Oxidation of benzylic alcohols and sulfides over $LaCoO_3$ and TBHP

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Abstract
A simple and efficient methodology has been described for the selective oxidation of secondary benzylic alcohols to the corresponding ketones. In contrast, primary benzylic alcohols afforded dimethyl acetals.

Keywords: Perovskite $LaCoO_3$, oxidation, benzylic alcohols, acetals

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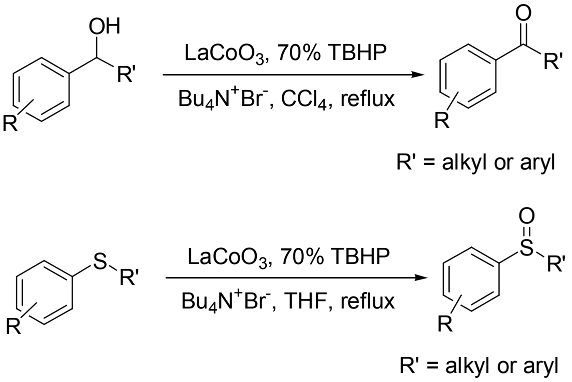
Introduction

The mineral perovskite, first described in the 1830s by the geologist Gustav Rose and named by him after the Russian mineralogist Count Lev Aleksevich von Perovski, is denoted by the chemical formula, ABO_3 wherein A is rare earth metal having +2 charge and B is transition metal such as Cr, Mn, Fe, Co, etc with +4 charge.[1] The perovskite-type oxides are non-toxic, easily handled and mild oxidizing catalysts. Despite of several advantages over traditional catalysts, they have been less explored in organic synthesis. The catalytic applications of perovskite-type oxides include hydrogenation, partial and complete oxidation of lower hydrocarbons, volatile organic compound abatement, NO reduction, fuel cells, benzylation and esterification.[1b,2] Due to the interest in the use of environmentally friendly catalysts for organic synthesis, we undertook a study of the utility of perovskite-type oxides for the oxidation of benzylic alcohols.

The oxidation of benzylic alcohols to the corresponding carbonyl compounds is a fundamental transformation in organic synthesis.[3] In spite of a number of reports employing conventional oxidizing catalysts for this transformation, the search for new catalyst is still actively pursued to address the problems like effluent pollution, loss of selectivity and tedious workup procedures.[4,5] We envisioned the use of non-toxic perovskite type metal oxides for the oxidation of benzylic alcohols to the corresponding carbonyl compounds in the presence of oxidants.

Results and Discussion

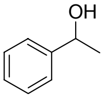
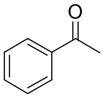
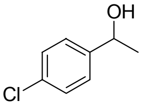
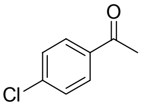
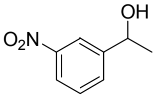
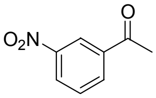
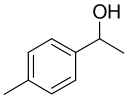
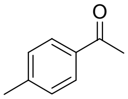
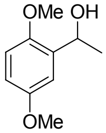
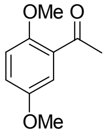
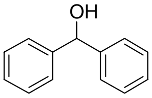
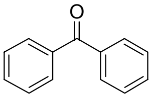
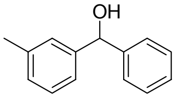
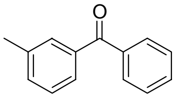
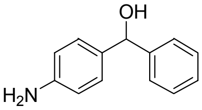
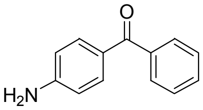
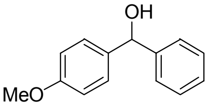
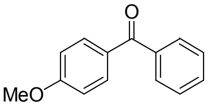
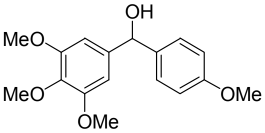
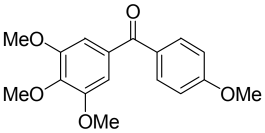
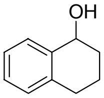
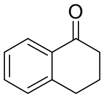
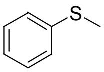
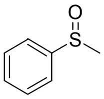
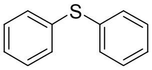
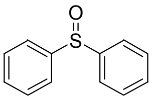
Among the various perovskite type metal oxides studied, $LaCoO_3$ was found to be very efficient catalyst for the oxidation of secondary benzylic alcohols in combination with 70% aq. TBHP (Scheme 1, table 1).[6] The catalyst $LaCoO_3$ was prepared and characterized according to the known procedure.[2b]



Scheme 1

Table 1 details the results of various secondary benzylic alcohols bearing electron withdrawing or donating groups. All substrates underwent smooth oxidation to produce corresponding ketones in excellent yields. Sterically hindered alcohols were oxidized in moderate yields (entry 5). Aromatic methyl groups were tolerated under these conditions without producing overoxidized products (entries 4 and 7). A notable feature of this methodology appeared when 4-aminobenzhydrol was subjected to oxidation under $LaCoO_3$-TBHP conditions to give 4-aminobenzophenone in 90% yield (entry 8). It is noteworthy to mention that CrS-2 zeolite along with 70% aq. TBHP has been known to catalyze oxidation of alcohols[5a] as well as amines[7] to the corresponding ketones and nitro compounds. Development of chemoselective methodology for the selective oxidation of benzylic alcohols would be of great importance in the synthesis of fine chemicals. $LaCoO_3$ is a mild yet very effective catalyst for the selective oxidation of secondary benzylic alcohols. Moreover CrS-2 is more expensive and also difficult to prepare than $LaCoO_3$. Additionally, $LaCoO_3$-TBHP system selectively produced sulfoxides from corresponding sulfides in good to moderate yields (entries 12 and 13).

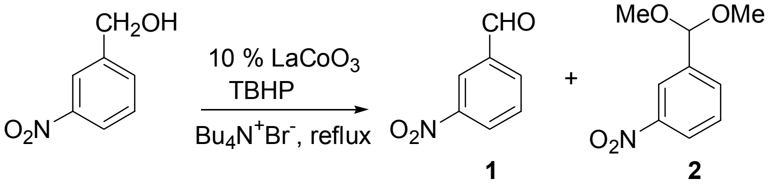
Table 1. Oxidation of benzylic alcohols and sulfides over $LaCoO_3$ using aq. TBHP

entry	substrate	product	time (h)	yield (%)[b]
1			6	95
2			4	84
3			10	95
4			10	92
5			10	65
6			6	95
7			10	95
8			6	90
9[c]			24	85
10			12	75
11[c]			14	57
12[c]			24	48
13[c]			24	55

[a] All reactions were carried out in CCl_4 under reflux unless otherwise mentioned. [b] Isolated yields. [c] THF reflux

Though $LaCoO_3$-aq. TBHP system holds certain advantages over known catalysts for the oxidation of secondary benzylic alcohols, it was less effective for the selective oxidation of primary benzylic alcohols. Attempts to standardize the reaction parameters for the oxidation of *m*-nitrobenzyl alcohol are summarized in table 2.

Table 2. Oxidation of m-nitrobenzyl alcohol using $LaCoO_3$-TBHP



Entry	Oxidant	Solvent	Time (h)	Product (conversion)
1[a]	TBHP[c]	CCl_4	24	complex mixture
2[a]	TBHP[c]	CCl_4	6	**1** (15)
3[b]	TBHP[c]	MeOH	24	**1** (20), **2** (5)
4[b]	TBHP[d]	MeOH	6	**1** (30), **2** (0)
5[b]	TBHP[d]	MeOH	24	**1** (0), **2** (35)
6[a]	TBHP[d]	CCl_4	24	**1** (10)

[a]Decomposition observed. [b]Significant amounts of the starting material was recovered. [c]70% aq. TBHP was used. [d] 5-6 M TBHP in decane was used.

In contrast to secondary benzylic alcohols, the oxidation of primary benzylic alcohol using $LaCoO_3$-70% aq. TBHP system in CCl_4 produced complex reaction mixture after 24 h (entry 1). Decreasing reaction time to 6 h afforded 15% of *m*-nitrobenzaldehyde (**1**) along with recovery of starting material (entry 2). Interestingly, while screening an effect of solvent, reaction in methanol yielded *m*-nitrobenzaldehye (**1**) and *m*-nitrobenzaldehyde dimethylacetal (**2**) with conversion up to 20 and 5% respectively (entry 3). Further, the use of anhydrous TBHP (5-6 M in decane) and $LaCoO_3$ in MeOH after 24 h showed slight increase in the conversion of *m*-nitrobenzaldehyde to *m*-nitrobenzaldehyde dimethylacetal (**2**) (up to 35%, entry 5). However, upon reducing the time period to 6 h only *m*-nitrobenzaldehyde was obtained with conversion up to 30% (entry 4). Acetals serve as very important protecting groups in natural product synthesis. Although in present study *m*-nitrobenzaldehyde dimethylacetal (**2**) was produced in low yield, this method might provide basis for further optimization to develop a new methodology towards direct synthesis of acetals from benzyl alcohols.[8]

Exact mechanism for the $LaCoO_3$-TBHP catalyzed oxidation is not known but it is believed that the lattice oxygen bound to the transition metal (cobalt) is responsible for this conversion.

In conclusion, we have demonstrated $LaCoO_3$-TBHP to be a mild, effective and highly chemoselective system for the oxidation of secondary benzylic alcohols and sulfides. Although primary benzylic alcohols produced low yields of corresponding benzaldehydes, the use of anhydrous TBHP afforded one-pot conversion of alcohols to acetals. Further studies to improve the yields of acetals are in progress.

Experimental Section

General Procedures. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer in $CDCl_3$ containing TMS as an internal standard. All solvents and reagents were purified and dried by standard procedures. TLC was carried out on silica gel plates prepared by spreading the slurry in CCl_4 and drying at room temperature. The plates were analyzed using an iodine chamber. Column chromatography was performed on silica gel (60-120 mesh). Petroleum ether refers to the fraction of boiling range 60-80 ºC.

Typical experimental procedure for oxidation of alcohols to ketones (Table 1)
A mixture of benzhydrol (552 mg, 3 mmol), 70% aq. TBHP (540 mg, 6 mmol), a pinch of tetrabutylammonium bromide and $LaCoO_3$ (55 mg, 10% by wt) in CCl_4 (10 mL) was refluxed until completion of reaction (6 h). The catalyst was filtered off and CCl_4 layer was washed three times with saturated sodium sulfite (10 mL) to remove excess TBHP. Purification by column chromatography afforded benzophenone (518 mg, 95%).
All known compounds showed satisfactory spectral data.

Typical procedure for the conversion of *m*-nitrobenzyl alcohol to *m*-nitrobenzaldehyde dimethylacetal (2). A mixture of *m*-nitrobenzyl alcohol (153 mg, 1 mmol), TBHP (5 M solution in decane, 1 mL, 5 mmol), a pinch of tetrabutylammonium bromide and $LaCoO_3$ (15 mg, 10% by wt) was refluxed in anhydrous methanol for 24 h. The catalyst was filtered off followed by evaporation of solvent and purification over neutral alumina to afford *m*-nitrobenzaldehyde dimethylacetal (**2**) (70 mg, 35%). (**Caution**: Peroxides should be handled with care, although no problems were experienced in present study).

Acknowledgements

SRM thanks CSIR, New Delhi for the award of junior research fellowship. We are grateful to Dr. V. H. Deshpande (National Chemical Laboratory, Pune, India) and Prof. Dr. Hiroaki Sasai (ISIR, Osaka University, Japan) for support and encouragement.

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6. Among the various solvents screened for the oxidation of secondary benzylic alcohols in the presence of $LaCoO_3$ and 70% aq. TBHP, best results were obtained when reaction was carried out in CCl_4. The use of phase transfer catalyst $Bu_4N^+Br^-$ further improved yields of the products.
7. Joseph, R.; Sasidharan, M.; Kumar, R.; Sudalai, A.; Ravindranathan, T. *J. Chem. Soc. Chem. Commun.* **1995**, 1341.
8. A small amount of acetal formation was observed during oxidation of primary alcohols using 90% TBHP and transition metal phthalocyanines as catalyst. Sanderson, J. R.; Marquis, E. T. US Pat. 5,132,465, **1992**.