Facile and Clean Oxidation of Alcohols in Water Using Hypervalent Iodine(III) Reagents

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Abstract: The facile and efficient oxidation of various alcohols such as benzylic alcohols, primary alcohols, secondary alcohols, and diols in water using the hypervalent iodine(III) reagent, iodosobenzene (PhI=O), with KBr is described. Electrospray ionization (ESI) mass spectrometric studies on the behavior of PhI=O-KBr in aqueous solution suggested that these reactions are induced by the formation of highly reactive iodine species $[PhI(Br)_nO^-]$. Further development to recyclable polymer-supported iodine(III) reagent extends the utility of this reaction to afford an environmentally benign method.

Keywords: alcohols; hypervalent compounds; iodine; oxidation; water as solvent

Introduction

Oxidation of alcohols to carbonyl compounds is a pivotal reaction in organic chemistry and numerous methods using a variety of reagents and conditions have been developed. Recent demands for eco-conscious chemical processes have encouraged the development of several clean and practical oxidation reactions,[1] and promote further development of high-yielding, clean, mild, safe, and economical methods for the oxidation of alcohols. Hypervalent iodine reagents have been used extensively in organic syntheses due to their low toxicity, ready availability and easy handling.[2] For example, the highly utilized pentavalent iodine reagents such as Dess–Martin periodinane (DMP)[3] and *o*-iodoxybenzoic acid (IBX)[4] mildly and efficiently oxidize alcohols to carbonyl compounds with high yields in organic solvents such as CH_2Cl_2, DMSO, and acetone. However, despite their utility, iodine(V) reagents are potentially explosive, cannot be stored for a long time, and the iodine(III) compounds (iodosobenzoic acid) generated after DMP (or IBX)-induced oxidations are usually not utilized for oxidation reactions. Therefore, facile and efficient use of the readily available and relatively stable iodine(III) reagents, in place of iodine(V) reagents, has been long desired. As part of our continued studies concerning the activation of trivalent iodine reagents using several additives and solvents,[5] we have briefly communicated a mild and efficient oxidation of alcohols using iodosobenzene (PhI=O) with an inexpensive inorganic salt, KBr, in water under neutral conditions and its extension to an environmentally benign oxidation process using poly(diacetoxyiodo)styrene (PDAIS).[6] In this paper, we present a full account of our studies on iodine(III)-induced oxidation of various alcohols such as benzylic alcohols, primary alcohols, secondary alcohols, and diols catalyzed by bromide salt in water, and a mechanistic consideration of reactive iodine species from the basis of ESI mass spectrometry (MS).

Results and Discussion

Oxidation of Benzylic, Primary and Secondary Alcohols

In contrast to oxidations with iodo(V)-based reagents such as DMP and IBX, only a few examples of the oxidation of alcohols using iodine(III) reagents have been described.[7] Existing oxidation methods are limited to organic solvents and usually involve activation of transition metal catalysts such as Ru, Yb, Co, and Cr[7a, b,c] or 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO)[7d] by an iodine(III) co-oxidant. As an exception, readily oxidizable benzylic alcohol derivatives do not require catalysts,[8a] and can be oxidized using I(III)-Al_2O_3 under microwave irradiation.[8b]

Various aqueous oxidation reactions have been developed[9] since economic and environmental concerns encourage the use of water as a reaction medium. Recently, we have achieved a novel catalytic activation of PhI=O using a cationic surfactant, cetyltrimethylammonium bromide (CTAB) under neutral conditions.[10] The low solubility of PhI=O in water and in most organic solvents normally limits the use of PhI=O, however, our micellar and reversed micellar systems have expanded the choice of solvents (from non-polar solvents to water) for hypervalent iodine oxidation. Thus, we first examined the oxidation of alcohol using PhI=O/CTAB in water. Oxidation of 2-octanol (**1e**) catalyzed by CTAB (20 mol %) in water gave 2-octanone (**2e**) in 67% yield. Thus, we re-investigated the activation of PhI=O in this reaction with a variety of additives including alkali metal salts. As a result, the addition of bromide ions such as NaBr, KBr, and LiBr was found to remarkably activate PhI=O to give **2e** in good yields [94% yield (KBr)], while salts other than bromide (Na_nX: X = F, Cl, I, HSO_4, BF_4, CO_3, ClO_4, OAc, NO_3) did not catalyze the reaction effectively.[11] We therefore chose KBr, the most economical alkali metal bromide, for further studies. The oxidation of activated alcohols such as benzylic or allylic alcohols proceeds in excellent yields simply by activating PhI=O with a small amount of water (10 equiv.), and without addition of KBr (entries 1 – 3, Table 1). With benzyl alcohol (**1c**), the reaction rate is enhanced remarkably by adding a catalytic amount of KBr (entries 3 – 4, Table 1). In contrast, a catalytic amount of KBr is indispensable for the oxidation of saturated primary and secondary alcohols (Table 1). This PhI=O/KBr system is applicable to the oxidation of various primary and secondary alcohols in water to directly afford the corresponding carboxylic acids and ketones in good yields. The results are listed in Table 1.

When using 1.1 equiv. PhI=O in the presence of 1.0 equiv. KBr, oxidation of primary alcohol **1k** yielded only carboxylic acid **2k** (28 % yield of **2k** and 68% of recovered **1k** for 5 h at r.t.) without yielding the corresponding aldehyde.

Oxidation of Diols to Lactones

During investigation of the above-mentioned reactions, we found that an oxidative condensation of primary alcohols mainly occurs as the water content decreases. For instance, oxidation of 1-pentanol (**1k**) using PhI=O/KBr afforded pentyl pentanoate **3a** in 77% yield along with 23% yield of pentanoic acid **2k** in the presence of water (10 equiv.). However, in the absence of water, the reaction rate slowed down due to the lowering of the efficiency of stirring. Thus, we subsequently applied this methodology to the oxidation of diols to lactones. Although many methods to prepare lactones by oxidative condensation of diols have been performed using various stoichiometric oxidants, enzymes, and transition metal catalysts, most of them have been carried out in organic solvents or aqueous organic solvents. Furthermore, the oxidations of diols, reported by Corey et al.,[12a] Bueno et al.,[12b] and Metz et al.[12c] in DMSO or CH_2Cl_2 using I(V) reagents, such as IBX and DMP, yield

Table 1. Oxidation of alcohols **1** (for structures, see Figure 1) with PhI=O/KBr in H_2O.

Entry	Substrate	Product	KBr [equiv.]	Time [h]	Yield [%][a]
1	**1a**	**2a**	none	30	quant.[b]
2	**1b**	**2b**	none	6	78(94)[d, e]
3	**1c**	**2c**	none	24	87[e]
4	**1c**	**2c**	0.2	2	quant.
5	**1d**	**2d**	1.0	4	quant.[e]
6	**1e**	**2e**	none	48	trace
7	**1e**	**2e**	0.2	24	94[e]
8	**1e**	**2e**	1.0	8	98[e]
9	**1f**	**2f**	1.0	4	quant.
10	**1g**	**2g**	1.0	3	quant.[e]
11	**1h**	**2h**	1.0	24	86
12	L-menthol **1i**	L-menthone **2i**	1.0	7	quant.[e]
13	3β-cholestanol **1j**	5α-cholestan-3-one **2j**	1.0	4	quant.
14	**1k**	**2k**	none	48	–[c]
15	**1k**	**2k**	1.0	5	83[c, e,f]
16	**1l**	**2l**	1.0	12	86[c, e,f]
17	**1m**	**2m**	1.0	3	92[c]
18	**1n**	**2n**	1.0	12	72[c, f]
19	**1o**	**2o**	1.0	3	70[c, f]
20	**1p**	**2p**	0.2	3	60[c, f]

[a] Yields are an average of two or more runs. Isolated yields unless otherwise noted.
[b] 2.5 equivalents of PhI=O were used.
[c] 3.0 equivalents of PhI=O were used.
[d] Yield in parenthesis is based on the consumed starting material.
[e] Yields were determined by GC.
[f] Small amount of ester was also obtained by oxidative condensation.

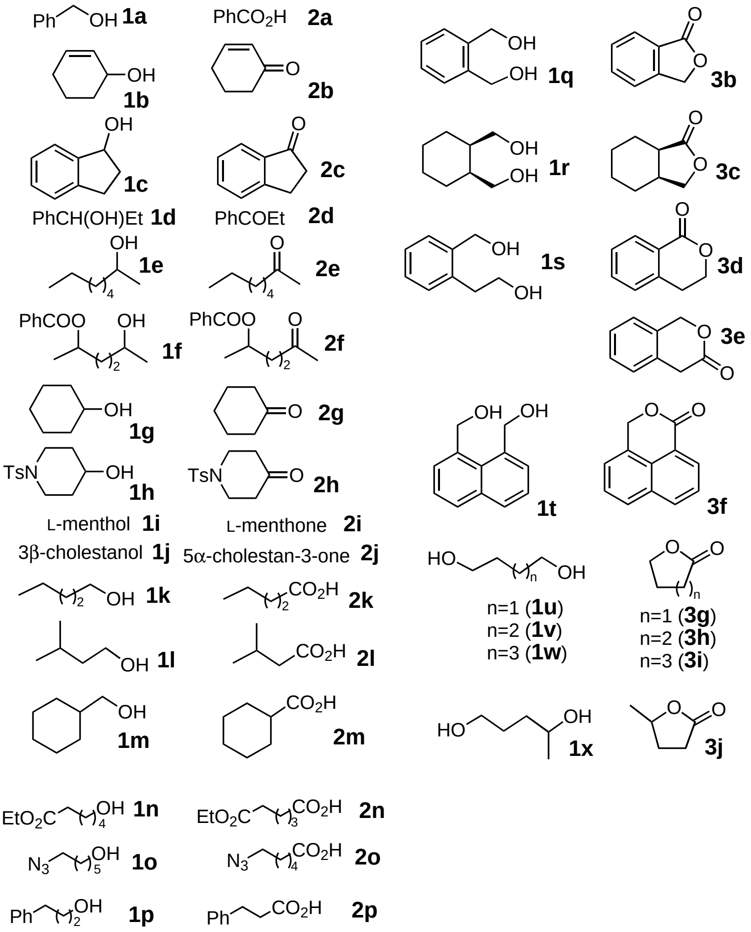


Figure 1. Structures of alcohols **1** investigated and the corresponding products **2** or **3.**

the corresponding lactol derivatives. First, we examined the oxidation of cyclic diols in the presence of a small amount of water (10 – 20 equiv.). Consequently, oxidation of various cyclic diols fixed by aromatic or aliphatic rings gave the corresponding lactones in good yields (entries 2 – 6, Table 2). On the other hand, oxidation of acyclic diols using PhI=O/KBr exclusively yielded 5- and 6-membered ring lactones (entries 9, 10, 12, Table 2). However, the yield of the 7-membered ring lactone **3i** was 49% due to accompanying formation of 6-hydroxycaproic acid (33% yield) and adipic acid (18% yield) under the reaction conditions (entry 11, Table 2). Addition of KBr was indispensable for the oxidation of saturated diol **1u** (entry 7, Table 2), while oxidative lactonization of benzylic diol **1q** proceeded slowly in the absence of KBr (entry 1, Table 2). This reaction also proceeded under diluted reaction conditions. However, an increase of the water content prolonged the reaction time.[13]

Mechanistic Study: Detection of Reactive Intermediate in Water

Regarding the behavior of iodine(III) reagents such as [hydroxy(mesyloxy)iodo]benzene and [hydroxy(tosyloxy)iodo]benzene in aqueous solution, Richter et al. demonstrated the presence of μ-oxodiiodine(III) species on the basis of UV-Vis and NMR spectroscopic measurements along with potentiometric titration data.[14] However, in our case, the addition of bromide salt complicated the mechanism. Thus, we considered the following three reaction mechanisms: (1) *in situ* generation of I(V) species by disproportionation of PhI=O to $PhIO_2$ and PhI in water, (2) *in situ* generation of bromine or bromonium ion by iodine(III)-induced oxidation of bromide ion, and (3) the formation of activated I(III) species that contain I-Br bonding. To identify the nature of the reactive species, first, we examined the oxidation of **1e** using $PhIO_2$/KBr, Br_2, and NBS. Consequently, only a trace amount of **2e** was obtained when using $PhIO_2$/KBr even after 24 h. This result meant that simple disproportionation of PhI=O does not occur. On the other hand, the reaction proceeded slowly when using Br_2 or NBS and afforded **2e** in 30% or 64% yield after 24 h. However, in both

Table 2. Oxidation of diols **1q – x** (See Figure 1) with PhI=O/KBr.

Entry	Substrate	Product	KBr [equiv.]	Time [h]	Yield [%][a]
1	**1q**	**3b**	none	24	54 (**1q**: 23)
2	**1q**	**3b**	0.2	5	89
3	**1q**	**3b**	1.0	2	91
4	**1r**	**3c**	1.0	3	quant.
5	**1s**	**3d** + **3e**	0.2	2	79 (**3d**:**3e** = 15:2)
6	**1t**	**3f**	1.0	7	92[b]
7	**1u**	**3g**	none	24	–
8	**1u**	**3g**	0.2	8	quant.[c]
9	**1u**	**3g**	1.0	3	quant.[c]
10	**1v**	**3h**	1.0	4	89[c]
11	**1w**	**3i**	1.0	6	49[c]
12	**1x**	**3j**	1.0	6	87[c]

[a] Yields are an average of two or more runs. 2.5 equivalents of PhI = O were used. Isolated yields unless otherwise noted.
[b] 3.0 equivalents of PhI=O were used.
[c] Yields were determined by GC.

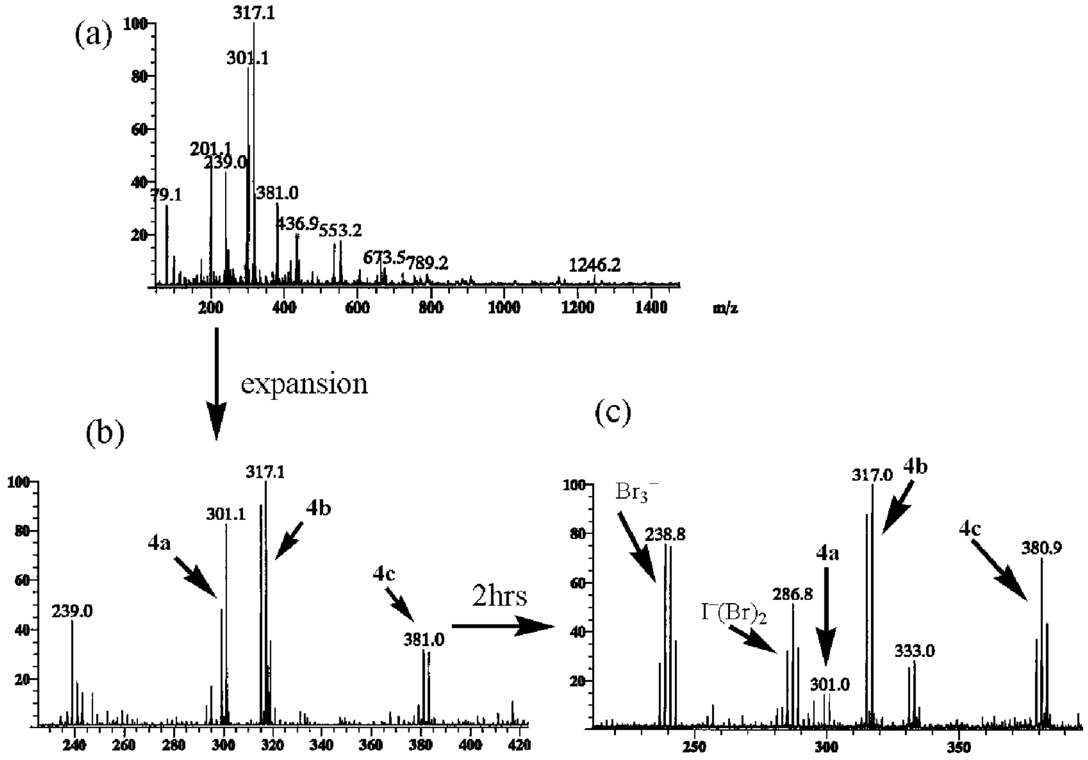


Figure 2. ESI-mass spectrum of reactive intermediates.

cases, brominated by-products were also obtained along with the recovery of **1e**. To clarify whether the actual reactive species are I-Br species or simple Br^+, next, we measured an ESI-mass spectrum of the aqueous solution of PhI=O/KBr in the absence of substrate. To measure the ESI-mass spectrum at room temperature, which is the same temperature as the reaction conditions, we adopted a technique using coldspray ionization (CSI)-MS, which was recently developed by Yamaguchi et al.,[15] since disproportionation of PhI=O seems to occur readily under normal ionization conditions (100 °C). Consequently, $PhIO^-(Br)$ (**4a**), $PhI(O^-)_2Br$ (**4b**) and $PhIOH(Br)_2$ (**4c**) were clearly detected by ESI negative ion detection (Figure 2). To ensure the presence of these species, we then examined the behavior of 4-iodosylanisole in an analogous aqueous solution by ESI negative ion detection (Figure 3). As expected, the analogous reactive species, $(p\text{-MeO})C_6H_4IO^-(Br)$, was detected. Furthermore, ESI positive ion detection of PhI=O/KBr in water showed that the activated species form oligomeric structures probably due to hydrophobic effects. Generation of Br_2 was not detected under the

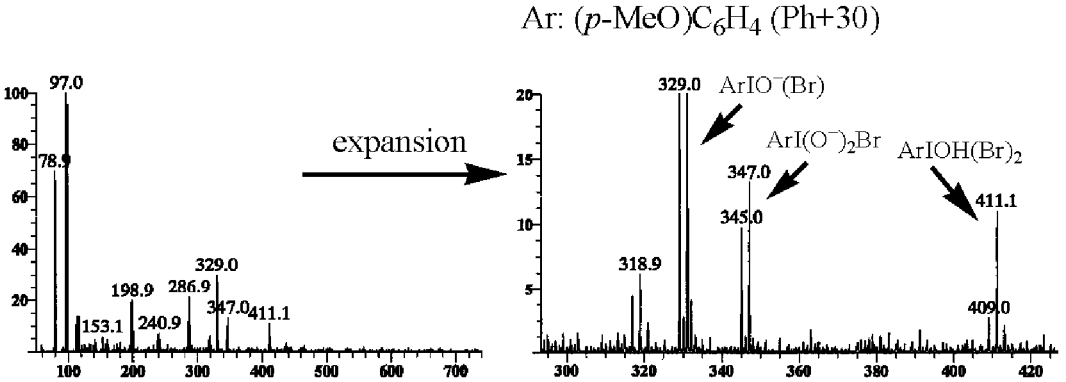
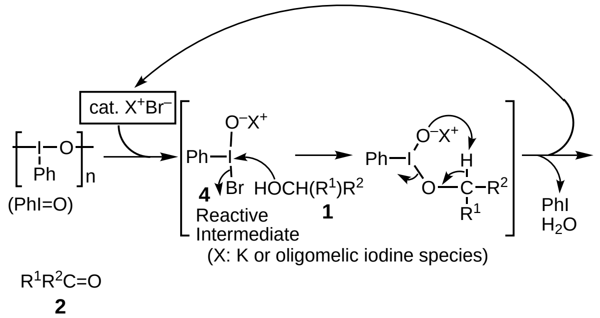


Figure 3. Detection of analogous reactive intermediates of (p-MeOC_6H_4)I=O/KBr by ESI-MS.

conditions for ESI-MS measurement, although detection of Br_2 was reported when phenyliodine(III) diacetate (PIDA) had been reacted with TMSBr in CH_2Cl_2.[11b] Therefore, at present, on the basis of above-mentioned experimental results and ESI-MS, the reagent containing an I-Br bond forms the reactive intermediate, while it is not clear whether I(III), Br(I), or mixed-valent iodine species are more likely to be the actual reactive intermediate. I(I) $[I^-(Br)_2]$ species similar to that reported by Kirschning et al.[16] also seemed to be a possible reactive intermediate from the basis of the ESI-MS. However, $I^-(Br)_2$ was found to be a decomposed product since a stoichiometric amount of PhI was always generated from the reactions, and polyiodostyrene was recovered quantitatively in the oxidation using PDAIS. In fact, the peak corresponding to $I^-(Br)_2$ appeared on allowing the reaction solution to stand for 2 h (Figure 2, c). Accordingly, in the presence of alcohols **1**, the reaction of **1** with **4** is expected to occur immediately without generating $I^-(Br)_2$.

Finally, a plausible reaction mechanism for the catalytic activation of PhI=O with KBr was deduced, and is depicted in Scheme 1. In this mechanism, polymeric iodosobenzene is initially decomposed to an oligomeric form by the addition of KBr to form the highly reactive intermediate **4**. Then, **4** reacts with alcohols **1** to yield the corresponding carboxylic acids or ketones with regeneration of KBr. This suggests that the activation of PhI=O with KBr involving **4** is very different from the mechanism involving transition metals or TEMPO, because in the latter cases, the metal oxide or N-oxoammonium salt functions as the reactive species.

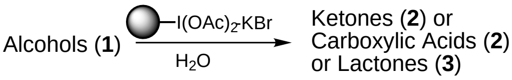


Scheme 1. A plausible reaction mechanism for the oxidation of alcohols.

Environmentally Benign Oxidation Reactions using a Polymer-Supported I(III) Reagent, PDAIS

Next, we modified this system to develop a practical and clean procedure for the oxidation of alcohols using a polymer-supported hypervalent iodine(III) reagent. Solid and polymer-supported reagents have applications in combinatorial chemistry, and the uses of such operationally simple and environmentally benign reagents are becoming more and more important in the pharmaceutical and agrochemical industries. Several polymer-bound oxidants have been reported,[17] and polymer-supported hypervalent iodine reagents should be a welcome addition due to their versatility, low toxicity, and high yields. Recently, Togo et al.,[18] Ley et al.,[19] and we[20] demonstrated that both poly(diacetoxyiodo)styrene (PDAIS)[21] and polybis(trifluoroacetoxyiodo)styrene (PBTIS)[19b,20a] show similar reactivity to phenyliodine(III) diacetate (PIDA) and phenyliodine(III) bis(trifluoroacetate) (PIFA), respectively, and utilized them in organic solvents as a replacement for the previously reported iodine(III) reagents. A method for the oxidation of alcohols using DMP with a thiosulfate resin was recently reported by Parlow et al.[22] but this required an excess amount of reagent. We re-examined the oxidation using PDAIS in water. The oxidation of saturated secondary alcohols using 1.1 equivalents of PDAIS and 0.2 equivalents of KBr proceeded in water at room temperature in a few hours to give the corresponding carbonyl compounds **2** in excellent yields (Table 3). In the oxidation of primary alcohols, the reaction rate was remarkably enhanced by heating at 80 °C (entries 8 – 11, Table 3). The present reaction was also found to be applicable to the oxidation of diols to the corresponding lactones (entries 12 – 14,

Table 3. Oxidation of alcohols **1** (see Figure 1) with PDAIS/KBr in H_2O.



Entry	Substrate	Product	KBr [equiv.]	Time [h]	Yield [%][a]
1	**1a**	**2a**	0.2	24	quant.[c]
2	**1d**	**2d**	0.2	4	quant.[b, c]
3	**1e**	**2e**	0.2	7	quant.[b, c]
4	**1e**	**2e**	0.2	7	93[b, c] (cycle 2)
5	**1e**	**2e**	0.2	7	91[b, c] (cycle 3)
6	**1g**	**2g**	0.2	3	86[b, c]
7	**1i**	**2i**	0.2	20	86[b, c]
8	**1k**	**2k**	1.0	12	91[b, d,e, f]
9	**1n**	**2n**	1.0	7	92[d, e,f]
10	**1o**	**2o**	1.0	8	74[d, e,f]
11	**1p**	**2p**	1.0	10	82[d, e,f]
12	**1q**	**3b**	1.0	3	88[d]
13	**1r**	**3c**	1.0	12	quant.[d]
14	**1u**	**3g**	1.0	10	93[b, d]

[a] Yields are an average of two or more runs. Isolated yields unless otherwise noted.
[b] Yields were determined by GC.
[c] 1.1 equivalents of PDAIS were used.
[d] 2.5 equivalents of PDAIS were used.
[e] Small amount of ester was also obtained by oxidative condensation.
[f] Reaction was carried out at 80 °C.

Table 3). Furthermore, the iodinated resin could be regenerated and recycled successfully without loss of activity (entries 3 – 5, Table 3). We also unexpectedly found that water is a suitable solvent for PDAIS-induced oxidation, and that PDAIS has considerable stability in water.[23] Since both water and Br^- are indispensable for reaction progression,[24] this reaction might also be proceeding *via* a reactive intermediate similar to **4** formed by ligand exchange of diacetate. However, considering that the reactivity of PDAIS is similar to that of PIDA, the mechanism *via* the formation of bromate(I) complex or BrOAc might also be possible.[16b,24]

The positive features of the use of PDAIS are summarized as follows: 1) ease of operation; 2) facile recyclability of the polymer-supported iodine(III) reagent; ease of re-oxidation of the recovered resin (polyiodostyrene) with peracetic acid (30% H_2O_2 and Ac_2O) and repeated use without loss of activity; 3) excellent yields; 4) environmental consciousness, such that no organic solvent is used in the reaction and only a small amount is needed in the work-up.

Conclusions

We have achieved a clean and efficient oxidation of alcohols using a mild and non-toxic oxidant, PhI=O, with KBr in water, and were able to detect the reactive intermediates by ESI-MS for the first time. Further expansion of the method using a polymer-supported I(III) reagent, PDAIS, enabled recycling of the oxidant as well as facile work-up. The present procedure will provide a facile and environmentally benign method for the catalytic activation of a variety of sluggishly reactive and/or sparsely soluble hypervalent iodine reagents in water under neutral conditions.

Experimental Section

General Remarks and Starting Materials

All melting points are uncorrected. Infrared (IR) absorption spectra (cm^{-1}) were recorded on a Shimadzu FTIR-8400 instrument. ^1H NMR (and ^{13}C NMR) spectra were recorded on JEOL JNM-EX 300 and JEOL JNM-EX 270 spectrometers with TMS as an internal standard. Analytical gas chromatography (GC) was carried out on a Shimadzu GC-1700 gas chromatograph with an HP-5 column (0.32 mm × 30 m, cross-linked 5% PH ME siloxane, Hewlett Packard) using helium as carrier gas. ESI-MS was carried out on a JEOL JMS-LCmate. Merck silica gel 60 was used for column chromatography, and E. Merck pre-coated TLC plates and silica gel F_{254} were used for preparative thin-layer chromatography. PhI=O was purchased from Tokyo Chemical Industry Co., Ltd. (TCI). Other commercially available compounds **1a – e**, **1g**, **1i – n**, **1p**, **1r**, **1t – x**, and KBr were purchased from Aldrich and TCI, and were used without further purification. Compounds **1f**,[25] **1o**,[26] **1q**,[27] and **1s**[28] were prepared according to known procedures. Compound **1h** was prepared by tosylation of 4,4-piperidinediol hydrochloride, followed by reduction with sodium borohydride. Oxidation products **2a – e**, **2g**, **2i – n**, **2p**, **3b**, **3e**, **3g – j** were identified by comparison with commercial samples. The known products **2f**,[25] **2o**,[29] **3c**,[30] **3d**,[31] and **3f**[30] were characterized by comparing their spectral and physical data with the literature values. Poly(diacetoxyiodo)styrene, PDAIS, was prepared by known procedures.[18a,21a]

A few corrections of both the reaction conditions and yields have been made in the oxidation of primary alcohols with PDAIS as well as PhI=O, because the ratio of carboxylic acid to ester was variable (that is, ester was sometimes obtained by an oxidative condensation reaction in $>40\%$ yield) and depended upon the efficiency of stirring under our previous conditions.[6] Therefore, we re-examined and optimized the reaction conditions leading to a more reliable and reproducible oxidation of primary alcohols.

5-Benzoyloxy-2-hexanol (1f):[25] Colorless oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.21$ (d, $J = 6.2$ Hz, 3H), 1.36 (d, $J = 6.2$ Hz, 3H), 1.52 – 1.86 (m, 6H), 3.83 (m, 1H), 5.16 – 5.20 (m, 1H), 7.29 – 7.57 (m, 3H), 8.03 – 8.05 (m, 2H); IR (KBr): $\tilde{\nu} = 3371$, 2972, 1713, 1277, 712 cm^{-1}; MS: $m/z = 222$ [M^+], 123, 105, 77; HRFABMS: m/z calcd. for $C_{13}H_{19}O_3$ ($M^+ + H$): 223.1334; found: 223.1317.

1-(4-Toluenesulfonyl)-4-piperidinol (1h): Colorless crystals; mp 130 – 132 °C (Et_2O); ^{1}H NMR ($CDCl_3$): $\delta = 1.37$ (d, $J = 4.2$ Hz, 1H), 1.58 – 1.71 (m, 2H), 1.90 – 1.96 (m, 2H), 2.43 (s, 3H), 2.81 – 2.88 (m, 2H), 3.27 – 3.35 (m, 2H), 3.74 – 3.78 (m, 1H), 7.32 (d, $J = 8.2$ Hz, 2H), 7.65 (d, $J = 8.2$Hz, 2H); IR (KBr): $\tilde{\nu} = 3557$, 2930, 1307, 1165, 729 cm^{-1}; MS: $m/z = 255$ [M^+]; anal. calcd. for $C_{12}H_{17}NO_3S$: C 56.45, H 6.71, N 5.49, S 12.56%; found: C 56.40, H 6.63, N 5.43, S 12.53%.

6-Azido-1-hexanol (1o):[26] Colorless oil; ^{1}H NMR ($CDCl_3$): $\delta = 1.38 – 1.42$ (m, 4H), 1.54 – 1.63 (m, 4H), 3.24 – 3.27 (m, 2H), 3.62 – 3.65 (m, 2H); IR (KBr): $\tilde{\nu} = 3329$, 2936, 2097, 1258, 1057 cm^{-1}; HRFABMS: m/z calcd. for $C_6H_{14}N_3O$ ($M^+ + H$): 144.1137; found: 144.1142.

1,2-Benzenedimethanol (1q):[27] Colorless crystal; mp 64 – 66 °C (Et_2O) (Lit. mp 64 – 65 °C); ^{1}H NMR ($CDCl_3$): $\delta = 3.25$ (br s, 1H), 4.70 (s, 4H), 7.32 (s, 4H); IR (KBr): $\tilde{\nu} = 3287$, 2882, 1454, 1005, 752 cm^{-1}; MS: $m/z = 138$ [M^+], 120, 91, 77.

2-Hydroxymethylphenethyl alcohol (1s):[28] Colorless oil; ^{1}H NMR ($CDCl_3$): $\delta = 2.94$ (t, $J = 5.9$ Hz, 2H), 3.88 (t, $J = 5.9$ Hz, 2H), 4.64 (s, 2H), 7.22 – 7.33 (m, 4H); IR (KBr): $\tilde{\nu} = 3317$, 2880, 1015, 750 cm^{-1}; MS: $m/z = 152$ [M^+], 134, 104, 77.

General Procedure for Oxidation of Benzylic Alcohols using PhI=O/KBr

H_2O (2.0 mmol) was added dropwise to a stirred mixture of allylic or benzylic alcohols **1a – d** (0.20 mmol) and PhI=O (0.50 mmol for **1a**; 0.22 mmol for **1b – d**). The mixture was stirred or sonicated for several hours while checking the reaction progress by gas or thin-layer chromatography. After completion, *n*-hexane (or AcOEt for **1a**) was added, the mixture was dried over Na_2SO_4, and then filtered. Evaporation of the solvent under vacuum afforded a crude product that was further purified by column chromatography (Et_2O/*n*-hexane) to give pure **2a – d** in the yields listed in Table 1. Yields of **2b – d** were determined by gas chromatography.

General Procedure for Oxidation of Secondary Alcohols using PhI=O/KBr

H_2O (2.0 mmol) was added dropwise to a stirred mixture of secondary alcohols **1e – j** (0.2 mmol), PhI=O (24.2 mg, 0.22 mmol), and KBr (23.8 mg, 0.2 mmol). The mixture was stirred or sonicated for several hours while checking the reaction progress by gas or thin-layer chromatography. After completion, *n*-hexane was added, the mixture was dried over Na_2SO_4, and then filtered. Evaporation of the solvent under vacuum afforded a crude product that was further purified by column chromatography [Et_2O (or AcOEt)/*n*-hexane] to give pure **2e – j** in the yields listed in Table 1. Yields of **2e**,**g**,**i** were determined by gas chromatography.

5-Benzoyloxy-2-hexanone (2f):[25] Colorless oil; yield: quant.; ^{1}H NMR ($CDCl_3$): $\delta = 1.28$ (d, $J = 6.1$ Hz, 3H), 1.91 (q, $J = 7.6$ Hz, 2H), 2.07 (s, 3H), 2.48 (dd, $J = 7.6$, 6.7 Hz, 2H), 5.09 (q, $J = 6.1$ Hz, 1H), 7.37 (dd, $J = 7.6$, 7.3 Hz, 2H), 7.46 – 7.52 (m, 1H), 7.96 (dd, $J = 7.0$, 1.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 20.2$, 29.8, 30.0, 39.5, 70.9, 128.3, 129.5, 130.4, 132.9, 166.1, 207.9; IR (KBr): $\tilde{\nu} = 1726$, 1717, 1277, 1133, 714 cm^{-1}; HRFABMS: m/z calcd. for $C_{13}H_{17}O_3$ ($M^+ + H$): 221.1178; found: 221.1154.

1-(4-Toluenesulfonyl)tetrahydro-4(1*H*)-pyridinone (2h): Colorless crystal; yield: 86%; mp 121 °C (Et_2O); ^{1}H NMR ($CDCl_3$): $\delta = 2.35$ (s, 3H), 2.42 – 2.47 (m, 4H), 3.27 – 3.32 (m, 4H), 7.26 (d, $J = 8.2$ Hz, 2H), 7.59 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 21.6$, 40.7, 45.9, 127.4, 129.8, 133.3, 144.0, 205.4; IR (KBr): $\tilde{\nu} = 1717$, 1362, 1337, 1165, 725 cm^{-1}; MS: $m/z = 253$ (M^+), 98; anal. calcd. for $C_{12}H_{15}NO_3S$: C 56.90, H 5.97, N 5.53, S 12.66%; found: C 56.87, H 5.93, N 5.55, S 12.67%.

General Procedure for Oxidation of Primary Alcohols using PhI=O/KBr

A suspension of PhI=O (132.0 mg, 0.6 mmol) and KBr (23.8 mg, 0.2 mmol) in H_2O (10 mL) was stirred for a few minutes at room temperature, then sonicated for a few minutes. Then, primary alcohol **1k – p** (0.2 mmol) was added to the mixture with stirring. After completion, AcOEt was added to the reaction mixture, then the mixture was acidified by a small amount of 1 N HCl, extracted with AcOEt, dried, and evaporated. The residue was purified by column chromatography on silica gel (AcOEt/*n*-hexane) to give **2k – p** in the yields listed in Table 1. Yields of **2k – l** were determined by gas chromatography.

6-Azido-1-hexanoic Acid (2o):[29] Colorless oil; yield: 70% (PhI=O); 74% (PDAIS); ^{1}H NMR ($CDCl_3$): $\delta = 1.34 – 1.42$ (m, 2H), 1.51 – 1.61 (m, 4H), 2.29 – 2.34 (m, 2H), 3.19 – 3.24 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 24.1$, 26.1, 28.5, 33.7, 51.2, 179.0; IR (KBr): $\tilde{\nu} = 2869$, 2099, 1715, 1456, 1258 cm^{-1}; HRFABMS: m/z calcd. for $C_6H_{12}N_3O_2$ ($M^+ + H$): 158.0935; found: 158.0928.

General Procedure for Oxidation of Diols to Lactones using PhI=O/KBr

H_2O (2.0 mmol) was added dropwise to a stirred mixture of diol **1q – x** (0.2 mmol), PhI=O (110.0 mg, 0.5 mmol), and KBr (23.8 mg, 0.2 mmol). The mixture was stirred or sonicated for several hours while checking the reaction progress by gas or thin-layer chromatography. After completion, *n*-hexane (or

AcOEt) was added, the mixture was dried over Na_2SO_4, and then filtered. Evaporation of the solvent under vacuum afforded a crude product that was further purified by column chromatography [Et_2O (or AcOEt)/*n*-hexane] to give pure **3b – j** in the yields listed in Table 2. Yields of **3g – j** were determined by gas chromatography.

***cis*-Hexahydrophthalide (3c):**[30] Colorless oil; yield: quant.; ^{1}H NMR ($CDCl_3$): δ = 1.13 – 1.19 (m, 3H), 1.53 – 1.75 (m, 4H), 2.02 – 2.07 (m, 1H), 2.41 – 2.57 (m, 2H), 3.88 (d, *J* = 8.9 Hz, 1H), 4.13 (dd, *J* = 6.9, 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 22.4, 22.8, 23.4, 27.1, 35.3, 39.4, 71.7, 178.5; IR (KBr): ṽ = 2859, 1790, 1375, 1130, 914 cm^{-1}; MS: *m/z* = 140 [M^+], 95, 85, 80, 69, 55.

Isochroman-1-one (3d):[31] Colorless oil; yield: 70%; ^{1}H NMR ($CDCl_3$): δ = 2.97 (t, *J* = 5.8 Hz, 2H), 4.44 (t, *J* = 5.8 Hz, 2H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 27.6, 67.2, 125.1, 127.1, 127.5, 130.1, 133.5, 139.4, 165.0; IR (KBr): ṽ = 1717, 1244 cm^{-1}; MS: *m/z* = 148 [M^+].

1,8-Naphthalide (3f):[30] Yellow crystals; yield: 92%; mp 153 – 155 °C (Lit. mp 154.5 – 156.0 °C); ^{1}H NMR ($CDCl_3$): δ = 5.83 (s, 2H), 7.36 – 7.38 (m, 1H), 7.53 – 7.58 (m, 1H), 7.62 – 7.67 (m, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.3 Hz, 1H), 8.39 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 69.9, 120.0, 121.3, 126.3, 126.5, 128.1, 128.9, 131.8, 133.3; IR (KBr): ṽ = 1720, 1244, 1086, 775 cm^{-1}; MS: *m/z* = 184 [M^+], 155, 127.

Iodination of Polystyrene

A mixture of polystyrene (5 g) (MW = 44,000, purchased from Aldrich), iodine (5 g), diiodine pentaoxide (2 g), carbon tetrachloride (10 mL), and 50% sulfuric acid (10 mL) in nitrobenzene (30 mL) was stirred at 90 °C for 60 h. The reaction mixture was precipitated by adding AcOEt (100 mL) and filtered. The residue was washed with AcOEt and methanol. The resulting solid was collected and dried under vacuum to give poly(4-iodostyrene); yield: 10.3 g. Elemental analysis (C 43.87, H 3.36, I 51.65%) revealed the resin loading to be 4.069 mmol g^{-1}, which indicated that 87% of the phenyl rings in polystyrene were iodinated.

Preparation of PDAIS

Hydrogen peroxide (30%, 64.4 mL) was added dropwise to acetic anhydride (233.6 mL) at 0 °C. The solution was slowly warmed to room temperature and stirred overnight. To this solution, poly(4-iodostyrene) (8.59 g) was added. Then, stirring was continued at 40 °C overnight. Et_2O was added to the reaction mixture and the whole was filtered. The residue was washed with Et_2O to give PDAIS; yield: 12.6 g. Elemental analysis (C 38.35, H 3.57, I 38.39%) revealed the resin loading to be 2.172 mmol g^{-1}, which indicated that 72% of the 4-iodophenyl rings in the resin were converted into 4-(diacetoxyiodo)phenyl rings. PDAIS was used without any pretreatment.

General Procedure for Oxidation of Primary Alcohols using PDAIS/KBr in H_2O

PDAIS (5.0 mmol) was added to a vigorously stirred suspension of **1** (2.0 mmol) and KBr (238 mg, 2.0 mmol) in H_2O (80 mL) at 80 °C, and the mixture was stirred for several hours. After work-up A or B, the respective product **2** was obtained.

Work-up A: After completion, the reaction mixture was acidified by 1 N HCl, and filtered. The residue was washed with AcOEt and a small amount of MeOH, then the filtrate was extracted with AcOEt, dried and evaporated. The residue was purified by column chromatography (AcOEt/*n*-hexane) to give **2**.

Work-up B: After completion, the reaction mixture was filtered through abselut^{TM} NEXUS (Varian) to remove aqueous KBr. Then, the polymer residue was washed (extracted) with MeOH, the filtrate was evaporated, and purified by column chromatography (AcOEt/*n*-hexane) to give **2**.

General Procedure for Oxidation of Secondary and Benzylic Alcohols using PDAIS/KBr in H_2O

PDAIS (8.5 mmol) was added to a stirred suspension of **1** (7.7 mmol) and KBr (183.2 mg, 1.5 mmol) in H_2O (40 mL), and the mixture was then stirred at room temperature for several hours. After completion, the reaction mixture was filtered and the residue containing **2** was washed with a small amount of water to remove KBr, then extracted with *n*-hexane or MeOH, and the filtrate was evaporated to give **2**. The product was purified by column chromatography, when necessary. In some cases, the use of BOND ELUT C2 or C8 (Varian) for filtration was effective for preventing leakage of **2** when washing the residue.

General Procedure for Oxidation of Diols using PDAIS/KBr in H_2O

H_2O (10 – 20 mmol) was added dropwise to a stirred mixture of diol **1q, r, u** (1.6 mmol), PDAIS (4.0 mmol), and KBr (1.6 mmol). The mixture was stirred or sonicated for several hours while checking the reaction progress by gas or thin-layer chromatography. After completion, the reaction mixture was filtered and extracted with *n*-hexane or AcOEt, and the filtrate was dried, evaporated, and purified by column chromatography to give **3b, c, g**. In some cases, the use of BOND ELUT C2 or C8 (Varian) for filtration was effective for preventing leakage of **2** when washing the residue.

ESI-MS Experiment

ESI-mass spectra were measured by a modification of the CSI-MS technique.[15] Typical measurement conditions for ESI-MS are as follows: acceleration voltage; 2.5 kV, orifice voltage; 0 V, resolution (10% valley definition); 1500, sample flow; 20 μL/min, solvent; water, the temperature of desolvation chamber (with cooling by pouring liquid nitrogen under the heater on to prevent freezing water); 30 °C.

The sample was prepared as follows; PhI=O (0.02 mmol) was added to a solution of KBr (0.02 mmol) in H_2O (1 mL) at room temperature. The mixture (suspension) was sonicated for a few minutes. After centrifugation, the supernatant was diluted with H_2O (1 mL) to yield the sample.

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