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2-Iodoxybenzenesulfonic Acid as an Extremely Active Catalyst for the Selective Oxidation of Alcohols to Aldehydes, Ketones, Carboxylic Acids, and Enones with Oxone

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Abstract: Electron-donating group-substituted 2-iodoxybenzoic acids (IBXs) such as 5-Me-IBX (**1g**), 5-MeO-IBX (**1h**), and 4,5-Me_2-IBX (**1i**) were superior to IBX **1a** as catalysts for the oxidation of alcohols with Oxone (a trademark of DuPont) under nonaqueous conditions, although Oxone was almost insoluble in most organic solvents. The catalytic oxidation proceeded more rapidly and cleanly in nitromethane. Furthermore, 2-iodoxybenzenesulfonic acid (IBS, **6a**) was much more active than modified IBXs. Thus, we established a highly efficient and selective method for the oxidation of primary and secondary alcohols to carbonyl compounds such as aldehydes, carboxylic acids, and ketones with Oxone in nonaqueous nitromethane, acetonitrile, or ethyl acetate in the presence of 0.05−5 mol % of **6a**, which was generated *in situ* from 2-iodobenzenesulfonic acid (**7a**) or its sodium salt. Cycloalkanones could be further oxidized to α,β-cycloalkenones or lactones by controlling the amounts of Oxone under the same conditions as above. When Oxone was used under nonaqueous conditions, Oxone wastes could be removed by simple filtration. Based on theoretical calculations, we considered that the relatively ionic character of the intramolecular hypervalent iodine−OSO_2 bond of IBS might lower the twisting barrier of the alkoxyperiodinane intermediate **16**.

Introduction

The oxidation of alcohols to the corresponding carbonyl compounds is one of the most fundamental and important transformations in synthetic organic chemistry. In particular, selective cascade oxidative transformations of alcohols to carbonyl compounds (i.e., primary alcohols → aldehydes → carboxylic acids; secondary alcohols → ketones → esters; cycloalkanols → cycloalkanones → lactones or cyclic α,β-enones, etc.) are attractive, since the target molecule can be obtained directly in one-pot sequences. To date, many excellent catalytic methods have been developed for alcohol oxidations.[1] However, there is a strong need for more efficient, chemoselective, and greener methods that do not require heavy metallic species for such transformations, particularly in the pharmaceutical industry.[2] Transition metal- or nitroxyl radical-catalyzed oxidation of alcohols to ketones or aldehydes has attracted great attention because aqueous H_2O_2 or gaseous O_2 can be used as a stoichiometric oxidant.[1,3] However, it is technically difficult to control the amount of gaseous O_2 added as an oxidant. Moreover, while aqueous H_2O_2 and gaseous O_2 are often concentrated under evaporation and high pressure, respectively, to increase their reactivity, such treatments are dangerous because these materials are explosive. In contrast, Oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, a trademark of DuPont) offers several great advantages, including stability, ease of transport, simple handling, controllable addition, nontoxic nature, etc.,[4] although aqueous H_2O_2 and gaseous O_2 are more atom-economically benign than Oxone.

Over the past decade there has been dramatic growth in the use of 2-iodoxybenzoic acid (**1a**), which is called IBX, in synthetic organic chemistry.[5,6] Its simple one-step preparation from 2-iodobenzoic acid (**2a**) and Oxone has made it a popular reagent (eq 1).[7]

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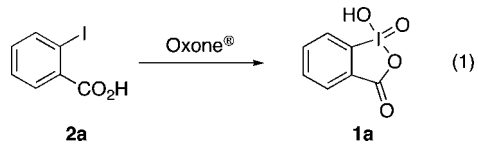
(1) (a) Tojo, G.; Fernandez, M. *Oxidation of Primary Alcohols to Carboxylic Acids*; Springer: Berlin, 2006. (b) Tojo, G.; Fernandez, M. *Oxidation of Alcohols to Aldehydes and Ketones*; Springer: Berlin, 2006. (c) Backwall, J. E. *Modern Oxidation Methods*; Wiley-VCH: New York, 2004. (d) Ley, S. V. *Comprehensive Organic Synthesis*, 3rd ed.; Pergamon: Oxford, 1999; Vol. 7, Chap. 2, pp 251−327. (e) Marko, I. E.; Giles, P. R.; Tsukazaki, M.; Brown, S. M.; Urch, C. J. *Science* **1996**, *274*, 2044. (f) ten Brink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636. (g) Enache, D. I.; Edwards, J. K.; Landoin, P.; Solsona-Espriu, B.; Carley, A. F.; Herzing, A. A.; Watanabe, M.; Kiely, C. J.; Knight, D. W.; Hutchings, G. J. *Science* **2006**, *127*, 8412. (h) Mu, R.; Liu, Z.; Yang, Z.; Liu, Z.; Wu, L.; Liu, Z.-L. *Adv. Synth. Catal.* **2005**, *347*, 1333.

(2) (a) Caron, S.; Dugger, R. W.; Ruggeri, S. G.; Ragan, J. A.; Ripin, D. H. B. *Chem. Rev.* **2006**, *106*, 2943. (b) Dugger, R. W.; Ragan, J. A.; Ripin, D. H. B. *Org. Proc. Res. Dev.* **2005**, *9*, 253.

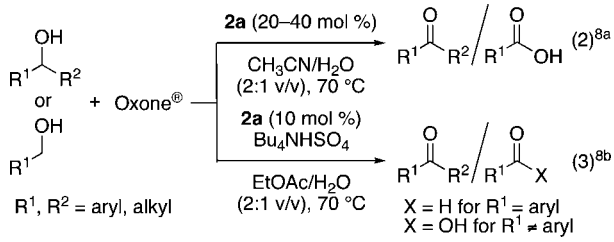
(3) (a) Shibuya, M.; Tomizawa, M.; Suzuki, I.; Iwabuchi, Y. *J. Am. Chem. Soc.* **2006**, *124*, 2245. (b) Adam, W.; Saha-Moller, C. R.; Ganeshpure, P. A. *Chem. Rev.* **2001**, *101*, 3499.

(4) Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031.

(5) For the first preparation of IBX, see: Hartman, C.; Meyer, V. *Chem. Ber.* **1893**, *26*, 1727.



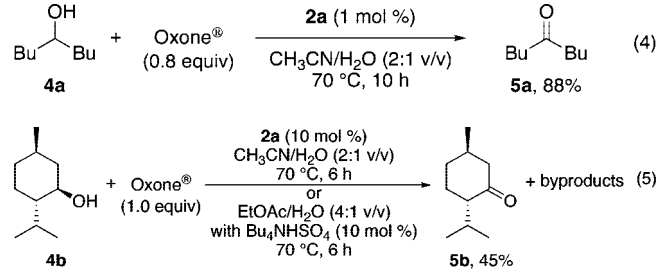
Recently, Vinod[8a] and Giannis[8b] independently reported the oxidation of alcohols catalyzed by **1a** which was generated *in situ* from **2a** in the presence of Oxone as a co-oxidant. Vinod's group used a water/acetonitrile biphasic solvent system, and primary and secondary alcohols were oxidized to ketones and carboxylic acids, respectively (eq 2).[8a] In contrast, Giannis' group used a water/ethyl acetate biphasic solvent system with an additional phase-transfer catalyst (Bu_4NHSO_4), and primary benzylic alcohols were oxidized to the corresponding aldehydes, which were not further oxidized (eq 3).[8b] These two reports declared that it was not necessary to isolate hypervalent iodine compounds, which are potentially shock-sensitive explosive oxidants, beforehand.[7]



To develop a more powerful hypervalent iodine catalyst for alcohol oxidation, we were interested in modification of the arene moiety of **1a**. Several arene-modified IBXs have been developed as stoichiometric oxidants (Chart 1). Vinod introduced a carboxyl group (CO_2H) at the 6-position of **1a**, which was called water-soluble IBX (**1b**).[9] Goddard proposed that 3-Me-IBX (**1c**) should be theoretically more active than **1a**.[10] After Goddard's report, Moorthy reported that 2-Me-4-MeO-IBX (**1d**), which dissolves in common organic solvents, could oxidize alcohols and sulfides at room temperature with short reaction periods.[11] Wirth also reported another soluble IBX analogue, 3,4,5,6-F_4-IBX (**1e**), which was more reactive than IBX in common organic solvents.[12] Several groups also reported solid-supported IBX analogues (**3**)[13] and stabilized IBXs,[14] which have some advantages including safety, easy workup, etc. However, there have been no reports on the catalytic use of modified IBX analogues. Thus, we sought to develop highly efficient IBX-analogous catalysts for the oxidation of alcohols with Oxone.

Results and Discussion

Optimization of Catalytic Oxidation Conditions. Initially, we optimized the reaction conditions for the known *in situ*-generated IBX-catalyzed oxidation with Oxone.[8] A mixture of 5-nonanol (**4a**) and 0.8 equiv of Oxone was heated under Vinod's conditions[8a] at 70 °C even in the presence of 1 mol % of **2a** to give 5-nonanone (**5a**) in good yield (eq 4). In sharp contrast, oxidation of a sterically hindered alcohol like (−)-menthol (**4b**) was problematic under the same conditions in our hand (eq. 5). Byproducts such as Baeyer−Villiger products were also observed in aqueous acetonitrile.



Although these byproducts were suppressed under the conditions described by Giannis,[8b] large amounts of acetic acid and ethanol were produced together with (−)-menthone (**5b**) through the hydrolysis of ethyl acetate. Thus, various solvent systems were examined for the *in situ*-generated **1a** (10 mol%)-catalyzed oxidation of **4b** with Oxone (Table 1). Surprisingly, the oxidation proceeded more cleanly and more rapidly in nonaqueous nitromethane than in organic solvent/water biphasic systems including Vinod's and Giannis' conditions,[8] although Oxone was almost insoluble in nitromethane (entry 6).

IBX-Substituent Effect. With these initial results in hand, we investigated the *in situ*-generated IBX-substituent effect under known aqueous[8a] and our nonaqueous conditions. The results are summarized in Scheme 1 and Table 2, and selected results are plotted in Figure 1. IBX (**1a**)-catalyzed oxidations of **4a** in aqueous acetonitrile and nonaqueous nitromethane gave **5a** in 88% and >99% yields, respectively. Although 3-Me-IBX (**1c**) and 3,4,5,6-F_4-IBX (**1e**) were reported to be more reactive oxidants than **1a**, their catalytic use gave **5a** in very low yields under both conditions (entries 2 and 3).[10−12] 4-Me-IBX (**1f**) showed catalytic activity similar to that of **1a** (entry 4 and Figure 1), and 5-Me-IBX (**1g**) was superior to **1a** (entry 5 and Figure

(6) For the first use of IBX as a selective oxidant for alcohols, see: (a) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019. For Nicolaou's excellent works with IBX, see: (b) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Barluenga, Z. S.; Hunt, K. W.; 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. (d) Nicolaou, K. C.; Montagnon, T.; Baran, P. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1386. (e) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5192. For recent reviews focused on hypervalent iodine chemistry, see: (f) Wirth, T., Ed. *Hypervalent Iodine Chemistry*; Topics in Current Chemistry *224*; Springer: Berlin, 2003. (g) Wirth, T. *Organic Synthesis Highlights V*; Wiley-VCH: Weinheim, 2003; p 144. For recent reviews focused on hypervalent idine chemistry, see:(h) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (i) Tohma, H.; Kita, Y. *Adv. Synth. Catal.* **2004**, *346*, 111. (j) Richardson, R. D.; Wirth, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4402. (k) Ladziata, U.; Zhdankin, V. V. *ARKIVOC* **2006**, *ix*, 26. (l) Ochiai, M.; Miyamota, K. *Eur. J. Org. Chem.* **2008**, 4229.
(7) For the synthesis of IBX with Oxone, see: Frigerio, M.; Santagostino, M.; Sputore, S. J. *J. Org. Chem.* **1999**, *64*, 4537.
(8) (a) Thottumkara, A. P.; Bowsher, M. S.; Vinod, T. K. *Org. Lett.* **2005**, *7*, 2933. (b) Schulze, A.; Giannis, A. *Synthesis* **2006**, 257.
(9) Thottumkara, A. P.; Vinod, T. K. *Tetrahedron Lett.* **2002**, *43*, 569.
(10) Su, J. T.; Goddard, W. A., III. *J. Am. Chem. Soc.* **2005**, *127*, 14146.
(11) Moorthy, J. N.; Singhal, N.; Senapati, K. *Tetrahedron Lett.* **2008**, *49*, 80.
(12) Richardson, R. D.; Zayed, J. M.; Altermann, S.; Smith, D.; Wirth, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 6529.
(13) (a) Lei, Z. Q.; Ma, H. C.; Zhang, Z.; Yang, Y. X. *React. Funct. Polym.* **2006**, *66*, 840. (b) Chung, W.-J.; Kim, D.-K.; Lee, Y.-S. *Synlett* **2005**, 2175. (c) Lei, Z.; Denecker, C.; Jegasothy, S.; Sherrington, D. C.; Slater, N. K. H.; Sutherland, A. J. *Tetrahedron Lett.* **2003**, *44*, 1635. (d) Reed, N. N.; Delgado, M.; Hereford, K.; Clapham, B.; Janda, K. D. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2047. (e) Sorg, G.; Mengel, A.; Jung, G.; Rademann, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4395. (f) Mülbaier, M.; Giannis, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4393.
(14) (a) Ozanne-Beaudenon, A.; Quideau, S. *Tetrahedron Lett.* **2006**, *47*, 5869. (b) Ozanne, A.; Pouysegu, L.; Depernet, D.; François, B.; Quideau, S. *Org. Lett.* **2003**, *5*, 2903.

Chart 1. Arene-Modified IBXs

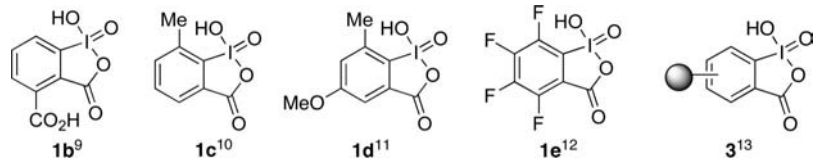
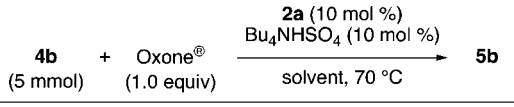


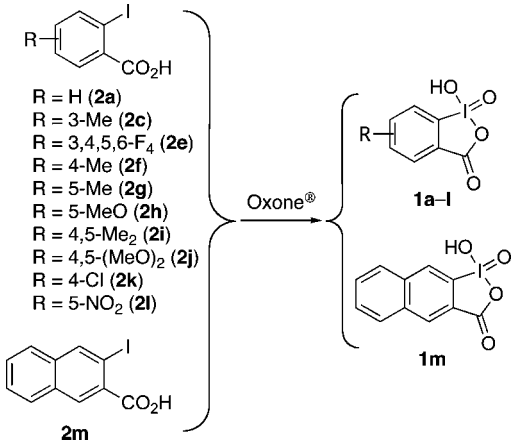
Table 1. Solvent Effects for the *in Situ*-Generated **1a**-Catalyzed Oxidation of **4b** with Oxone[a]



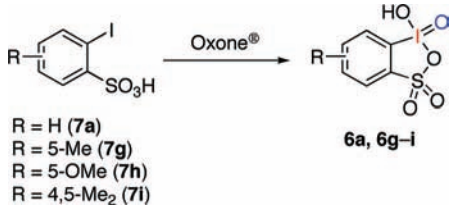
entry	solvents, time	Bu_4NHSO_4 (mol %)	yield **5b**, (%)
1	C_6H_6/H_2O (10 mL/2.5 mL), 6 h	10	33
2	DCE/H_2O (10 mL/2.5 mL), 6 h	10	70
3	*i*-Pr_2O/H_2O (10 mL/2.5 mL), 6 h	10	7
4	CH_3NO_2/H_2O (10 mL/2.5 mL), 6 h	10	90
5	CH_3NO_2/H_2O (10 mL/2.5 mL), 6 h	0	97
6	CH_3NO_2 (12.5 mL), 4 h	0	>99

[a] A mixture of **4b** (5.0 mmol) and Oxone (5.0 mmol) in the indicated solvent system was heated at 70 °C in the presence of **2a** (0.5 mmol) and Bu_4NHSO_4 (0.5 mmol) under open air. For details see Supporting Information.

Scheme 1. Substituted IBX Analogues **1** Generated *in Situ* from **2** with Oxone

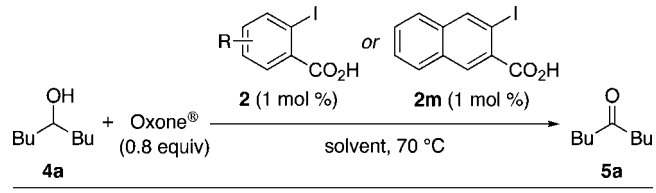


Scheme 2. Substituted IBSs **6** Generated *in Situ* from **7** with Oxone



1) under both conditions, while 4,5-Me_2-IBX (**1i**) was inferior to **1a** in aqueous acetonitrile and superior to **1a** in nitromethane (entry 7 and Figure 1). Electron-donating group-substituted IBXs such as 5-MeO-IBX (**1h**) and 4,5-$(MeO)_2$-IBX (**1j**) and 3-iodoxy-2-naphthalenecarboxylic acid (**1m**) showed good catalytic activities but gradually decomposed under aqueous conditions (entries 6, 8, and 11 and Figure 1). In sharp contrast, the catalytic use of **1h** and **1m** in nitromethane gave **5a** quantitatively within 4 h (entries 6 and 11 and Figure 1). Electron-withdrawing group-substituted IBXs such as 4-Cl-IBX (**1k**) and 5-NO_2-IBX (**1l**)

Table 2. Comparison of **1** Generated *in Situ* from **2** in Aqueous Acetonitrile and Nonaqueous Nitromethane[a]



		5a, time, conv (%)[b]	
entry	precatalyst **2** (R)	in CH_3CN/H_2O	in CH_3NO_2
1	**2a** (H)	10 h, 88	6.3 h, >99
2	**2c** (3-Me)	10 h, 33	10 h, 14
3	**2e** (3,4,5,6-F_4)	10 h, <5	10 h, <5
4	**2f** (4-Me)	10 h, 87	6.3 h, >99
5	**2g** (5-Me)	10 h, 94	4.3 h, >99
6	**2h** (5-MeO)	10 h, 37	3 h, >99
7	**2i** (4,5-Me_2)	10 h, 78	4.1 h, >99
8	**2j** [4,5-$(MeO)_2$]	10 h, 77	10 h, 20
9	**2k** (4-Cl)	10 h, 40	10 h, 66
10	**2l** (5-NO_2)	10 h, 36	10 h, 45
11	**2m**	10 h, 48	4 h, >99
12	–	24 h, <5	24 h, <5

[a] A mixture of **4a** (5.0 mmol) and Oxone (4.0 mmol) in CH_3CN (4 mL)/H_2O (2 mL) or CH_3NO_2 (6 mL) was heated at 70 °C in the presence of **2** (0.05 mmol) under open air. [b] ^1H NMR analysis. For details, see Supporting Information.

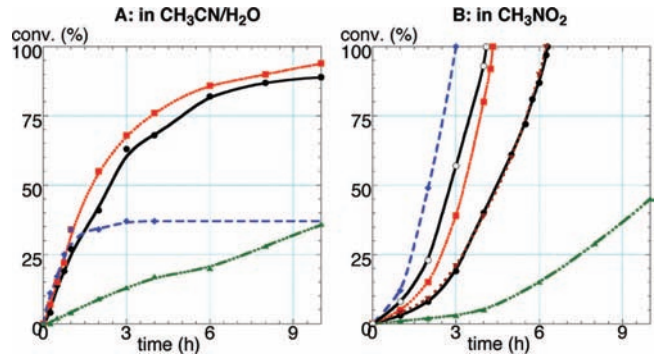
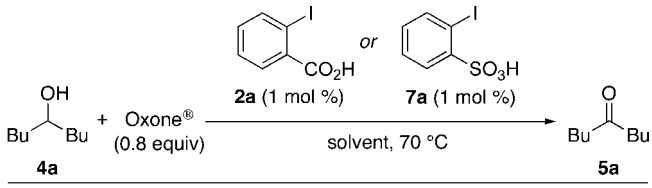


Figure 1. Comparison of the catalytic efficiencies of **1** generated *in situ* from **2** and Oxone in aqueous CH_3CN and nonaqueous CH_3NO_2: **1a** (R = H; black ●), **1f** (R = 4-Me; brown▼), **1g** (R = 5-Me; red ■), **1h** (R = 5-OMe; blue ◆), **1i** (R = 4,5-Me_2; ○), and **1l** (R = 5-NO_2; green ▲). For details, see Supporting Information.

showed low reactivity under both conditions (entries 9 and 10 and Figure 1). In the absence of precatalyst, only a trace amount of ketone was detected, even after 24 h (entry 12). The stability of IBX catalysts was strongly influenced by the solvents and substituents of IBXs. **1c** and **1j** were decomposed under both aqueous and nonaqueous conditions (entries 2 and 6), and **1h** and **1m** were decomposed under aqueous conditions (entries 8 and 11). The reaction mixture became yellowish red or brown when catalysts were decomposed, although any decomposed products of catalysts could not be identified.[15] These results indicated that, in general, I(V)-catalyzed oxidation was faster and cleaner under nonaqueous conditions, although Oxone was

Table 3. Catalytic Efficiency of *in Situ*-Generated **6a** and **1a**[a]



entry	solvents	5a, time, conv (%)[b] with 7a	with 2a
1	CH_3CN/H_2O (2:1 v/v)	12 h, 24	10 h, 88
2	$EtOAc/H_2O$ (4:1 v/v)[c]	12 h, <5	12 h, 45
3	CH_3NO_2	2 h, >99	6.3 h, >99
4	CH_3CN	1.6 h, >99	24 h, <5
5	EtOAc	10 h, >99	24 h, <5

[a] A mixture of **4a** (5.0 mmol) and Oxone (4.0 mmol) in solvents (6 mL) described in the table was heated at 70 °C in the presence of precatalyst (0.05 mmol) under open air. [b] ^1H NMR analysis. [c] In the presence of Bu_4NHSO_4 (10 mol %). For details, see Supporting Information.

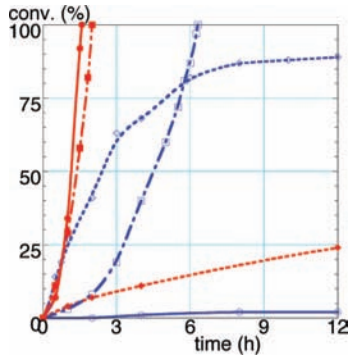


Figure 2. Catalytic efficiency of **1a** (blue) and **6a** (red) generated *in situ* from **2a** and **7a**, respectively: **6a** in CH_3CN-H_2O (red ◆), **6a** in CH_3NO_2 (red ■), **6a** in CH_3CN (red ●), **1a** in CH_3CN-H_2O (blue ◇), **1a** in CH_3NO_2 (blue □), **1a** in CH_3CN (blue ○). For details, see Supporting Information.

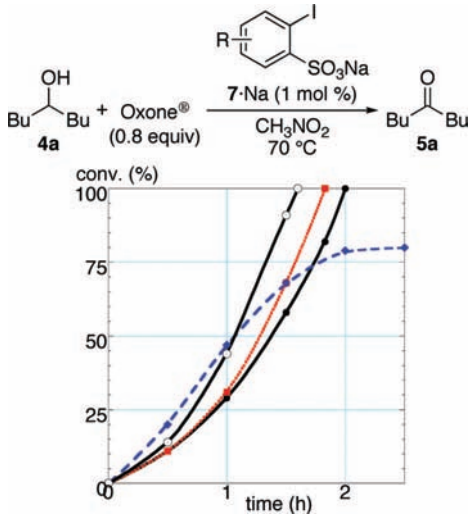


Figure 3. Comparison of catalytic efficiency of **6** generated *in situ* from **7** in nonaqueous CH_3NO_2 (method B): **6a** (R = H; black ●), **6g** (R = 5-Me; red ■), **6h** (R = 5-MeO; blue ◆), and **6i** (R = 4,5-Me_2; black ○). For details, see Supporting Information.

almost insoluble in CH_3NO_2. In addition, in most cases, the reaction proceeded straightforwardly under nonaqueous conditions, and the reaction rate was not reduced, regardless of the conversion (Figure 1B).

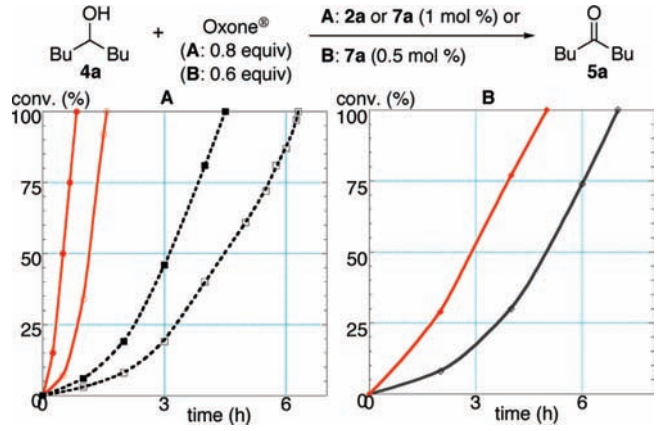


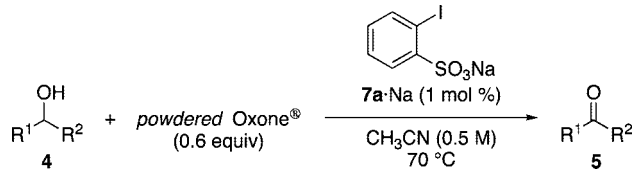
Figure 4. (A) Acceleration of the oxidation rate of **4a** with *powdered* Oxone (0.8 equiv): **6a** with *commercial* Oxone in CH_3CN (red ○), **6a** with *powdered* Oxone in CH_3CN (red ●), **1a** with *commercial* Oxone in CH_3NO_2 (black □), and **1a** with *powdered* Oxone in CH_3NO_2 (black ■). (B) Effect of the addition of Na_2SO_4 on the catalytic efficiency of **6a** (0.5 mol %) in the oxidation of **4a** with *powdered* Oxone (0.6 equiv) in CH_3CN in the presence of 0.5 g/mmol of **4a** (red ◆) versus without Na_2SO_4 (black ◆). For details, see Supporting Information.

2-Iodoxybenzenesulfonic Acid (IBS, 6a). To develop an even more powerful catalyst for alcohol oxidation, we were interested in 2-iodoxybenzenesulfonic acid (IBS, **6a**), an analogue of **1a**. Although **6a** has been synthesized from 2-iodobenzenesulfonic acid (**7a**)[16] and Oxone in water by Zhdankin and co-workers, its oxidative ability has not been investigated due to its low stability (Scheme 2).[17] We envisaged that **6**, which could be prepared from **7** and Oxone *in situ*, might have greater catalytic activity than **1**, since the Lewis acidity of the I(V) atom in **6** would be higher than that in **1** due to its strong electron-withdrawing sulfo group.[18]

To investigate the catalytic efficiency of **6**, a mixture of **4a** and 0.8 equiv of Oxone was heated in known aqueous[8] and our nonaqueous solvent systems at 70 °C in the presence of 1 mol % of precatalysts **7a** and **2a**. The results are summarized in Table 3, and selected results are plotted in Figure 2. Unexpectedly, **5a** was obtained in yields of only 24% (Figure 2, red diamond) and <5%, respectively (entries 1 and 2). Surprisingly, the **6a**-catalyzed oxidation of **4a** was dramatically accelerated in nonaqueous nitromethane and acetonitrile, and **5a** was obtained quantitatively within 2 h (entries 3 and 4 and Figure 2, red square and red circle respectively; TOF[19] reached to 63 h^{-1}). In nonaqueous nitromethane, **6a** was superior to **1a** (Figure 2, red square vs blue open-square; TOF = 50 h^{-1} vs 16 h^{-1}, respectively). In sharp contrast, the oxidation with the use of 1 mol % of **2a** in aqueous solvent systems gave **5a** in good yield (entries 1 and 2 and Figure 2, blue open diamond), albeit only a trace amount of **5a** was obtained in acetonitrile, even after 24 h (entry 4 and Figure 2, blue open circle). Moreover, **6a** was sufficiently active in less polar but more environmentally

(15) For oxidative decomposition of IBX, see: Bunton, C. A.; Foroudian, H. J.; Gillitt, N. D. *J. Phys. Org. Chem.* **1999**, *12*, 758.
(16) For the synthesis of **7a**, see: (a) Chau, M. M.; Kice, J. L. *J. Org. Chem.* **1977**, *42*, 3265. (b) Dolenc, D.; Plesnicar, B. *J. Org. Chem.* **2006**, *71*, 8025. (c) Minami, T.; Ito, S.; Ohuchida, S.; Naganawa, A.; Maruyama, T. *PCT Int. Appl.* **2001**, WO2001008674. **7a** is commercially available from CarboMer, Inc. (San Diego, CA).
(17) Koposov, A. Y.; Litvinov, D. N.; Zhdankin, V. V.; Ferguson, M. J.; McDonald, R.; Tykwinski, R. R. *Eur. J. Org. Chem.* **2006**, 4791.

Table 4. Selective Oxidation of Secondary Alcohols **4** to Ketones **5** Using Method A[a]



entry	alcohol **4**	product **5**	time, yield (%)
1	**4b**	**5b**	2 h, 99
2	**4c** $n = 1$	**5c**	2 h, 99[b]
3	**4d** $n = 7$	**5d**	2 h, 99
4	**4e** (>95% ee)	**5e** (>95% ee)	1 h, 98
5	**4f** R= OSiPh$_2$*t*-Bu	**5f**	2 h, 99
6	**4g** R= *t*-Bu	**5g**	2 h, 92
7	**4h**	**5h**	8 h, 91[c]
13	**4i**	**5i**	1 h, 99
8	**4j**	**5j**	2 h, 99[b]
9	**4k**	**5k**	1.5 h, 99
10	**4l**	**5l**	1 h, 99
11	**4m**	**5m**	12 h, 80
12	**4n**	**5n**	1 h, 99

[a] Method A (unless otherwise noted): a mixture of **4** and *powdered* Oxone (0.6 equiv) in CH_3CN (0.5 M) was heated at 70 °C in the presence of **7a**·Na (1 mol %) under open air. [b] ^{1}H NMR analysis. [c] 1.2 equiv of Oxone was used.

benign ethyl acetate (entry 5).[8b] However, the **1a**-catalyzed oxidation of alcohols did not give any products in nonaqueous solvents such as ethyl acetate or acetonitrile (entry 5). Sodium 2-iodobenzenesulfonate (**7a**·Na) could be used as a precatalyst for **6a**, and **7a**·Na at a catalyst loading of 0.05 mol % was enough for the oxidation of **4a** in acetonitrile (20 mmol scale, 32 h, 99% isolated yield, TON[19] $\geq$ 2000).

Next, we investigated the substituent effect of IBS (**6a**) on the oxidation of alcohols in nonaqueous nitromethane. As shown in Figure 3, the same tendency seen with IBX was observed for IBS. Electron-donating group-substituted IBSs such as 4,5-Me_2-IBS (**6i**, black open circle) and 5-Me-IBS (**6g**, red square) were superior to **6a** (black solid circle). Although 5-MeO-IBS (**6h**, blue diamond) showed the highest activity initially, catalyst decomposition was observed.

The oxidation rates in reactions catalyzed by IBXs **1** and IBSs **6** were further accelerated by the use of *powdered* Oxone due to its increased surface area (Figure 4A; for powder size of Oxone, see Supporting Information) and/or by the addition of anhydrous sodium sulfate (Figure 4B, red square versus black circle). TOF of **6a** was increased from 63 to 120 h^{-1} by using powdered Oxone in acetonitrile (Figure 4A, red open circle vs red solid circle], and TOF of **1a** was also increased from 16 to 22 h^{-1} in nitromethane (Figure 4A, black open square vs black solid square).

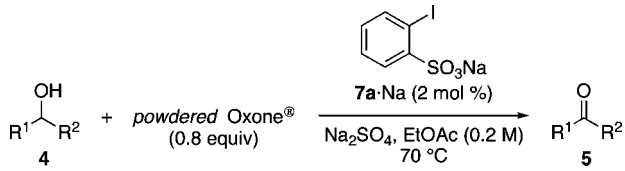
IBS (6a)-Catalyzed Selective Oxidation of Alcohols. To explore the generality of the *in situ*-generated **6a**-catalyzed oxidation of alcohols with Oxone, various structurally diverse secondary and primary alcohols **4** and **8** were examined as substrates under optimized conditions (Tables 47).

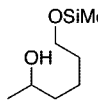
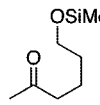
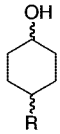
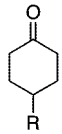
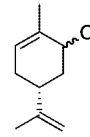
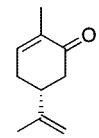
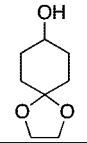
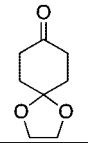
As shown in Table 4, not only sterically demanding secondary alcohols **4b**−**k** but also α,β-unsaturated secondary alcohols **4l**−**n** were oxidized to the corresponding ketones **5b**−**n** using method **A** [**7a**·Na (1 mol %); solvent, acetonitrile; no additive].

As shown in Table 5, method B [**7a**·Na (2 mol%); solvent, ethyl acetate; additive, anhydrous sodium sulfate] was more effective for the oxidation of acid-senstitive secondary alcohols **4o**−**t** to the corresponding ketones **5o**−**t** in high yields, although lower catalytic activity was observed. In contrast, the oxidation of **4o**, **4p**, and **4t** using method A gave corresponding ketones **5o**, **5p**, and **5t** in low yields because acid-sensitive TES, TBS, and ketal groups were decomposed rapidly (entries 1, 2, and 5).

According to previous reports,[1,3,8] it is difficult to oxidize primary alcohols selectively to the corresponding aldehydes or carboxylic acids with the same catalyst and reagents. Fortunately, as shown in Table 6, α,β-unsaturated primary alcohols **8a**−**i**, such as allylic, propargylic, and benzylic alcohols, could be selectively oxidized to the corresponding aldehydes **9** and carboxylic acids **10** in excellent yield by controlling the amount of Oxone added in the presence of precatalyst **7a**·Na (1−2 mol %) using method A: 0.6 and 1.2 equiv of Oxone were used for the selective oxidation to **9** and **10**, respectively. In contrast, α,β-saturated primary

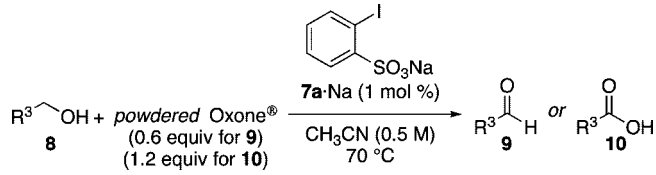
Table 5. Selective Oxidation of Acid-Sensitive Secondary Alcohols **4** to Ketones **5** Using Method B[a]

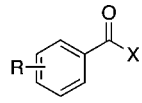
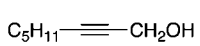
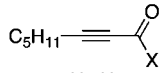
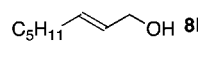
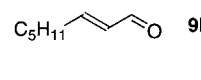
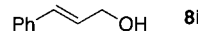
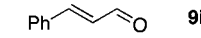
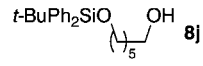
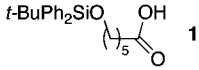
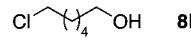
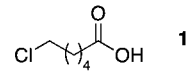
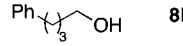
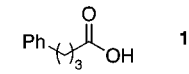
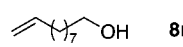
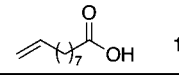


entry	alcohol **4**	product **5**	time, yield (%)
1	 **4o**	 **5o**	8 h, 95 (1 h, ~30%)[b]
2	 **4p** R= $OSiEt_3$	 **5p**	7 h, 78 (1 h, <5%)[b]
3	**4r** R= OBn	**5r**	8 h, 94
4	 **4s**	 **5s**	8 h, 91
5	 **4t**	 **5t**	8 h, 86 (1 h, ~15%)[b]

[a] Method B (unless otherwise noted): a mixture of **4**, *powdered* Oxone (0.8 equiv), and anhydrous Na_2SO_4 in EtOAc (0.2 M) was heated at 70 °C in the presence of **7a**·Na (2 mol %) under N_2. [b] With method A.

Table 6. Selective Oxidation of Primary Alcohols **8** to Aldehydes **9** or Carboxylic Acids **10** Using Method A[a]



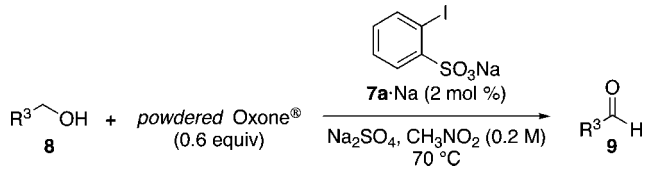
entry	alcohol **8**	product **9**, **10**	time, yield (%)
1	 **8a** R= H	 **9a** X= H	2 h, 99
2	**8b** R= 4-Me	**9b** X= H	3 h, 95
3	**8b**	**10b** X= OH	4 h, 94[b]
4	**8c** R= 4-NO_2	**9c** X= H	2 h, 87
5	**8c**	**10c** X= OH	4 h, 99[b]
6	**8d** R= 2,4-Cl_2	**9d** X= H	1.5 h, 92
7	**8e** R= 3-Br	**9e** X= H	2 h, 95
9	 **8f**	 **9i** X= H	3 h, 84
10	**8f**	**10i** X= OH	8 h, 93[b]
11	 **8g**	 **9g**	5 h, 93
12	 **8h**	 **9h**	3 h, 95
13	 **8i**	 **9i**	3 h, 92
14	 **8j**	 **10j**	4 h, 90[c]
15	 **8k**	 **10k**	6 h, 96[c]
16	 **8l**	 **10l**	6 h, 94[c]
17	 **8m**	 **10m**	7 h, 96[c]

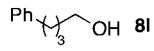
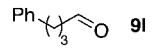
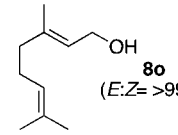
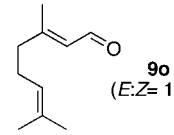
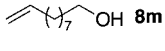
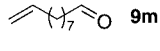
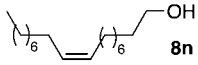
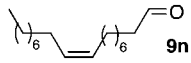
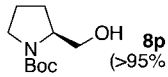
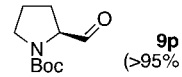
[a] Method A (unless otherwise noted): a mixture of **8** and *powdered* Oxone (0.6 equiv for **9**, 1.2 equiv for **10**) in CH_3CN (0.5 M) was heated at 70 °C in the presence of **7a**·Na (1 mol %) under open air. [b] After **8** was completely consumed (after 1 h), H_2O was added to accelerate the further oxidation of **9** to **10** with Oxone. [c] **8** was slowly added to the reaction mixture to prevent ester formation in the oxidation to **9** and **10**.

alcohols **8j**−**m** with 0.6 equiv of Oxone gave a mixture of **9j**−**m** and **10j**−**m**, although α,β-saturated primary alcohols **8j**−**m** with 1.2 equiv of Oxone were oxidized to **10j**−**m** in high yields. It was difficult to oxidize aliphatic primary alcohols to aldehydes selectively, because the reactivity of aliphatic aldehydes with Oxone was higher than that of aromatic ones.

As shown in Table 7, methods B and C [**7a**·Na (2 mol%); solvent, nitromethane; additive, anhydrous sodium sulfate] were also effective for the selective oxidation of acid-sensitive primary alcohols. Method B used milder conditions for oxidation of alcohols than method C. Fortunately, aliphatic primary alcohols were selectively oxidized to aldehydes in excellent yield in the presence of anhydrous Na_2SO_4 by using method B or C. It is known that aldehydes easily react with water to give hemiacetals, which are oxidized to carboxylic acids in the presence of Oxone.[4] Thus, the addition of anhydrous Na_2SO_4 prevented the hydration of aldehydes to hemiacetals. Notably,

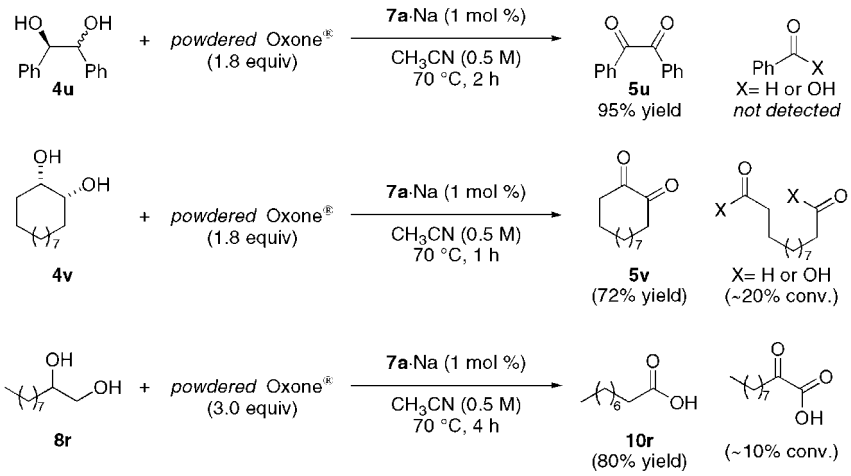
Table 7. Selective Oxidation of Primary Alcohols **8** to Aldehydes **9** Using Method C or B[a]



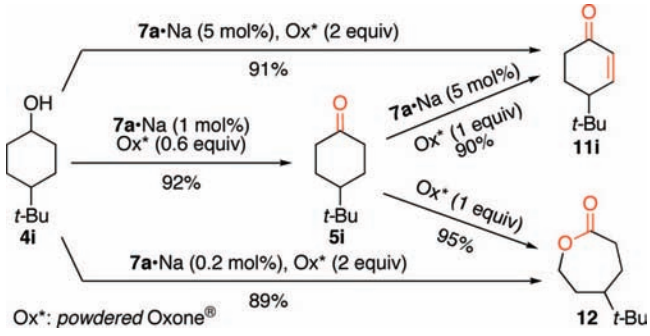
entry	alcohol **8**	product **9**	time, yield (%)	entry	alcohol **8**	product **9**	time, yield (%)
1	 **8l**	 **9l**	2 h, 90[b]	4	 **8o** (*E*:*Z*= >99:1)	 **9o** (*E*:*Z*= 16:1)	2 h, 86
2	 **8m**	 **9m**	2 h, 92[b]				
3	 **8n**	 **9n**	2 h, 90[b]	5	 **8p** (>95% ee)	 **9p** (>95% ee)	8 h, 85[b,c]

[a] Method C (unless otherwise noted): a mixture of **8**, *powdered* Oxone (0.6 equiv), and anhydrous Na_2SO_4 in CH_3NO_2 (0.2 M) was heated at 70 °C in the presence of **7a**·Na (2 mol %) under N_2. [b] **8** was slowly added to the reaction mixture to prevent ester formation in the oxidation to **9** and **10**. [c] EtOAc was used as solvent (method B) and 5 mol % **7a**·Na was used.

Scheme 3. **6a**-Catalyzed Oxidation of 1,2-Diols with Oxone



Scheme 4. **6a**-Catalyzed Cascade Oxidation of **4i** to **11i** or **12** in CH_3NO_2



the oxidation of *N*-Boc-L-prolinol (**8p**) gave *N*-Boc-L-prolinal (**9p**) without racemization in ethyl acetate (method B, entry 5).

The present protocol could be applied to the chemoselective oxidation of alcohols bearing several functional or protective groups such as *tert*-butyldiphenylsilyloxy (**4f** and **8j**, method A), *tert*-butyldimethylsilyloxy (**4o**, method B), triethylsilyloxy (**4p**, method B), benzyloxy (**4r**, method B), ketal (**4t**, method B), alkenyl (**4s**, method B; for **8h**, **8i**, and **8m** to **10**, method A; for **8m**−**o** to **9**, method C), alkynyl (**4n** and **8f**, method A), halo (**8d**, **8e**, and **8k**, method A), pyridinyl (**4m**, method A), and thiophene groups (**8g**, method A) (Tables 4−7). In the

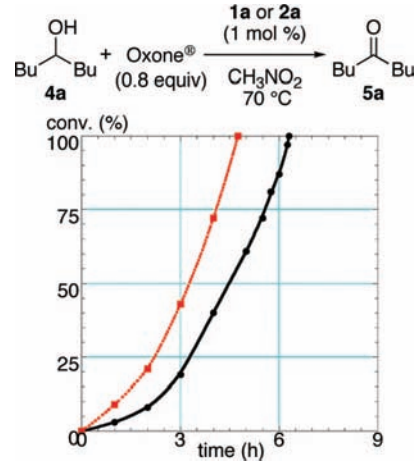
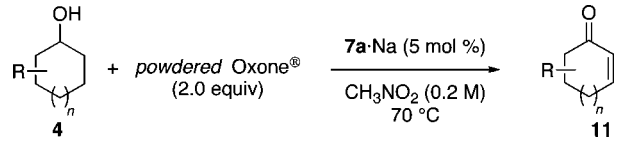
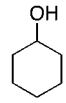
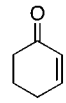
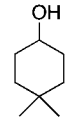
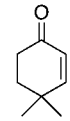
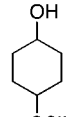
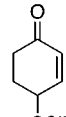
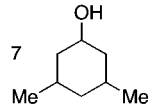
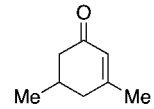
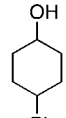
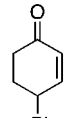
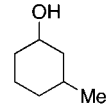
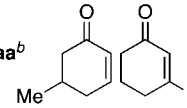
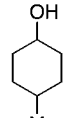
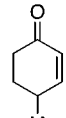


Figure 5. Comparison of the catalytic activity of isolated **1a** with that of *in situ*-generated **1a**: **1a** (red ■) and **2a** (black ●).

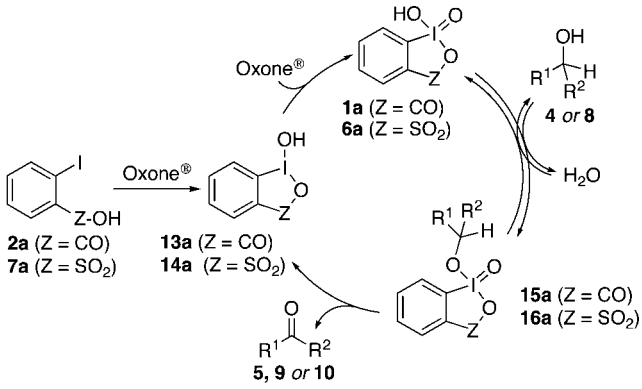
Table 8. Cascade Oxidative Dehydrogenations of **4** to **11**[a]



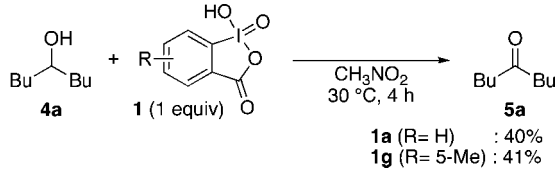
entry	cycloalkanol **4**	enone **11** time, yield (%)	entry	cycloalkanol **4**	enone **11** time, yield (%)
1	 **4c**	 **11c** 8 h, 82	6	 **4y**	 **11y** 8 h, 61
2	 **4f**[b]	 **11f** 6 h, 88	7	 **4z**[b]	 **11z** 24 h, 74
4	 **4w**[b]	 **11w** 8 h, 88	8	 **4aa**[b]	 **11aa** 12 h, 86 (4:1)[c]
5	 **4x**[b]	 **11x** 8 h, 83	9	 **4ab**	 **11ab** 24 h, ca. 70[d]

[a] For experimental details, see Supporting Information. [b] A *cis*/*trans* isomeric mixture of **4** was used. [c] 3-Me- and 5-Me-regioisomers of **11aa** were obtained in 1:4 ratio. [d] ^{1}H NMR analysis.

Scheme 5. *In Situ* Generation of IBX (**1a**) or IBS (**6a**) and Catalytic Cycle of Alcohol Oxidation



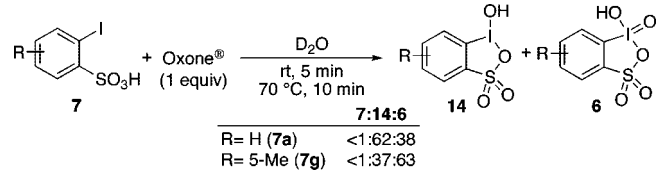
Scheme 6. Stoichiometric Control Experiments



nonaqueous solvent system, the desired carbonyl products were obtained in nearly pure form by simple filtration of most wastes derived from Oxone and washing with water to remove catalyst derivatives.

The oxidation of several 1,2-diols was also examined (Scheme 3). Benzylic secondary/secondary 1,2-diol **4u** was oxidized to the diketone **5u** in excellent yield without oxidative cleavage

Scheme 7. *In Situ* Generation of **6** and **14** from **7** and Oxone



products. Aliphatic secondary/secondary 1,2-diol **4v** was oxidized to the diketone **5v** in 72% yields, and oxidative cleavage products 1,12-dodecanedial, 12-oxododecanoic acid, and 1,12-dodecanedioic acid were also obtained in ~20% yields. On the other hand, oxidation of aliphatic primary/secondary 1,2-diol **8r** gave oxidative cleavage product **10r** as major product in 80% yield.

IBS (6a)-Catalyzed Cascade Oxidative Dehydrogenation of Cycloalkanols. Although many methods have been reported for the synthesis of α,β-unsaturated carbonyl compounds, it is quite difficult to catalytically dehydrogenate saturated carbonyl compounds to α,β-unsaturated carbonyl compounds.[20] Nicolaou and co-workers recently reported direct oxidative dehydrogenation with the stoichiometric use of IBX (**1a**) in DMSO via a single-electron-transfer (SET) mechanism.[6c,d] During the course of our research on the oxidation of cycloalkanols, we found that IBS (**6a**) efficiently catalyzed the cascade oxidative dehydrogenation of cycloalkanols to cycloalkenones. The selective oxidation of 4-*tert*-butylcyclohexanol (**4i**) to 4-*tert*-butylcyclohexanone (**5i**) and successive oxidation of **5i** to 4-*tert*-butylcyclohex-2-enone (**11i**) and 5-*tert*-butyloxepan-2-one (**12**)[21] proceeded in excellent yields when we controlled the amounts of **7a**·Na and Oxone (Scheme 4). In contrast, the oxidation of

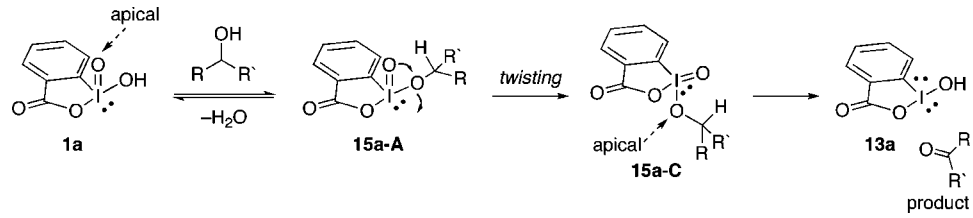


Figure 6. Goddard's hypervalent twisting mechanism of IBX-mediated alcohol oxidation.[10]

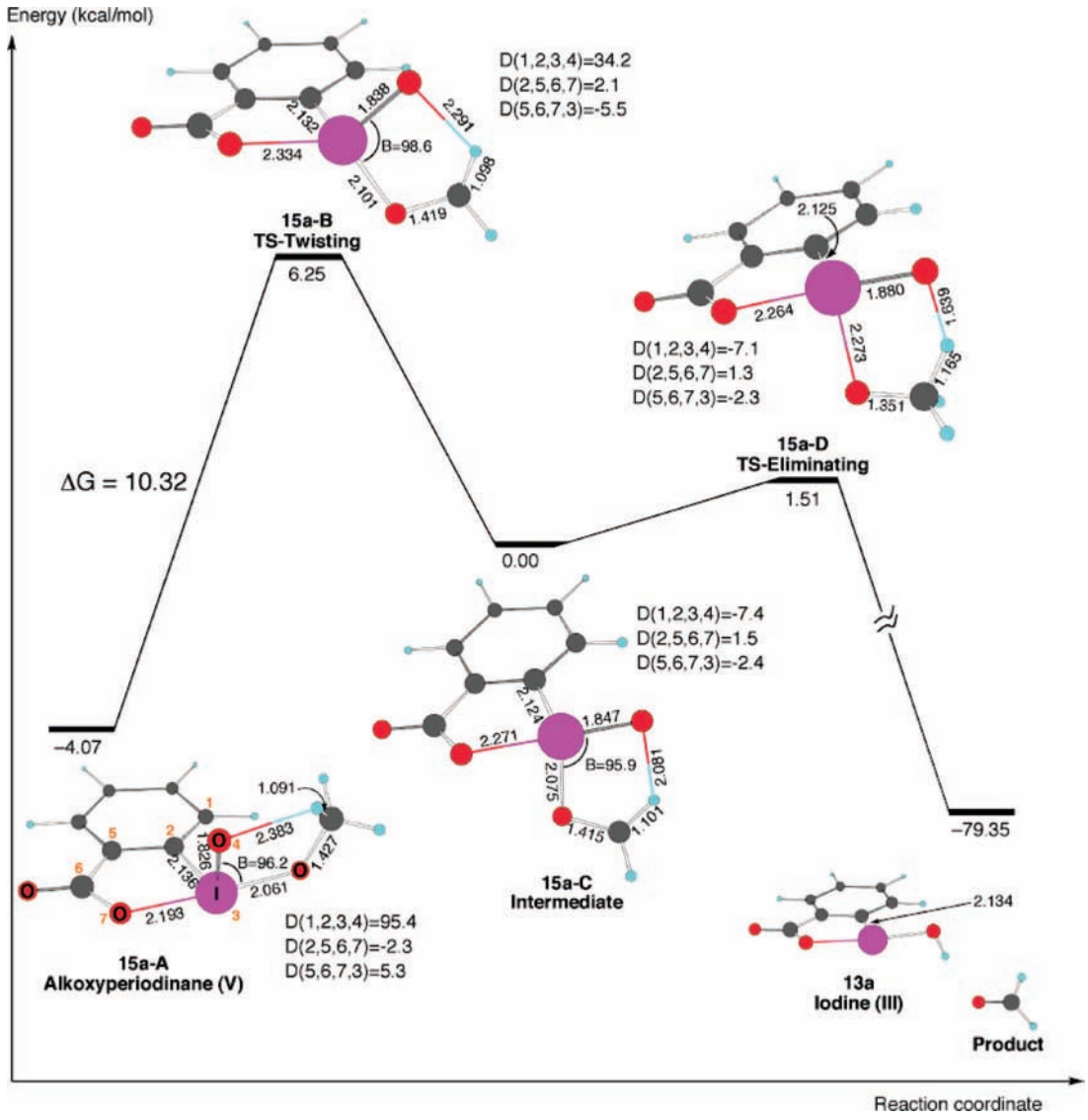


Figure 7. Free energy profiles relevant to **15a→13a**. Gibbs free energies (kcal/mol), selected bond lengths (Å), bite angles (B, °), and dihedral angles (D, °) for optimized structures **15a-A**−**15a-D** and **13a** are shown.

5i with Oxone in the presence of 10 mol % of **2a** gave **11i** in ≤10% yield under aqueous or nonaqueous conditions (see Supporting Information). *To the best of our knowledge, this is the first example of the catalytic cascade oxidative dehydrogenation of saturated alcohols to the α,β-unsaturated carbonyl compounds.*[22]

Other examples of cascade oxidation of **4** to **11** are shown in Table 8. Five- and six-membered cycloalkanols were transformed to the corresponding enones in good yield. Unfortunately, **6a**-catalyzed oxidative dehydrogenation of linear carbonyl compounds to the linear α,β-unsaturated carbonyl compounds with Oxone was not successful under these conditions.

Mechanism. As shown in Scheme 5, Santagostino has proposed a mechanism for the oxidation of alcohols with IBX (**1a**) via two steps: a fast pre-equilibrium step (**1a→15a**) and a

(18) There are many examples of the activation of hypervalent aryl-λ^3-iodanes by strong Lewis acids that increased its oxidation power. For a review, see: Ochiai, M. *Chem. Rec.* **2007**, *7*, 12.

(19) TON and TOF are based on precatalysts **2** and **7**.

(20) For the synthesis of α,β-unsaturated carbonyl compounds, see: (a) Larock, R. C. *Comprehensive Organic Transformations*; John Wiley & Sons: New York, 1999; pp 251−256. (b) Buckle, D. R.; Pinto, I. L. In *Comprehensive Organic Synthesis*; TrostB. M., Ed.; Pergamon: Oxford, 1991; Vol. 7, pp 119146.

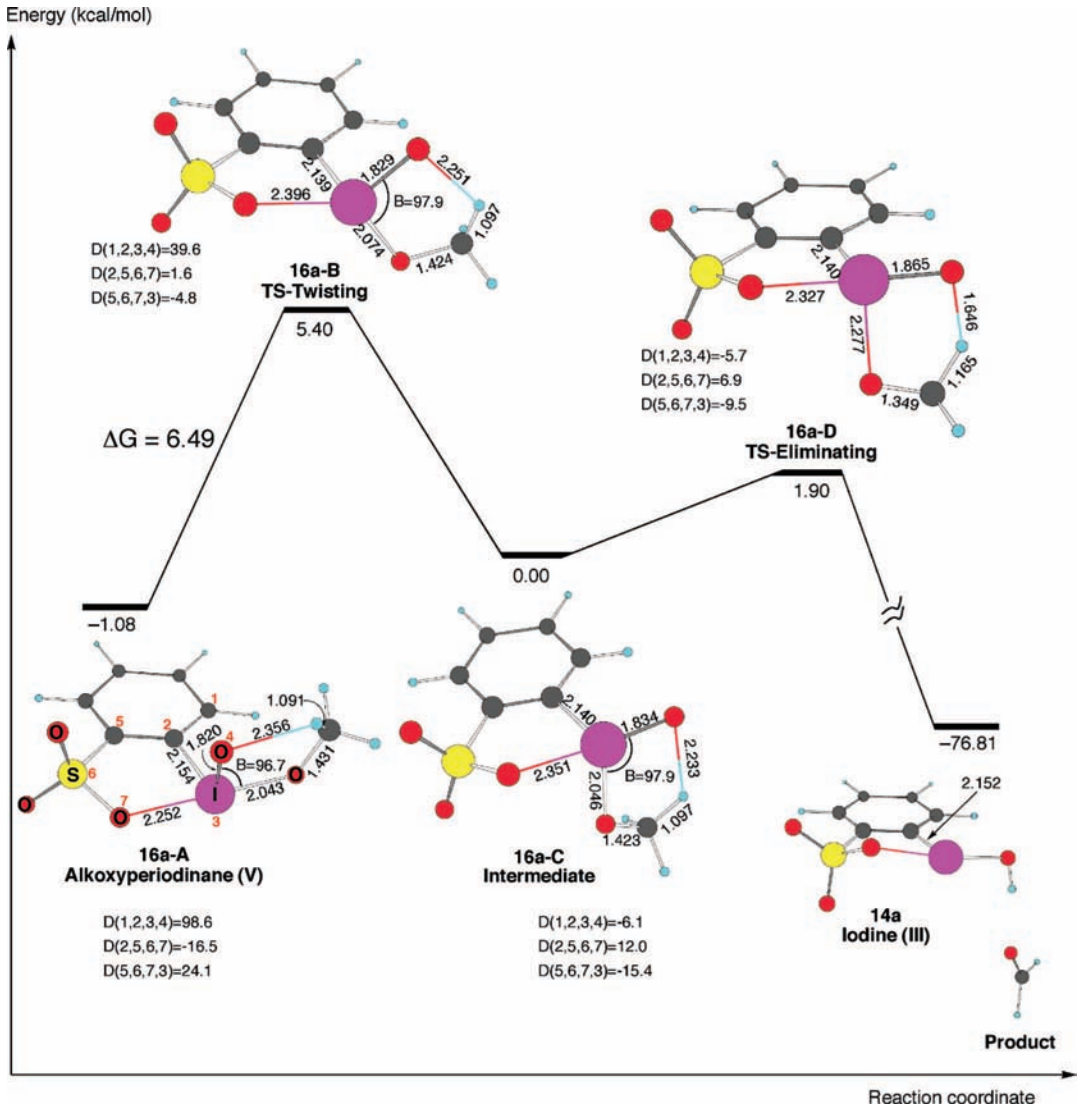


Figure 8. Free energy profiles relevant to **16a→14a**. Gibbs free energies (kcal/mol), selected bond lengths (Å), bite angles (B, °), and dihedral angles (D, °) for optimized structures **16a-A**−**16a-D** and **14a** are shown.

rate-determining disproportionation step (**15a→13a**).[8,23] The catalytic cycle of **1a**, which was prepared *in situ* from **2a**, could be accomplished by regenerating **1a** through the oxidation of **13a** with Oxone.[8]

The initial oxidation rate of alcohols using **2a** as a precatalyst was relatively slower than that using **1a** isolated (Figure 5). The oxidation rate of alcohols was accelerated under nonaqueous conditions, because powdered Oxone was further ground-up by mechanical stirring during the oxidation reaction (Figures 15). It was experimentally confirmed that IBS (**6a**) as well as **1a** were the true active species and the intramolecular relationship between the "I(V)" and "SO_3H" groups of **6a** was essential in our new catalytic system (Scheme 4, see Supporting Information). The catalytic cycle of IBS-catalyzed oxidation should be essentially identical to that of IBX.

The oxidation of **4a** with **1a** or **1g** as a stoichiometric oxidant in nitromethane at 30 °C gave **5a** in similar yields, although **1g** was superior to **1a** for the catalytic oxidation (Figure 1 vs Scheme 6). These results indicated that the electron-donating groups on IBX had no effect on the oxidation step in the reaction of alcohols with IBX. In contrast, IBS (**6a**) was not stable enough to isolate in pure form and examine in stoichiometric reactions.[17] Thus, we could not compare IBS with IBX as stoichiometric oxidants.

The substituent effect of **7** on the oxidation of **7** with Oxone to I(III) species **14** and I(V) species **6** was also confirmed by ^{1}H experiments in D_2O, because **7**, **14**, **6**, and Oxone were not dissolved completely in other solvents except for water (Scheme 7). The oxidations of **7g** to I(III) species **14g** and I(V) species **6g** were faster than those of **7a**. These results indicated that the electron-donating group on IBS accelerated the regeneration of **14a** to **6a**. Unfortunately, we could not compare the regeneration rates of IBS and IBX, due to the insolubility of **13a** in D_2O. Nevertheless, it was reasonable that the rate-determining step of I(V)-catalyzed oxidations might be the regeneration of I(V) speices, because the catalytic oxidation of alcohols was accelerated with powdered Oxone (Figure 4A). However, we could not rule out the possibility of the disproportionation step as the rate-determining step, without experimental evidence.

(21) For the oxidation of alicyclic ketones with Oxone in the presence of wet-alumina to the lactones, see: Hirano, M.; Oose, M.; Morimoto, T. *Chem. Lett.* **1991**, 331.

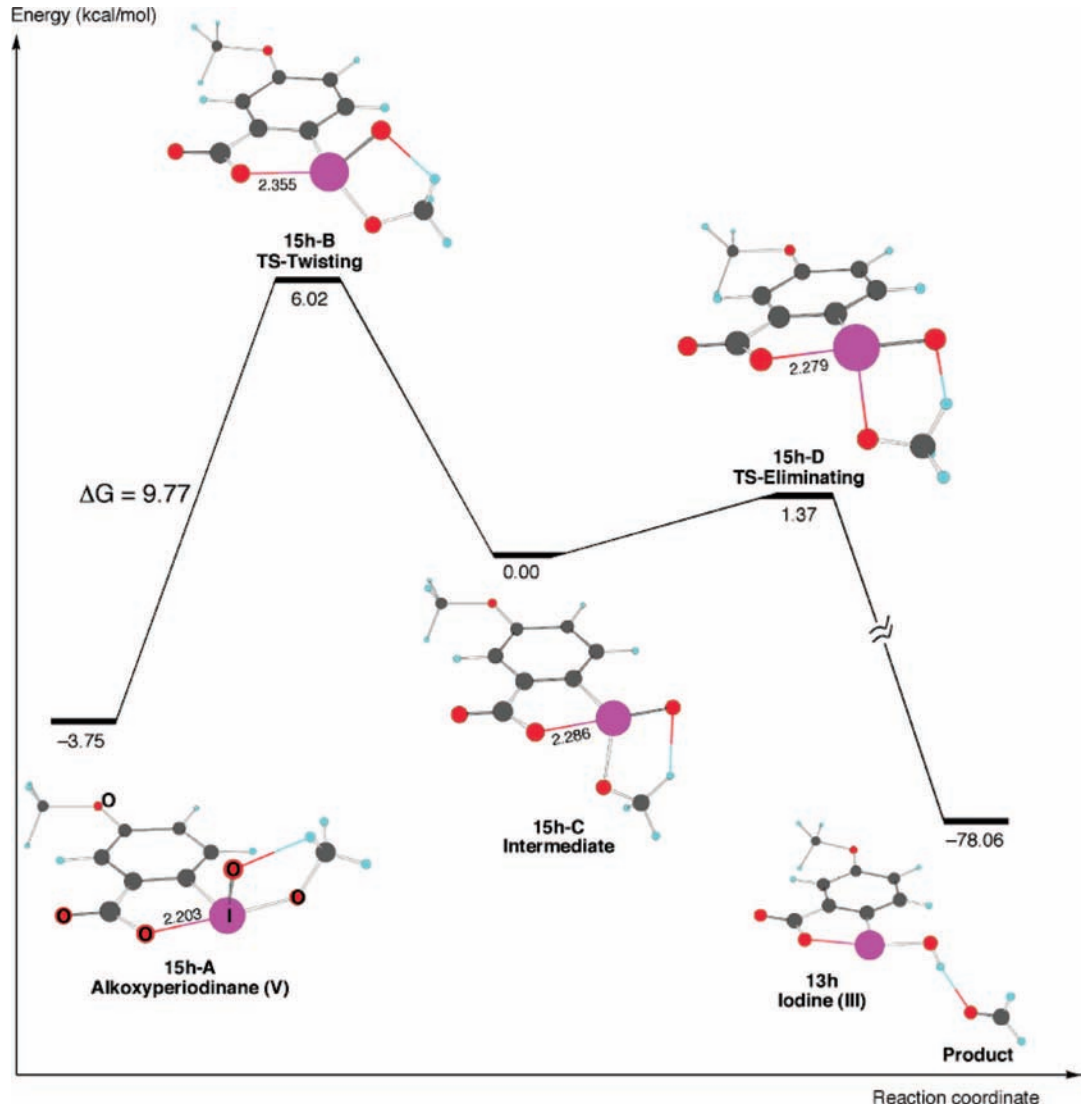


Figure 9. Free energy profiles relevant to **15h→13h**. Gibbs free energies (kcal/mol) and selected bond lengths (Å) for optimized structures **15h-A**−**15h-D** and **13h** are shown.

The *ortho*-sulfo group of IBS functions dually as *activator* and *deactivator*. The *ortho*-sulfo group as deactivator would decrease the electron density of the iodine(I) center, and the oxidation rate of iodine(I)→I(III)→I(V) would be lowered. In contrast, when IBS was generated, the *ortho*-sulfo group as activator would increase the Lewis acidity and oxidizing power of the iodine(V) center.[18] Because IBS-catalyzed oxidation of alcohols was much faster than that with IBX, the regeneration of IBS should be faster than that of IBX. IBS might be generated through an intramolecular oxygen transfer from the 1-peroxysulfo group to the 2-iodo(I or III) group. On the other hand, IBX might be generated through an intramolecular oxygen transfer from the 1-peroxycarboxyl group to the 2-iodo(I or III) group or an intermolecular oxygen transfer from Oxone to the 2-iodo(I or III) group. However, we could not rule out the possibility that Brønsted acidity of the 1-sulfo group might activate the regeneration of IBS.

Goddard has proposed that *hypervalent twisting* is the rate-determining step for oxidation of alcohols with stoichiometric amounts of IBX. According to Goddard's explanation, hypervalent twisting is a coordinated motion of the ligands attached to iodine driven by the necessity of generating a stable and planar form of IBA (**13a**) from its precursor alkoxyperiodinane intermediate **15a-A** (**15a-A**→**15a-C**, Figure 6).[10] After acid-catalyzed water/alcohol exchange on IBX (**1a**), alkoxyperiodinane **15a-A** must twist to its isomeric structure **15a-C** to eliminate the carbonyl compound to form planar compound **13a** (Figure 6).[10]

Based on Goddard's theoretical study on the oxidation of alcohols with IBX (**1a**),[10] each of the geometries of intermediates and transition states in the disproportionation steps **15a**→**13a**, **15h**→**13h**, and **16a**→**14a** were optimized by DFT calculations. These results are summarized as free energy profiles in Figures 79. Because alkoxyperiodinane **15a-A** should be favored in the reversible water/alcohol exchange under nonaqueous conditions, we excluded the ligand-exchange step from the calculation. The twisting steps from alkoxyperiodinanes **15-A** and **16-A** to the intermediates **15-C** and **16-C** were the rate-limiting steps, in agreement with Goddard's results.[10] Interestingly, **16a** has a much lower twisting barrier than **15a** (10.3 kcal/mol for **15a-A**→**15a-B** vs 6.5 kcal/mol for **16a-A**→**16a-B**). Although **15h** also has a lower twisting barrier than **15a**, the difference between the two twisting barriers was not

so large (9.8 kcal/mol for **15h-A**→**15h-B**). The hypervalent iodine−oxygen(7) atom distances in **15a-A**, **16a-A**, and **15 h-A** are correlated with the twisting barriers: 2.252 Å for **16a-A** > 2.203 Å for **15 h-A** > 2.193 Å for **15a-A**. This tendency suggests that the intramolecular hypervalent iodine−oxygen(7) bond of **16a-A** is more ionic than that of **15a-A**, and the weaker bond is more favorable for the twisting step. After twisting, the elimination steps from the intermediates **15-C** and **16-C** to **13a** or **14a** occur over low barrier (Figures 79). Notably, the elimination barrier would be correlated to the Lewis basicity of the oxo ligand of iodine (I═O): **15 h-D** > **15a-D** > **16a-D**. Thus, the Lewis basicity of I═O would be increased by the substitution of electron-donating groups (MeO and Me) on IBX.

Electron-donating groups on IBXs had no effect on the oxidation of alcohol (Scheme 6). These experimental results were supported by theoretical calculations (Figure 7 vs 9; the twisting barriers of **15a** and **15h** had very similar values). In contrast, electron-donating groups on IBS activated the catalyst regeneration step (Scheme 7). Furthermore, theoretical calculations indicated that IBS should be a stronger oxidant than IBX (Figure 7 vs 8).

In conclusion, electron-donating group-substituted IBXs such as 5-Me-IBX (**1g**), 5-MeO-IBX (**1h**), and 4,5-Me_2-IBX (**1i**) were superior to IBX (**1a**) as catalysts for the oxidation of alcohols with Oxone under nonaqueous conditions, although Oxone is nearly insoluble in most organic solvents. The catalytic oxidation proceeded more rapidly and cleanly in nitromethane. Furthermore, IBS (**6a**), which was generated *in situ* from **7a** and Oxone, was much more active than modified IBXs. Thus, we succeeded in developing a highly efficient and selective oxidation of primary or secondary alcohols to aldehydes, carboxylic acids, ketones, and α,β-cycloalkenones with powdered Oxone promoted by the catalytic use of **7a** or **7a**·Na under nonaqueous conditions. After the reaction was complete, Oxone wastes could be removed by simple filtration. On the basis of theoretical calculations, it was supposed that the relatively ionic character of the intramolecular hypervalent iodine−OSO_2 bond of IBS might lower the twisting barrier of the alkoxyperiodinane intermediate **16**. It was confirmed that Goddard's *hypervalent twisting* would be rate-determining for *stoichiometric* oxidation of alcohols with not only **1a** but also **1h** and **6a**. In contrast, it was reasonable that the rate-determining step of *I(V)-catalyzed* oxidations might be the regeneration of I(V) speices, because the catalytic oxidation of alcohols was accelerated with powdered Oxone. This new protocol should be registered as a practical method for the oxidation of not only simple but also diverse alcohols bearing functional or protective groups.

Computational Details

Theoretical calculations were performed using the Gaussian03[24] programs. The geometries of the stationary points were optimized in gradient-corrected density functional theory (DFT) calculations with Becke's three-parameter exchange with the Lee, Yang, and Parr correlation functional (B3LYP).[25] For iodine atom, effective core potentials (ECPs) were used. In the present research, we adopted the Stuttgart/Dresden double-ζ (SDD) ECP basis sets.[26] In these basis sets, the core electrons (46 for I) for iodine atom are replaced by ECP, which include relativistic effects that are known to be important for the heavy atoms. For the valence electrons (7 for I), the SDD ECP basis sets can be designated (4s5p/2s3p). The 6-311+G(3df) basis set was used for S, and the 6-311+G(2df,2p) basis set was used for C, O, and H. Appropriate vibrational analyses were also carried out at the same level of theory. The nature of the stationary points was then checked by counting no imaginary frequency for stable species and a single such frequency for transition states. Starting from the harmonic frequencies, thermal corrections, enthalpies, and Gibbs free energies were computed using standard statistical approaches. Transition-state geometries and confirmation calculations, involving intrinsic reaction coordinate (IRC) calculations, were performed to identify the pathways between transition states and their connecting minima.

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Supporting Information Available: Experimental procedures, full characterization of new compounds, Cartesian coordinates of stational point structures in calculation, and complete ref 24. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) To the best of our knowledge, there are only two examples on the direct catalytic oxidative dehydrogenation of carbonyl compounds. (a) Pd catalyst with Cu co-catalyst: Theissen, R. J. *J. Org. Chem.* **1971**, *36*, 752. (b) Pd catalyst with stoichiometric allyl diethyl phosphate reagents in the presence of stoichiometric bases: Shvo, Y.; Arisha, A. H. I. *J. Org. Chem.* **1998**, *63*, 5640.

(23) Munari, S. D.; Frigerio, M.; Santagostino, M. *J. Org. Chem.* **1996**, *61*, 9272.

(24) Frisch, M. J.; et al. *Gaussian 03*, revision D.02; Gaussian, Inc.: Wallingford, CT, 2004.

(25) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *96*, 5648. (b) Stevens, P. J.; Devlin, J. F.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1998**, *B 37*, 785.

(26) Andrae, D.; Haüssermann, U.; Dolg, M.; Stoll, H.; Preuss, H. *Theor. Chim. Acta* **1990**, *77*, 123.