild reaction conditions, and affords excellent yields of the products. Frigerio and Santagostino primarily demonstrated the synthetic use of IBX for the selective transformation of alcohols to carbonyl compounds [18]. However, it has few limitations, such as poor solubility in common organic solvents, explosive nature at high temperature, and shock sensitivity [19]. To overcome these limitations, numerous modified IBXs (mIBXs) [20], IBX on solid support [21], tetrafluoro-IBX (FIBX) [21], 2-iodoxybenzoic acid organosulfonates (IBX-OTs) [22], and 2-iodoxybenzoic acid ditriflate (IBX-ditriflate) [23] were reported with improved solubility in common organic solvents [24]. These mIBXs are neither explosive at elevated temperatures nor shock sensitive [25]. Dess and Martin have reported the oxidation of alcohols using Dess Martin Periodinane (DMP) with excellent yields [26]. DMP was also found to be a mild and chemoselective reagent, as primary alcohols and amino alcohols can be oxidized to aldehydes and amino carbonyls respectively, without over-oxidation, and avoiding the protection of the amino group. Similarly, 1,2-diols can be converted to α-ketols or α-diketones without oxidative cleavage. Additionally, β-hydroxy ketones have been successfully oxidised to 1,3-diketones at elevated temperatures in ethylacetate [27]. To avoid the structural modification of IBX, few additives like oxone [28], acetic acid [29], trifluoroacetic acid [30], β-cyclodextrin in water/acetone mixture [31] etc., are used with pleasant efficiency. Several reports suggest that IBX is a powerful oxidant when used in ionic liquids [32], or solvents like ethyl acetate/acetone (2:1) [33], 1,2-DCE [33], acetone or acetonitrile [33], DMSO [34], and DMF [35] (Fig. 1).

While synthesizing biologically important molecules [36,37], we required few aldehyde and ketone substrates. However, the alc

efficiently. Thus, we developed a facile and mild reaction protocol for the oxidation of alcohols to carbonyl compounds, using a catalytic amount of TfOH in 1,4-dioxane containing a stoichiometric amount of IBX at room temperature.

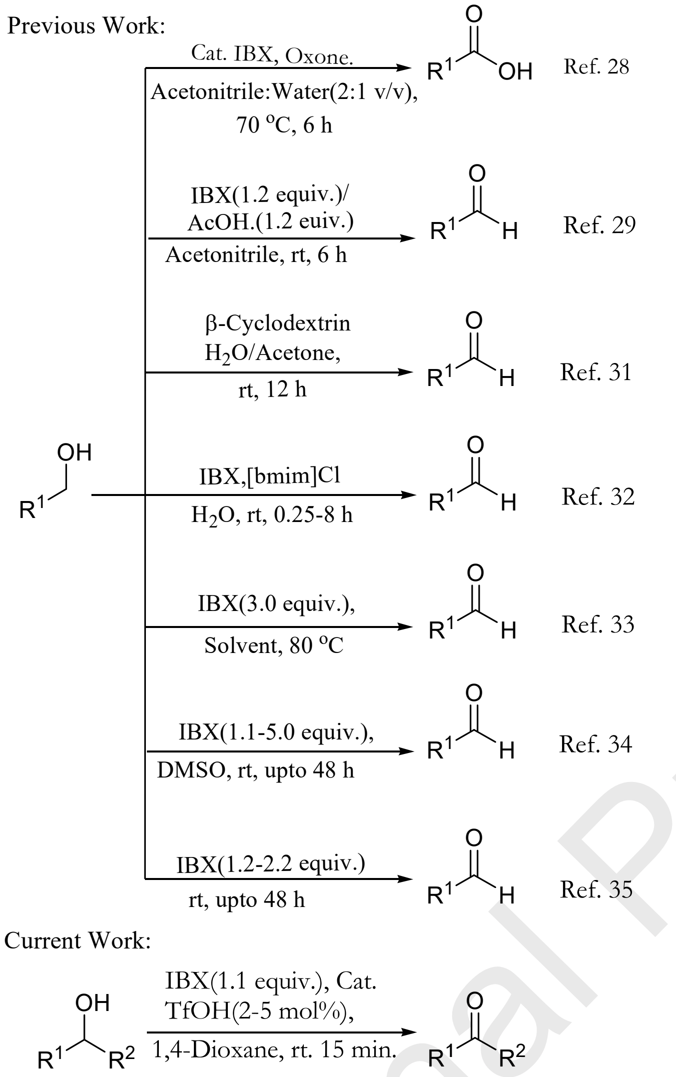
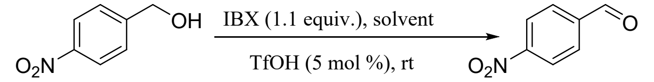


Figure 1: IBX mediated oxidation of alcohols

2. Results and discussion

To optimize the reaction conditions without modifying the structure of *o*-iodoxybenzoic acid, we screened a few additives, and we used 4-nitrobenzyl alcohol as a model substrate for the oxidation reaction. The different additives such triflic acid, *p*-toluenesulfonic acid, trifluoroacetic acid, trifluoroacetic anhydride, and triflic anhydride were employed in catalytic amounts (1 to 10 mol%). The best results were obtained when 5 mol% TfOH was used with 1.1 equiv. IBX in DCM at room temperature (Table 1; entry 5). Further, to improve the efficiency of reaction, we screened various polar protic and aprotic solvents: water, acetonitrile, toluene, 1,4-dioxane, dimethylformamide, dimethylsulfoxide, acetone and ethyl acetate (Table 1; entries 1-4, 6-9). It was observed that the reaction in 1,4-dioxane containing IBX-TfOH completed in 15 minutes (as indicated by TLC), and yielded 4-nitrobenzaldehyde in 98% yield (Table 1; entry 4). Next, progress of reaction was studied by varying the mol% of TfOH and it was found that 2-5 mol% of TfOH with 1.1 equiv. IBX in 1,4-dioxane is the best condition to oxidized 4-nitrobenzyl alcohol to 4-nitrobenzaldehyde at room temperature.

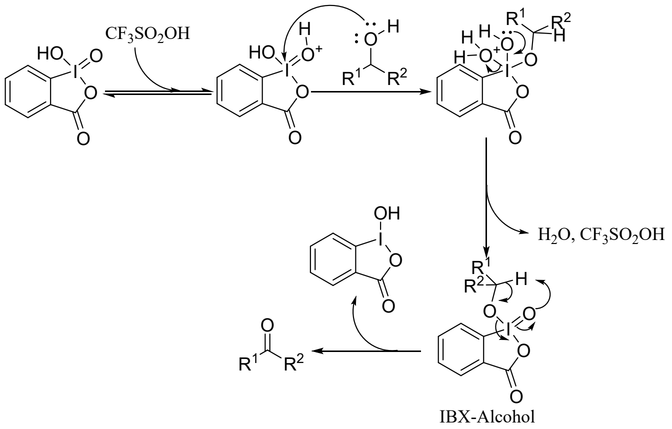


Entry	IBX (equiv.)	Solvent	Time (min)	Yield (%)
1.	2.5	Water	630	32
2.	2.0	Acetonitrile	150	57
3.	2.1	Toluene	235	60
4.	**1.1**	**Dioxane**	**15**	**98**
5.	1.5	DCM	20	96
6.	2.0	DMF	40	67
7.	1.7	DMSO	45	70
8.	2.0	Acetone	130	65
9.	1.5	Ethyl acetate	170	78

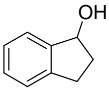
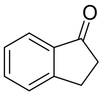
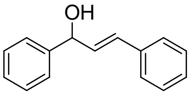
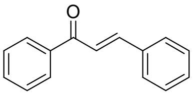
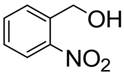
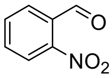
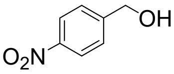
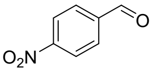
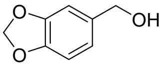
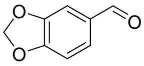
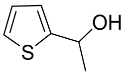
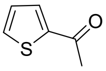
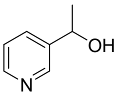
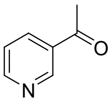
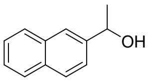
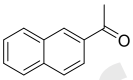
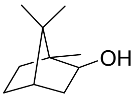
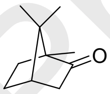
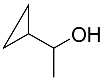
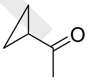
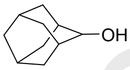
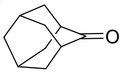
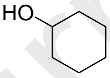
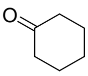
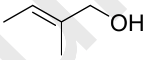
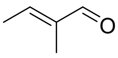
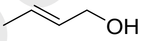
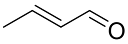
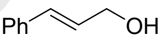
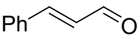
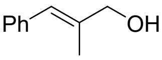
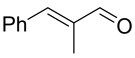
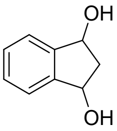
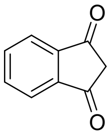
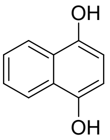
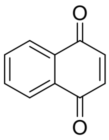
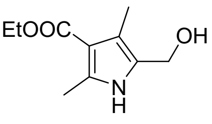
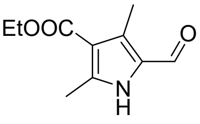
The ^1H NMR studies revealed that the oxidation of 4-nitrobenzyl alcohol using IBX-TfOH in 1,4-dioxane was much faster than that of IBX alone under identical reaction conditions (Fig. S1 & S2). The ^1H NMR which was recorded at different time intervals, clearly showed the disappearance of the benzylic protons signal (at δ 4.69 ppm), and the appearance of a new signal (at δ 10.06 ppm), confirms the oxidation of alcohol. The newly developed oxidative system was very efficient and 92% conversion was observed in 15 min, whereas in the absence of TfOH, the oxidation was found to be sluggish and only 22.9% consumption of starting material was observed after 15 minutes.

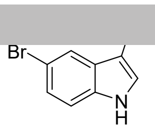
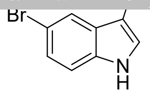
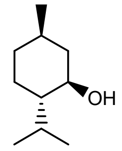
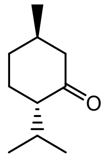
The addition of TfOH to the reaction mixture caused a rapid downfield shift of the benzylic proton signal in ^1H NMR. This may be due to the protonation of oxygen atom (I=O of IBX) by TfOH, which makes the iodine centre highly electron-deficient, and hastens the nucleophilic attack of alcohol, followed by the loss of water molecule, as suggested by Goddard et al. [38], and subsequently regeneration of TfOH. Ultimately there is a formation of IBX-alcohol intermediate, which yields the carbonyl compound *via* an intramolecular cleavage mechanism (Fig. 2). Unfortunately, all our efforts to trap the reactive intermediate were unsuccessful, due to the high reactivity of present catalytic system.

Figure 2. Plausible mechanism of acid catalysed oxidation of alcohol with IBX.



After optimizing the reaction conditions, we established the versatility of the IBX-TfOH system by oxidizing a wide array of alcohols. It was noted that primary aliphatic and aromatic alcohols were oxidized to their corresponding carbonyl compounds, and no over-oxidized side products were observed. Indanone-1 was obtained in excellent yield by the oxidation of 1-Indenol, within 15 minutes (Table 2, entry 1).

S. No.	Substrate	Product	Time (minutes)	Yield (%)	Melting Point (^{o}C)
1			15	96	39-40
2			20	98	55-58
3			25	90	39-40
4			17	98	105-106
5			10	92	35-36
6			12	95	-
7			12	89	-
8			8	99	-
9			28	93	-
10			15	98	-
11			15	97	223-225
12			6	98	-
13			15	87	-
14			9	96	-
15			20	94	-
16			26	85	-
17			20	92	129-132
18			5	96	123-124
19			15	88	164-166

20			23	91	204-206
21			45	75	

The oxidation of (*E*)-1,3-diphenylprop-2-en-1-ol (Table 2, entry 2) in 1.1 equiv. IBX and 3 mol% TfOH, afforded (*E*)-chalcone in 98% isolated yield in 20 minutes. The *o*- and *p*- nitro benzyl alcohols on oxidation yielded the corresponding aldehydes in 90% and 98% isolated yields, respectively (Table 2, entry 3 and 4). Heterocycle-substituted primary and secondary alcohols were oxidized smoothly, and provided the corresponding carbonyl compounds in 88-95% yields, without forming any side product (Table 2; entry 6, 7, 19, 20). The oxidation of 1-cyclopropylethanol yields cyclopropylmethyl ketone in 98% yield (Table 2, entry 10) without forming the rearranged product as reported in previous report [39]. The oxidation of piperonyl alcohol required 2.5 equiv. of IBX to yield 78% of piperonal but addition of 2 mol% of TfOH increased the yield of piperonal to 92% in 10 minutes. Adamantan-2-ol (Table 2, entry 11) was oxidized to adamantan-2-one by 4 equiv. of IBX with 37% yield in 14 hours but when reaction was carried out in the presence of 5 mol% TfOH and 1.3 equiv. IBX, the isolated yield of corresponding ketone was 97% in 15 minutes. *Trans*-menthol was successfully oxidized to *trans*-menthone in 75% yield (Table 2, entry 21) and no racemization was observed as evident by ^{1}H NMR, specific rotation and CD experiments (please see SI) [40].

Conclusion

In conclusion, we have developed an efficient IBX-TfOH mediated method for the oxidation of a wide range of functionalized alcohols to carbonyl compounds in 1,4-dioxane at room temperature. Notably, the present method is readily accessible, has a broad substrate scope and good functional group tolerance under mild reaction conditions.

Acknowledgments

DSR thanks Council of Scientific and Industrial Research, India (File Number: 02(0318)/17/EMR-II) for financial support. We thank USIC-CIF, University of Delhi for assisting to acquire analytical data.

References and notes

1. (a) T. Mallat, A. Baiker, Chem. Rev. 104 (2004) 3037–3058; (b) M. S. Sigman, D. R. Jensen, Acc. Chem. Res. 39 (2006) 221-229; (c) M. J. Schultz, M. S. Sigman, Tetrahedron 62 (2006) 8227-8241; (d) T. Daisuke, T. Masayuki, M. Katsuhiko, H. Togo, Tetrahedron 68 (2012) 6849-6855.
2. (a) G. J. T. Brink, I. W. C. E. Arends, R. A. Sheldon, Science, 287 (2000) 1636-1639; (b) L. Tebben, A. Studer, Angew. Chem. Int. Ed. 50 (2011) 5034-5068; (c) D. I. Enache, J. K. Edwards, P. Landon, B. Solsona-Espriu, A. F. Carley, A. A. Herzing, M. Watanabe, C. J. Kiely, D. W. Knight, G. J. Hutchings, Science, 311 (2006) 362-365; (d) H. Li, F. Qin, Z. Yang, X. Cui, J. Wang, L. Zhang, J. Am. Chem. Soc., 139 (2017) 3513-3521; (e) M. Rafiee, K. C. Miles, S. S. Stahl, J. Am. Chem. Soc. 137 (2015) 14751-14757. (f) A. Badalyan, S. S. Stahl, Nature 535 (2016) 406-410; (g) I. Enache, J. K. Edwards, P. Landon, B. Solsona-Espriu, A. F. Carley, A. A. Herzing, M. Watanabe, C. J. Kiely, D. W. Knight, G. J. Hutchings, Science 311 (2006) 362-365; (h) J. M. Hoover, S. S. Stahl, J. Am. Chem. Soc. 133 (2011) 16901-16910.
3. N. Kaur, D. Kishore, Catalysis Surveys From Asia 17 (2012) 20-42.
4. R. A. Sheldon, I.W.C.E. Arends, G. J. Ten Brink, Dijksman, Acc. Chem. Res. 35 (2002) 774-781.
5. L. Cheng, J. Wang, M. Wang, Z. Wu, Inorg. Chem. 49 (2010) 9392-9399.
6. S.S. Stahl, Angew. Chem. Int. Ed. 43 (2004) 3400-3420.
7. (a) T. Matsumoto, M. Ueno, N. Wang, S. Kobayashi, Chem. Asian J. 3 (2008) 196-214; (b) C. Parmeggiani, F. Cardona, Green Chem. 14 (2012) 547-564
8. F. A. Luzzio, F. S. Guziec, Org. Prep. Proced. Int. 20 (1988) 533-584.
9. S. D. Meyer, S. L. Schreiber, J. Org. Chem. 59 (1994) 7549-7552.
10. K. Omura, D. Swern, Tetrahedron 34 (1978) 1651-1660.
11. A. J. Mancuso, D. S. Brownfain, D. Swern, J. Org. Chem. 44 (1979) 4148-4150.
12. A. J. Mancuso, S. L. Huang, D. Swern, J. Org. Chem. 43 (1978) 2480–2482.
13. K. E. Pfitzner, J. G. Moffatt, J. Am. Chem. Soc. 85 (1963) 3027-3028.
14. J. G. Moffatt, "Sulfoxide-Carbodiimide and Related Oxidations" in *Oxidation* vol. 2, R. L. Augustine, D. J. Trecker, Eds. (Dekker, New York, 1971) pp 1–64.
15. E. J. Corey; C. U. Kim, J. Am. Chem. Soc. 94 (1972) 7586-7587.
16. R. Noyori, M. Aoki, Chem. Commun. (2003) 1977-1986.
17. C. Hartmann, V. Meyer, Chem. Ber. 26 (1893) 1727-1732.
18. (a) M. Frigerio, M. Santogostino, S. Sputore, J. Org. Chem. 64 (1999) 4537-4538; (b) M. Frigerio, M. Santagostino, Tetrahedron Lett. 35 (1994) 8019-8022
19. J. B. Plumb, D. J. Harper, Chem. Eng. News 68 (1990) 3.
20. (a) D. B. Dess, J. C. Martin, J. Am. Chem. Soc. 113 (1991) 7277–7287; (b) D. Macikenas, E. Skrzypczak-Jankun, J. D. Protasiewicz, Angew. Chem., Int. Ed. 39 (2000) 2007–2010; (c) G. Sorg, A. Mengei, G. Jung, J. Rademann, Angew. Chem., Int. Ed. 40 (2001) 4395–4397; (d) A. P. Thottumkara, T. K. Vinod, Tetrahedron Lett. 43 (2002) 569–572; (e) V. V. Zhdankin, A. Y. Koposov, B. C. Netzel, N. V. Yashin, B. P. Rempel, M. J. Ferguson, R. R. Tykwinski, Angew. Chem. Int. Ed. 42 (2003) 2194–2196; (f) W.-J.Chung, D.-K.Kim, Y.-S. Lee, Tetrahedron Lett. 44 (2003) 9251–9254; (g) U. Ladziata, A. Y. Koposov, K. Y. Lo, J. Willging, V. N. Nemykin, V. V. Zhdankin, Angew. Chem. Int. Ed. 44 (2005) 7127–7131; (h) B. V. Meprathu, M. W. Justik, J. D. Protasiewicz, Tetrahedron Lett. 46 (2005) 5187–5190; (i) A. Y. Koposov, D. N. Litvinov, V. V. Zhdankin, M. J. Ferguson, R. McDonald, R. R. Tykwinski, Eur. J. Org. Chem. (2006) 4791–4795; (j) R. D. Richardson, J. M. Zayed, S. Altermann, D. Smith, T. Wirth, Angew. Chem. Int. Ed. 46 (2007) 6529–6532; (k) L.-Q. Cui, Z.-L. Dong, K. Liu, C. Zhang, Org. Lett. 13 (2011) 6488–6491; (l) J. N. Moorthy, K. Senapati, K. N. Parida, S. Jhulki, K. Sooraj, N. N. Nair, J. Org. Chem. 76 (2011) 9593–9601; (m) S. Seth, S. Jhulki, J. N. Moorthy, Eur. J. Org. Chem., 2013, 2445–2452; (n) J. N. Moorthy, K.Senapati, K. N.Parida. J. Org. Chem. 75 (2010) 8416–8421.
21. (a) M. M¨ulbaier, A. Giannis, Angew. Chem., Int. Ed. 40 (2001) 4393–4394; (b) A. Ozanne, L. Pouyse´gu, D. Depernet, B. Francüois, S. Quideau. Org. Lett. 5 (2003) 2903-2906.
22. M. S. Yusubov, D. Y. Svitich, A. Yoshimura, V. N. Nemykin, V. V. Zhdankin. Chem. Commun. 49 (2013) 11269-11271.
23. M. S. Yusubov, N. S. Soldatova, P. S. Postnikov, R. R. Valiev, A. Yoshimura, T. Wirth, V. N. Nemykin, V. V. Zhdankin. Chem. Commun. 55 (2019) 7760-7763.
24. R. D. Richardson, J. M. Zayed, S. Altermann, D. Smith, T. Wirth, Angew. Chem. Int. Ed. 46 (2007) 6529-6532.
25. J. N. Moorthy, K. Senapati, K. N. Parida, S. Jhulki, K. Sooraj, N. N. Nair, J. Org. Chem. 76 (2011) 9593-9601.
26. D. B. Dess, J. C. Martin, J. Org. Chem. 48 (1983) 4155-4156.
27. S. L. Bartlett, C. M. Beaudry, J. Org. Chem. 76 (2011) 9852−9855.
28. A. P. Thottumkara, M. S. Bowsher, T. K. Vinod, Org. Lett. 7 (2005) 2933-2936.
29. C.-K. Lin, T.-J. Lu, Tetrahedron, 60 (2010) 9688-9693.

(2007) 767–771.

31. K. Surendra, N. S. Krishnaveni, M. A. Reddy, Y. V. D. Nageswar, K. R. Rao, J. Org. Chem. 68 (2003) 2058-2059.
32. (a) G. Karthikeyan, P. T. Perumal, Synlett, (2003) 2249-2251; (b) Z. Liu, Z. C. Chen, Q. G. Zheng, Org. Lett. 5 (2003) 3321-3323; (c) J. S. Yadav, B. V. S. Reddy, A. K. Basak, A. V. Narsaiah, Tetrahedron, 60 (2004) 2131-2135.
33. J. D. More, N. S. Finney, Org. Lett. 17 (2002) 3001-3003.
34. M. Frigerio, M. Santagostino, S. Sputore, G. Palmisano, J. Org. Chem. 60 (1995) 7272-7276.
35. M. A. Lapitskaya, L. L. Vasiljeva, K. K. Pivnitsky, Mendeleev Commun. 18 (2008) 309–311.
36. K. Arya, U. C. Rajesh, D. S. Rawat, Green Chem. 14 (2012) 3344-3351.

vat,
Eur. J. Med. Chem. 46 (2011) 2816-2827.

38. J. T. Su, W. A. Goddard, J. Am. Chem. Soc., 127 (2005) 14146-14147.
39. S. Sarell, J. Yovell, M. Sarel-Imber, Angew. Chem. Int. Ed. 7 (1987) 577-578.
40. (a) R. P. Bell, B. G. Cox, J. Chem. Soc. B, (1970) 194-196 (b) H. C. Geiger, J. S. Donohoe, J. Chem. Educ. 89 (2012) 1572-1574. (c) K. Yoshikai, T. Hayama, K. Nishimura, Ken-ichi Yamada, K. Tomioka J. Org. Chem. 70 (2005) 681-683.

De

Authors declare no conflict of interest.

Hig

- IBX-TfOH mediated oxidation of primary and secondary alcohols to carbonyls is reported.
- The catalytic system is compatible with a variety of substrates having arene, heteroarene and alkene functionalities.
- The developed synthetic protocol can be used for the oxidation of alcohols at 1 gm scale.