



Highly efficient oxidation of benzyl alcohols using the catalytic system sulfoxide/oxo-complexes

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ABSTRACT

This work reports a novel and highly efficient method for the oxidation of benzyl alcohols to the corresponding aldehydes catalyzed by HReO_4 (5 mol %) using 4-methylphenyl sulfoxide as the oxidizing agent.

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The synthesis of aldehydes is a fundamental process in Organic Chemistry, in particular, for the chemical and pharmaceutical industries, where aldehydes find wide applications as intermediates. The Swern oxidation (using DMSO coupled with the electrophile oxalyl chloride) is an efficient and widely used method for the oxidation of alcohols.^{1,2} However, these reagents bring some disadvantages: the by-product dimethyl sulfide is volatile (bp 37 °C) and has an unpleasant smell; the electrophile oxalyl chloride is moisture sensitive, toxic and its vapor is a powerful irritant, particularly to the respiratory system; the activation of DMSO can be violent and exothermic, and it must occur at low temperatures (–60 °C). Several modifications on the Swern methodology have been accomplished in order to overcome some of these disadvantages.^{3–7}

Another traditional method for the oxidation of alcohols involves the use of stoichiometric inorganic oxidants such as Cr(VI) based reagents, which generate a large amount of heavy metal waste.⁸ Several oxo-vanadium,^{9,10} oxo-molybdenum,^{11–13} and oxo-rhenium¹⁴ complexes have also proved to be efficient catalysts for the oxidation of alcohols in the presence of molecular oxygen or using hydroperoxide compounds as the oxidizing agent. Only a few studies have also been reported for the oxidation of alcohols with DMSO catalyzed by oxo-molybdenum or -rhenium complexes.^{15–18}

In continuation of our work about the use of oxo-complexes as catalysts for oxidation/reduction reactions,^{19–27} in this communi-

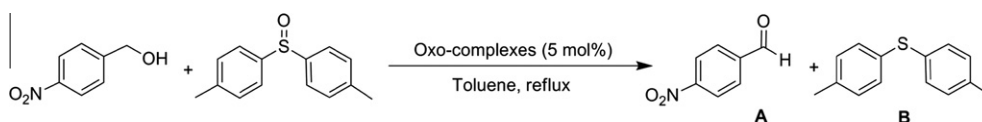
cation we report the selective oxidation of benzyl alcohols to the corresponding aldehydes catalyzed by oxo-complexes using a sulfoxide as the oxidizing agent.

Initially we investigated the oxidation of 4-nitrobenzyl alcohol with the oxo-complexes HReO_4 , $\text{MoO}_2(\text{acac})_2$, MoO_2Cl_2 , $\text{VO}(\text{acac})_2$, and WO_2Cl_2 via oxygen transfer from a sulfoxide. The reactions were carried out in refluxing toluene under air atmosphere (Table 1), and the progress of the oxidations was monitored by thin layer chromatography and by ¹H NMR. HReO_4 (5 mol %) proved to be the best catalyst, affording 4-nitrobenzaldehyde in 99% yield after 17 h (Table 1, entry 1). The oxo-molybdenum complexes MoO_2Cl_2 and $\text{MoO}_2(\text{acac})_2$ produced good yields of the aldehyde (86–89%) (Table 1, entries 2 and 3). The oxo-vanadium complex $\text{VO}(\text{acac})_2$ gave moderate yield (60%) of 4-nitrobenzaldehyde (Table 1, entry 4), and finally WO_2Cl_2 only produced low yield of the product (Table 1, entry 5). In the reactions catalyzed by HReO_4 , MoO_2Cl_2 , and $\text{MoO}_2(\text{acac})_2$, 4-methylphenyl sulfide was isolated in high yield (91–96%) (Table 1, entries 1–3).

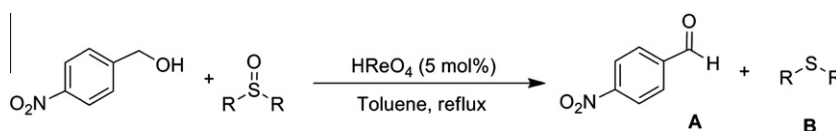
The oxidation of 4-nitrobenzyl alcohol was also studied with several sulfoxides as the oxidizing agent catalyzed by 5 mol % of HReO_4 in reflux of toluene under air atmosphere. Among all the sulfoxides tested, the reactions with 4-methylphenyl sulfoxide, diphenyl sulfoxide, and 4-chlorophenyl sulfoxide produced the best yields of 4-nitrobenzaldehyde (Table 2, entries 1–3). Good yields of the sulfides were also isolated in the reactions with sulfoxides like 4-methylphenyl sulfoxide, diphenyl sulfoxide, and 4-chlorophenyl sulfoxide (Table 2, entries 1–3). In the presence of DMSO, 4-nitrobenzyl alcohol was not oxidized (Table 2, entry 4).

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Table 1Oxidation of 4-nitrobenzyl alcohol catalyzed by oxo-complexes using 4-methylphenyl sulfoxide as the oxidizing agent^a

Entry	Catalyst	Time (h)	Yield A/B (%) ^b
1	HReO ₄	17	99/96
2	MoO ₂ Cl ₂	24	89/92
3	MoO ₂ (acac) ₂	20	86/91
4	VO(acac) ₂	20	60/65 (26) ^c (31) ^d
5	WO ₂ Cl ₂	24	36/45 (52) ^c (40) ^d

^a All reactions were carried out with 1.0 mmol of sulfoxide and 1.0 mmol of alcohol.^b Isolated yield.^c Alcohol recovered.^d Sulfoxide recovered.**Table 2**Oxidation of 4-nitrobenzyl alcohol catalyzed by HReO₄ using different sulfoxides as the oxidizing agent^a

Entry	Sulfoxide	Time (h)	Yield (%) ^b (A/B)
1		17	99/96
2		17	90/92
3		17	86/90
4		24	No reaction

^a All reactions were carried out with 1.0 mmol of sulfoxide and 1.0 mmol of alcohol.^b Isolated yield.

To assess the scope and limitations of this novel methodology, we carried out the oxidation of several benzyl alcohols bearing different functional groups using 4-methylphenyl sulfoxide as the oxidizing agent catalyzed by 5 mol % of HReO₄.²⁸ The reactions were carried out at refluxing toluene under air atmosphere (Table 3). As shown in Table 3, 4-nitrobenzyl, 4-bromobenzyl, 4-fluorobenzyl, 4-iodobenzyl, benzyl, 4-chlorobenzyl alcohols, and methyl 4-(hydroxymethyl)benzoate were oxidized in excellent yields (70–99%), affording selectively the corresponding aldehydes with no further oxidation to acids (Table 3, entries 1–7). Cinnamyl alcohol was also chemoselectively oxidized to cinnamaldehyde in moderate yield without affecting the double bond (Table 3, entry 8).

In contrast, the oxidation of the secondary diaromatic alcohols (4-nitrophenyl)(phenyl)methanol and bis(4-chlorophenyl)methanol afforded the corresponding ketones in low to moderate yields (Table 3, entries 9 and 10). For most reactions, the sulfide was isolated in high yields (80–99%).

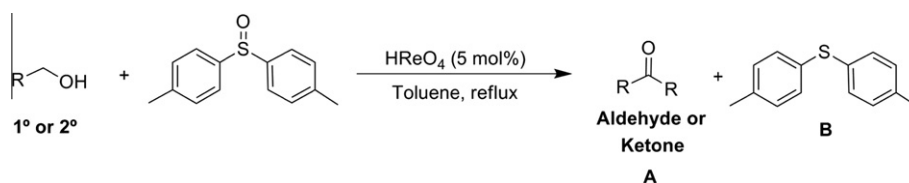
The results obtained demonstrate that the catalytic system 4-methylphenyl sulfoxide/HReO₄ (5 mol %) is very efficient for the oxidation of benzyl alcohols to the corresponding aldehydes.

Compared to other methods reported in the literature, this procedure does not require the use of DMSO as the oxidizing agent, avoiding the production of the volatile and unpleasant dimethyl sulfide. Another advantage of this method is that 4-methylphenyl sulfide, obtained as by-product in high yields, can be used as a substrate in other reactions or can be oxidized and reused in this procedure.

In conclusion, we have developed a novel and an efficient method for the selective oxidation of benzyl alcohols to the corresponding aldehydes catalyzed by oxo-complexes using 4-methylphenyl sulfoxide as the oxidizing agent. Other advantages of this method include: 1) high isolated yields of aldehyde; 2) applicability to a variety of alcohols; 3) use of commercial and easy-to-handle catalyst; 4) use of a sulfoxide (other than DMSO) as the oxidizing agent; 5) high isolated yields of the sulfide that can be used in other reactions or oxidized and reused in this method; and 6) simple experimental operation.

Further mechanistic studies and new applications of this methodology to the oxidation of other substrates are now under investigation in our group.

Table 3
Oxidation of alcohols catalyzed by HReO_4 using 4-methylphenyl sulfoxide as the oxidizing agent^a



Entry	Alcohol	Carbonyl compound	Time (h)	Yield (%) ^b A/B
1			17	99/96
2			17	98/99
3			17	90/97
4			17	88/99
5			24	85/97
6			17	83/95
7			17	70/99
8			24	68/80 (15) ^c
9			24	55/85 (33) ^c
10			24	35/60 (49) ^c

^a All reactions were carried out with 1.0 mmol of sulfoxide and 1.0 mmol of alcohol.

^b Isolated yield.

^c Alcohol recovered.

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28. In a typical experiment, to a solution of HReO₄ (5.0 mol %) in toluene (3 mL) was added the 4-methylphenyl sulfoxide (1.0 mmol) and the alcohol (1.0 mmol). The reaction mixture was heated at reflux temperature under air atmosphere (the reaction times are indicated in the Tables 1–3) and the progress of the reactions was monitored by TLC or ¹H NMR. Upon completion, the reaction mixture was evaporated and purified by silica gel column chromatography with *n*-hexane to afford the carbonyl compounds and 4-methylphenyl sulfide, which are all known compounds.