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Catalytic oxidations of alcohols to carbonyl compounds by oxygen under solvent-free and transition-metal-free conditions

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Abstract—A green catalytic oxidation of alcohols to carbonyl compounds by oxygen was developed by using catalytic amounts of [bis(acetoxy)iodo]benzene/TEMPO/KNO_2. In addition, the use of a catalytic amount of poly[4-(bis(acetoxy)iodo)]styrene led to yields (up to 99%) comparable to the non-supported hypervalent iodine reagent, while offering the advantage of an efficient recovery and the subsequent recycling of the hypervalent iodine reagent.

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1. Introduction

Oxidations in general and oxidation of alcohols in particular are key reactions in the synthesis of complex organic molecules and fine chemicals.[1] Most oxidation reactions in organic chemistry are contradictory to the principles of Green Chemistry and Sustainable Developments[2] due to the lack of selectivity, the use of toxic metal reagents or catalysts that are persistent pollutants, or the use of halogenated solvents. Therefore, there is a great interest in the development of green oxidations for chemical manufacturing. In this regard, the use of organocatalysts for oxidation of organic compounds, avoiding transition-metals completely, appears very appealing and constitutes a significant challenge. Recently, Hu et al. described an efficient aerobic transition-metal-free catalytic oxidation of alcohols in water.[3] The oxidation was carried out under a high pressured-air atmosphere and promoted by a mixture of TEMPO/1,3-dibromo-5,5-dimethylhydantoin/$NaNO_2$ in catalytic amounts. The use of NO activates the molecular oxygen, thus completing the catalytic oxidation cycle. On the other hand, recently we have explored the use of selective oxidation of alcohols by oxygen in the presence of organocatalysts. To be successful, we need a highly efficient organic oxidant that has proven high oxidation efficiency and chemoselectivity and can be regenerated in situ without using any transition metal. To meet such a challenge, we chose hypervalent iodine reagents for the oxidation of alcohols.

Hypervalent iodine reagents are becoming increasingly appreciated by organic chemists for their mild and highly chemoselective oxidizing properties.[4] For example, the Dess–Martin periodinane (DMP), and to a lesser extent, its precursor 2-iodoxybenzoic acid (IBX) (both are iodine(V)-based reagents) have been widely used as oxidants for the chemoselective transformation of alcohols to their corresponding carbonyl compounds.[5] In spite of the extensive use of these compounds in synthesis, their potentially explosive nature constitutes a serious disadvantage. Thus, a facile and efficient use of the readily available and relatively stable iodine(III)-based reagents has been desired in place of iodine(V)-based reagents. However, only a few examples of effective oxidations of alcohols using iodine(III)-based reagents have been described.[6] One such example is the highly selective and efficient oxidation of alcohols to carbonyl compounds carried out by Piancatelli et al.,[6a] without overoxidation to carboxylic compounds. They used, as reagents, a combination of [bis(acetoxy)iodo]benzene (BAIB) in a stoichiometric amount together 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO), a nitroxyl radical and the species responsible for the selective oxidation of alcohols,[7,8] in a catalytic amount, leading to a procedure highly selective for the oxidation of primary alcohols to aldehydes and highly chemoselective in the presence of secondary alcohols and other oxidizable functional groups. This same reaction has been carried

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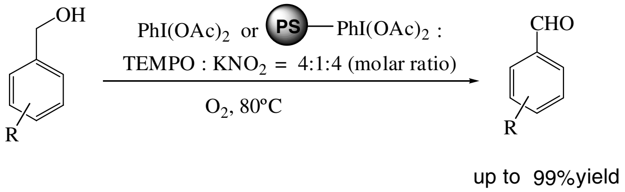
out using poly[4-(bis(acetoxy)iodo)]styrene (PBAIS) instead of BAIB.[9] PBAIS has recently attracted much attention because of its similar reactivity to BAIB but with the additional advantages of simple workup procedure and easy recovery and recycling.[10] Building upon these achievements, we have developed a green catalytic oxidation of alcohols to carbonyl compounds under oxygen atmosphere using catalytic amounts of a mixture of BAIB or PBAIS/TEMPO/KNO_2 (Eq. 1).



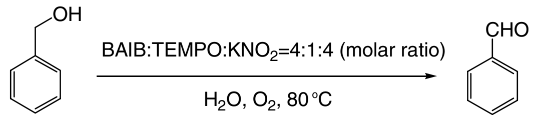
(1)

2. Results and discussion

The initial experiments were carried out using benzyl alcohol as the model substrate utilizing 4 mol % of BAIB, 1 mol % of TEMPO and 4 mol % of KNO_2 as catalysts in water and under an oxygen atmosphere (Table 1).

Our first result (Table 1, entry 1), using 3 mL of water as solvent, showed clearly the catalytic nature of this reaction since the yield (26%) is higher than the percentage of the catalyst used. The reduction of the amount of water increased the yield of the product significantly and the best results are obtained when no solvent was used. A 96% yield of the oxidation product was achieved when neat conditions were utilized in spite of the low solubility of KNO_2 in the alcohol. These results could be explained by the known dehydrogenating properties of BAIB due to the highly electrophilic character of iodine(III), and the fact that the presence of water hydrolyzes BAIB to give iodosylbenzene (PhI=O) or other species[11] deprived of catalytic properties. In addition, the use of less solvent or neat conditions allows a better contact between the catalysts and the oxygen. As a result, efficient agitation of the reaction mixture is also critical to achieve the maximum yield.

Table 1. Oxidation of benzyl alcohol using water as solvent[a]



Entry	H_2O (mL)	Time (h)	Yield (%)[b]
1	3	3	26
2	1	3	57
3	0.1	3	68
4	0	3	96

[a] Reactions were carried out using the following conditions: benzyl alcohol (10 mmol), BAIB (0.4 mmol), TEMPO (0.1 mmol), KNO_2 (0.4 mmol), O_2 (balloon), 80 °C.

[b] Yield was determined by ^1H NMR using mesytilene as internal standard.

With the optimized neat reaction conditions [BAIB:TEMPO:KNO_2 = 4:1:4 (mol %) and a temperature of 80 °C], we applied the procedure to a wide range of alcohols in order to evaluate the versatility of this novel catalytic system. The preparation of PBAIS allowed us to compare the results of homogeneous and heterogeneous conditions. Table 2 shows the range of oxidized alcohols under these conditions.

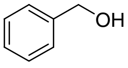
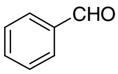
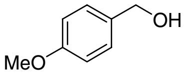
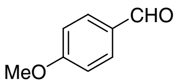
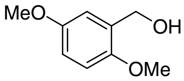
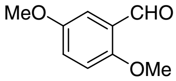
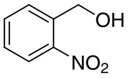
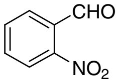
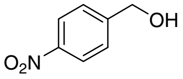
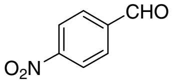
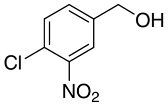
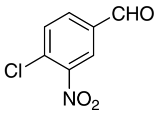
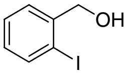
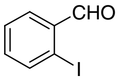
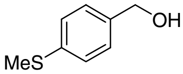
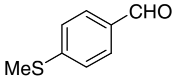
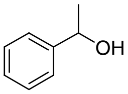
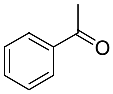
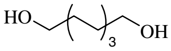
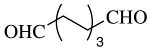
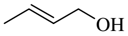
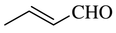
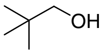
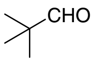
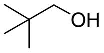
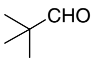
As it was shown, moderate to excellent yields were obtained when benzylic alcohols were used, and the overoxidized carboxylic acid was not observed in any case. However, the yields were affected by the electronic properties of the substituents and their position in the aromatic ring: while an electron-donating group on the aryl ring leads to satisfactory yields, an electron-withdrawing group decreases the yields (Table 2, entries 2–8). It has been reported that iodine(III) and TEMPO/primary oxidant systems oxidize sulfur functional groups.[12] Surprisingly, the current catalytic system exhibited high chemoselectivity toward the alcoholic moiety even in the presence of a sulfur heteroatom (Table 2, entry 8). An α-methyl benzyl alcohol can be also be oxidized into acetophenone with a reasonable yield (Table 2, entry 9). The use of PBAIS led to similar results, albeit a longer reaction time was needed. At the end of the reaction, the polymer species was recovered by precipitation with diethyl ether, filtration from the reaction medium, and regeneration by treatment with peracetic acid. The polymer was successfully recycled in three successive reactions (Table 2, entry 1).

In spite of the good results with benzylic alcohols, the yields obtained with aliphatic or allylic alcohols under the same conditions are quite low. Hu et al. described[10] that the use of a larger amount of catalyst in their system improved the yield. Indeed using 10% of each catalytic component (Table 2, entries 10–13), our catalytic mixture afforded a 61% yield of the aldehyde for the neopentyl alcohol.

These results suggested a potential chemoselectivity between primary and secondary alcohols and also between primary benzylic and aliphatic alcohols. The competing reaction of an equimolecular mixture of benzyl alcohol and α-methyl benzyl alcohol resulted in 97% of yield in the aldehyde whereas the yield of the ketone was very low (Table 3, entry 1). The presence of benzylic and aliphatic alcohols in the same molecule led to the formation of the benzyl aldehyde derivative as the only oxidation product (Table 3, entry 2).

A tentative mechanism of this catalytic oxidation based on previous studies[8] is shown in Scheme 1. The oxoammonium cation, which is oxidized from TEMPO, would be the active oxidant in this reaction. The role of BAIB is to regenerate TEMPO, and subsequently, BAIB would be also reoxidized to its initial state by KNO_2. The oxidation of NO into NO_2 can be carried out easily

Table 2. Oxidation of alcohols[a]

Entry	Substrate	Product	Yield (%)[b]	
			PhI(OAc)$_2$	(PS)—PhI(OAc)$_2$
1			96 (3 h)	98 (15 h) (1st) 100 (15 h) (2nd) 98 (15 h) (3rd)
2			97 (15 h)	99 (24 h)
3			70 (15 h)	88 (24 h)
4			73 (15 h)	65 (24 h)
5			59[c] (15 h)	55 (24 h)
6			60 (15 h)	50 (24 h)
7			77[c] (15 h)	72 (24 h)
8			75 (15 h)	73 (24 h)
9			51 (15 h) 75[e] (15 h)	29 (24 h)
10			20[e] (15 h)	—
11	 (Z and E)	 (Z and E)	23[e] (15 h)	—
12			26[d] (15 h)	—
13			61[e] (15 h)	32[e] (24 h)

[a] Neat reactions were carried out using the following conditions: (A) With BAIB:alcohol (10 mmol), BAIB (0.4 mmol), TEMPO (0.1 mmol), KNO_2 (0.4 mmol), O_2 (balloon), 80 °C; (B) With PBAIS:alcohol (5 mmol), BAIB (0.2 mmol), TEMPO (0.05 mmol), KNO_2 (0.2 mmol), O_2 (balloon), 80 °C.

[b] Yield was determined by ^1H NMR using mesitylene as internal standard.

[c] Reaction carried out at 90 °C to allow the alcohol to reach liquid state.

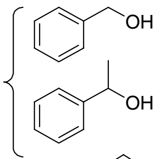
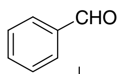
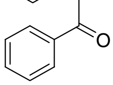
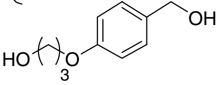
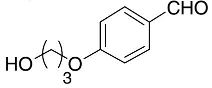
[d] Alcohol:BAIB:TEMPO:KNO_2 10:0.5:0.5:0.5 (mmol).

[e] Alcohol:BAIB/PBAIS:TEMPO:KNO_2 10:1:1:1 (mmol).

with molecular oxygen and completed the catalytic cycles in the absence of any transition metal. The identity of the reduced BAIB species has not been determined yet. Iodobenzene was detected at the end of the reaction; however several reactions utilizing this compound, either alone or with different amounts of BAIB, failed to display any catalytic activities.

In conclusion, we have developed an effective catalytic system for the oxidation of alcohols under an oxygen

Table 3. Oxidation of primary benzylic alcohols in the presence of secondary or aliphatic alcohols

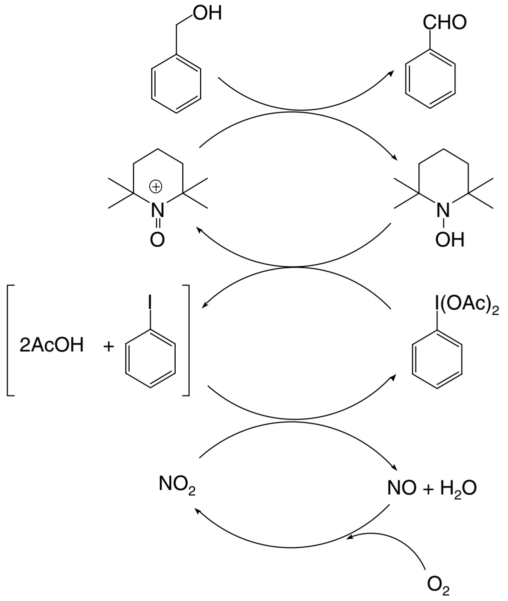
Entry	Substrate	Product	Yield (%)[a]
1[b]			97 (15 h)
			15 (15 h)
2[c]			21[d] (15 h)

[a] Yield was determined by ^{1}H NMR using mesitylene as internal standard.

[b] Reaction was carried out using the following conditions: benzyl alcohol (10 mmol), methyl benzyl alcohol (10 mmol), BAIB (0.4 mmol), TEMPO (0.1 mmol), KNO_2 (0.4 mmol), O_2 (balloon), 80 °C.

[c] Reaction was carried out using the following conditions: 3-(4-hydroxymethylphenoxy)propan-1-ol[13] (2 mmol), BAIB (0.08 mmol), TEMPO (0.02 mmol), KNO_2 (0.08 mmol), O_2 (balloon), 100 °C.

[d] Isolated yield.



Scheme 1. Tentative mechanism for the oxidation of benzyl alcohol with BAIB/TEMPO/KNO_2/O_2.

atmosphere using TEMPO and a hypervalent iodine reagent as organic catalysts. The reaction was carried out without the need of any additional solvent or transition metal catalyst. In addition, the immobilization of BAIB in polystyrene allowed the successful recycling of this essential catalytic component. The obtained results showed the versatility of this catalytic system since it can be used to promote the oxidation of different kinds of alcohols in the presence of other functional groups and also, the oxidation of primary benzylic alcohols in the presence of secondary and aliphatic ones. All primary alcohols can be oxidized to the corresponding aldehydes without any noticeable overoxidation to the carboxylic acids, even when an excess amount of oxidant was utilized.

3. General experimental procedure

The corresponding alcohol (10 mmol), BAIB (0.4 mmol, 128.8 mg), TEMPO (0.1 mmol, 15 mg), and KNO_2 (0.4 mmol, 34 mg) were added in a 25 mL round-bottom flask. The mixture was put into an oil bath pre-heated at 80 °C, kept under an oxygen atmosphere (with a balloon) and stirred vigorously for the desired reaction time. Then, the reaction mixture was cooled to room temperature and mesitylene was added as an internal standard for the determination of the results by ^{1}H NMR.

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