

Catalytic hypervalent iodine oxidation of alcohols to corresponding aldehydes or ketones using 2,2,6,6-tetramethylpiperidinyl-1-oxy and potassium peroxodisulfate

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Abstract An efficient, facile, and mild oxidation of alcohols to the corresponding aldehydes or ketones with potassium peroxodisulfate and 2,2,6,6-tetramethylpiperidinyl-1-oxy in the presence of a catalytic amount of iodobenzene is reported. The oxidation proceeded in a mixed solvent to afford carbonyl compounds in moderate to excellent yields. A possible mechanism for the oxidation is proposed.

Keywords Alcohols · Catalysis · Hypervalent iodine · Oxidations · TEMPO

Introduction

The selective oxidation of alcohols to the corresponding carbonyl compounds is a fundamental transformation in both laboratory synthesis and industrial production [1–3]. Numerous hypervalent iodine compounds, e.g., 1,1,1-tri-*acetoxy*-1,1-dihydro-1,2-benzodioxol-3H-one (DMP), 1-hydroxy-1,2-benzodioxol-3H-one 1-oxide (IBX), $\text{PhI}(\text{OAc})_2$, and PhIO , in stoichiometric amounts have been traditionally employed to accomplish this transformation [4, for reviews see 5–10]. However, some of these reagents are potentially explosive, and use of stoichiometric amounts of iodine reagents leads to the production of equimolar amounts of organic iodine waste. From economic and environmental perspectives, the development of catalytic systems based on hypervalent iodine has received great attention (for reviews see [11–15]). Many highly efficient systems have been developed for catalytic hypervalent iodine oxidation using

co-oxidants such as *m*-chloroperbenzoic acid (mCPBA) [16–28], oxone ($2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$) [29–36], H_2O_2 [37, 38], tetraphenylphosphonium monoperoxysulfate (TPPP) [39], $\text{NaBO}_3 \cdot \text{H}_2\text{O}$ [40], O_2 [41], Ru [42], peracetic acid [43], or combinations with the nitroxyl radical 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) [44]. To the best of our knowledge, there is no report on the use of $\text{K}_2\text{S}_2\text{O}_8$ as co-oxidant for catalytic hypervalent iodine oxidation. The advantages of using $\text{K}_2\text{S}_2\text{O}_8$ are due in part to its stability, nontoxic nature, low cost, and easy and safe handling.

On the other hand, it is well known that nitroxyl radicals such as TEMPO and *N*-hydroxyphthalimide (NHPI) promote oxidation of various alcohols to the corresponding carbonyl compounds effectively under mild reaction conditions (for reviews see [45–48]). Piancatelli and co-workers have reported a mild and selective method for the oxidation of primary and secondary alcohols using TEMPO and stoichiometric bis(acetoxy)iodobenzene [$\text{PhI}(\text{OAc})_2$] as a reoxidant [49].

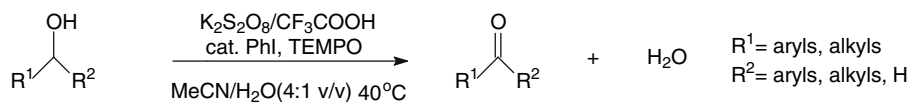
In continuation of our interest in exploring systems for the oxidation of organic compounds [50–53], we report herein a facile procedure for the oxidation of alcohols to the corresponding carbonyl compounds with $\text{K}_2\text{S}_2\text{O}_8$ in the presence of CF_3COOH , catalytic amounts of PhI , and TEMPO (Scheme 1).

Results and discussion

Initial experiments were carried out using 4-nitrobenzyl alcohol as the model substrate. When 4-nitrobenzyl alcohol was oxidized with $\text{K}_2\text{S}_2\text{O}_8/\text{PhI}/\text{CF}_3\text{COOH}/\text{TEMPO}$ in $\text{MeCN}/\text{H}_2\text{O}$ at 40 °C for 4 h, 92% conversion of the alcohol and 98% selectivity to the corresponding aldehyde were observed (Table 1, entry 1). However, in the absence

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Scheme 1

**Table 1** Oxidation of 4-nitrobenzyl alcohol

Entry	PhI (equiv)	K ₂ S ₂ O ₈ (equiv)	Acid	Additive	Conv./sel. (%) ^a
1	0.1	3	CF ₃ COOH	TEMPO	92/98
2 ^b	0.1	3	CF ₃ COOH	TEMPO	71/99
3	0.1	3	CF ₃ COOH	None	21/63
4	0.1	3	None	TEMPO	36/96
5	0.1	None	CF ₃ COOH	TEMPO	<10/–
6	None	3	CF ₃ COOH	TEMPO	33/90
7	0.05	3	CF ₃ COOH	TEMPO	90/99
8	0.1	3	AcOH	TEMPO	<10/–
9	0.1	3	HCl	TEMPO	<10/–
10	0.1	3	(CF ₃ CO) ₂ O	TEMPO	54/93
11	0.1	3	CF ₃ COOH	NHPI	88/59
12	0.1	3	CF ₃ COOH	BF ₃ ·Et ₂ O	<10/–
13 ^c	0.1	3	CF ₃ COOH	3 Å MS	<10/–

Reactions were performed by using 1 mmol 4-nitrobenzyl alcohol, 3 mmol K₂S₂O₈, 1 cm³ acid, 0.2 mmol additive, and 0.1 mmol PhI in MeCN/H₂O (4 cm³/1 cm³) at 40 °C for 4 h unless otherwise noted

^a GC conversion and selectivity

^b Without H₂O

^c 0.1 g 3 Å molecular sieve was added

of H₂O the conversion of the alcohol was decreased to 71% (Table 1, entry 2). This result suggests that the presence of H₂O as a co-solvent is beneficial for the dissolution of K₂S₂O₈. As control experiments, the same reaction was carried out in the absence of TEMPO, CF₃COOH, K₂S₂O₈, or PhI. In all cases, the conversion of the alcohol was much lower (Table 1, entries 3–6). It was possible to decrease the amount of PhI to as low as 0.05 equivalent without significant loss in catalytic efficiency (Table 1, entry 7). Use of other acids or anhydrides instead of CF₃COOH in this reaction was not successful (Table 1, entries 8–10). Moreover, a range of additives were tested for this reaction. However, all of them were unsatisfactory except for TEMPO (Table 1, entries 10–13). Besides, we also tested other co-oxidants such as NaBO₃·H₂O, NaIO₄, urea hydrogen peroxide adduct (UHP), and Na₂CO₃·3H₂O₂ in this experiment, all of which were not successful.

In order to evaluate the versatility of this novel catalytic system, we applied the procedure to the oxidation of a wide range of alcohols, including benzylic, allylic, heterocyclic, and aliphatic alcohols. As shown in Table 2, most alcohols underwent oxidation to afford the corresponding aldehydes or ketones in excellent yield. The present protocol afforded aldehydes from primary alcohols (Table 2, entries 1, 2, 3,

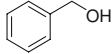
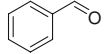
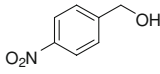
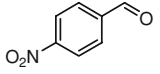
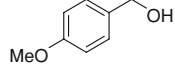
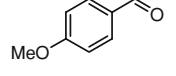
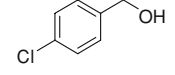
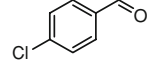
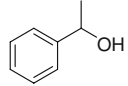
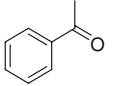
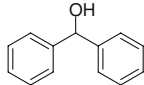
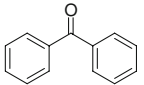
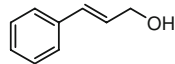
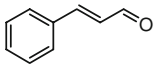
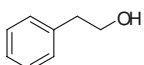
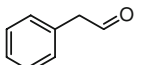
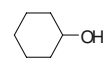
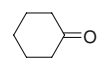
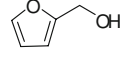
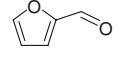

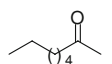
4, 8, 11, and 13) and ketones from secondary alcohols (Table 2, entries 5, 6, 9, and 12). For the oxidation of primary alcohols, no noticeable overoxidation of aldehyde to carboxylic acids was detected. Benzylic alcohols underwent smooth oxidation (Table 2, entries 1–6). An allylic alcohol, cinnamyl alcohol (Table 1, entry 7), was also oxidized efficiently without any observable reaction at the double-bond functionality. Even for the oxidation of furan-2-ylmethanol an excellent yield was also obtained (Table 1, entry 10). The electronic properties of the substituents in the aromatic ring had remarkable influence on the rate of the oxidation of alcohols. Strong electron-withdrawing groups, e.g., a nitro group, lowered the reaction rate (Table 2, entry 2). Strong electron-donating groups, such as a –OCH₃ group, accelerated the oxidation (Table 2, entry 3). Use of the present procedure for the oxidation of aliphatic alcohols under the same conditions gave moderate yields (61–77%) in prolonged reaction times (Table 2, entries 8, 11, 12, and 13). In view of the fact that the oxidation of aliphatic alcohols is much more difficult than the oxidation of benzylic alcohols, results obtained with the present procedure were also satisfactory.

Table 3 shows the results of the competitive oxidation of primary and secondary alcohols. The competing oxidation of an equimolar mixture of benzyl alcohol and 1-phenylethanol resulted in a 93% yield of benzaldehyde and less than 5% yield of acetophenone (Table 3, entry 1). Oxidation of an equimolar mixture of octan-1-ol and octan-2-ol gave 67% caprylic aldehyde, whereas no ketone could be detected (Table 3, entry 2). These results suggest that chemoselective oxidation of primary alcoholic functionality in the presence of secondary alcoholic functionality is possible with the present oxidation system.

Recently, Kitamura and co-workers reported a facile experimental procedure for the direct preparation of ArI(OCOCF₃)₂ from the respective iodoarenes in CF₃COOH, using potassium peroxodisulfate (K₂S₂O₈) as the oxidant (Scheme 2) [56]. Inspired by the preliminary research, in our present procedure, PhI and CF₃COOH may be initially oxidized by K₂S₂O₈ to form the highly reactive hypervalent iodine(III) compound PhI(OCOCF₃)₂. The role of PhI(OCOCF₃)₂ is to regenerate TEMPO from TEMPOH, then TEMPO is responsible for the actual oxidation in this reaction to oxidize alcohols to the corresponding aldehydes or ketones. A plausible mechanism for this reaction is depicted in Scheme 3.

In conclusion, a novel and mild catalytic system for the oxidation of alcohols to the corresponding aldehydes or

Table 2 $K_2S_2O_8$ /PhI/TEMPO catalyzed oxidation of alcohols

Entry	Alcohols	Products	Time (h)	Yield ^a (%)	Ref. ^c
1			1	95	[54a, 55a]
2			4	90	[54b, 55b]
3			2	97	[54c, 55c]
4			4	91	[54d, 55d]
5			2.5	93	[54e, 55e]
6			5	96	[54f, 55f]
7			5	92	[54g, 55g]
8			8	77	[54h, 55h]
9			8	71 ^b	[54i, 55i]
10			5	88 ^b	[54j, 55j]
11	$CH_3(CH_2)_7OH$	$CH_3(CH_2)_6CHO$	12	75 ^b	[54k, 54k]
12			12	70 ^b	[54l, 55l]
13	$n-C_{11}H_{23}-CH_2OH$	$n-C_{11}H_{23}-CHO$	12	61 ^b	[54m, 55m]

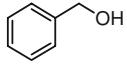
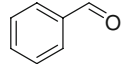
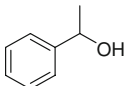
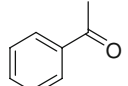
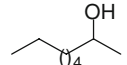
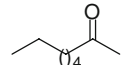
Reaction conditions: 1 mmol alcohol, 3 mmol $K_2S_2O_8$, 0.1 mmol PhI, 1 cm³ CF_3COOH , 0.2 mmol TEMPO, MeCN/H₂O (4 cm³/1 cm³), 40 °C

^a Yields of isolated products unless otherwise noted

^b Yields were determined by GC

^c References for isolated products

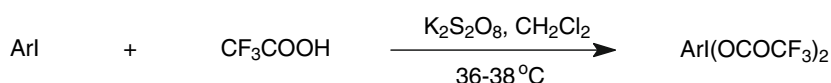
Table 3 Competitive oxidation of primary and secondary alcohols^a

Entry	Substrate	Product	Time (h)	Yield ^a (%)
1			1	93
				<5
2	$CH_3(CH_2)_7OH$	$CH_3(CH_2)_6CHO$	8	67
				not detectable

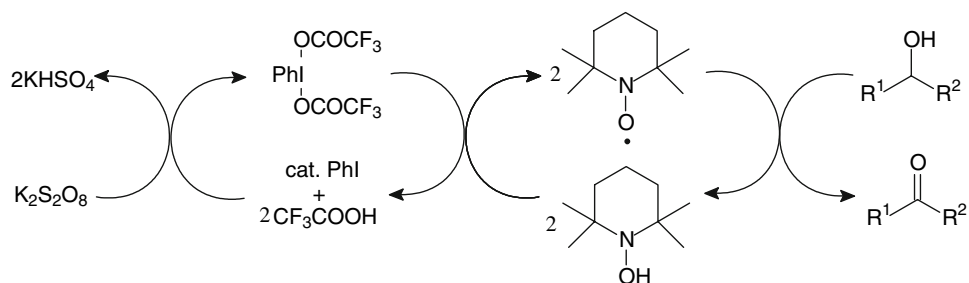
Reactions were carried out on a 1:1 mixture of primary and secondary alcohols, on a 1 mmol scale

^a GC yield

Scheme 2



Scheme 3



ketones with $\text{K}_2\text{S}_2\text{O}_8/\text{PhI}/\text{TEMPO}$ was developed. PhI was oxidized by $\text{K}_2\text{S}_2\text{O}_8$ in situ to highly active hypervalent iodine(III) species, a reoxidant of TEMPO, which allowed the oxidation of various kinds of alcohols, including benzylic, alicyclic, heterocyclic, and aliphatic alcohols to afford carbonyl compounds in moderate to excellent yields. The procedure can be used for the synthesis of aldehydes from primary alcohols or ketones from secondary alcohols. Selective oxidation of primary alcohols in the presence of secondary alcohols was also achieved.

Experimental

All chemicals (AR grade) were obtained from commercial resources and used without further purification. Products were all known compounds and were identified by comparing their physical and spectroscopic data with those reported in literature. Gas chromatography (GC) analysis was performed on an Agilent GC-6820 chromatograph equipped with a $30\text{ m} \times 0.32\text{ mm} \times 0.5\text{ }\mu\text{m}$ HP-Innowax capillary column and a flame ionization detector. Progress of the reactions was followed by TLC (petroleum ether/ethyl acetate/acetate acid = 5/15/1) using silica-gel polygrams SIL G/UV 254 plates. Mass spectra were recorded on a Shimadzu GC MS-QP 1000 EX apparatus.

Typical experimental procedure for oxidation of alcohols

To a mixture of 1 mmol alcohol, 20 mg iodobenzene (0.1 mmol), 31 mg TEMPO (0.2 mmol), 1 cm^3 CF_3COOH , 4 cm^3 MeCN, and 1 cm^3 H_2O was added 810 mg $\text{K}_2\text{S}_2\text{O}_8$ (3 mmol). The mixture was stirred at 40°C for several hours while checking the reaction progress by gas or thin-layer chromatography. After completion, aqueous sodium thiosulfate and ether were sequentially added to the residue, and then the mixture was stirred vigorously for 10 min. The

organic layer was separated, and the aqueous layer was extracted with ether. The combined ether phase was concentrated under vacuum. The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to provide the analytically pure product. The identity of products was determined either by comparison with authentic samples using gas chromatography or by GC/MS analysis.

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