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## Novel and Efficient Oxidation of Benzyl Ethers to Benzaldehydes by DMSO/49% Aq. HBr

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**Abstract:** Dimethylsulfoxide (DMSO) oxidizes benzyl ethers into corresponding benzaldehydes at 110°C; the reaction is accelerated by 49% aq. HBr. The conditions work well for different aryl-substituted benzyl ethers. This protocol is inert toward dialkyl ethers.

**Keywords:** benzaldehydes, benzyl ethers, DMSO/49% aq. HBr

### INTRODUCTION

Investigation from our laboratory has revealed the new paradigms for dimethylsulfoxide (DMSO) in effecting the oxidation of benzylic substrates. We successfully employed the oxidation of primary benzyl amines to benzoic acids by DMSO/aq. HBr/NaNO<sub>2</sub>.<sup>[1]</sup> In context of our ongoing program, we sought to develop DMSO-based synthetic technology over benzyl ethers to their corresponding benzaldehydes under acidic conditions.

Although a few methods to achieve the oxidation of benzyl ethers are known, none are both simple and effective. The reported methods involve use of reagents such as expensive UF<sub>6</sub>,<sup>[2]</sup> metallic nitrates,<sup>[3]</sup> experimentally incontinent reagents in a common laboratory such as HOF·CH<sub>3</sub>CN complex,<sup>[4]</sup> and dimethyldioxirane,<sup>[5]</sup> which requires a specially designed

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apparatus and reagents for its preparation. The only method that offers a good yield of benzaldehyde is the use of  $\text{HNO}_3$ <sup>[6]</sup> at  $0^\circ\text{C}$  in dichloromethane (DCM). The disadvantage encountered in this method is the formation of nitrated product at elevated temperature.

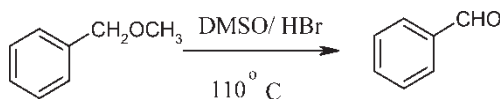
## RESULTS AND DISCUSSION

As we noted, the inherent reactivity of DMSO under acidic conditions is sufficient for oxidation of benzyl ethers. To explore the DMSO-based synthetic paradigm of oxidation, a quick experiment was done with benzyl methyl ether as our prime substrate. On heating benzyl methyl ether with DMSO and 49% aq. HBr at  $110^\circ\text{C}$  for 4 h, partial conversion of the substrate into benzaldehyde occurred (gas chromatography (GC)). On continuous heating for an additional 3 h, complete conversion of the substrate to benzaldehyde was achieved. After workup, the crude product was purified on silica-gel column chromatography and characterized by  $^1\text{H}$  NMR, GC-MS, and IR spectral analysis by comparing with that of authentic benzaldehyde (Scheme 1).

To optimize the reaction conditions, we demonstrated the reaction of benzyl methyl ether under different acidic conditions such as con. HCl, con.  $\text{H}_2\text{SO}_4$ ,  $\text{H}_3\text{PO}_4$ ,  $\text{CH}_3\text{COOH}$ ,  $\text{CF}_3\text{COOH}$ , and 49% aq. HBr. Among these, only 49% aq. HBr gave the pure product with excellent yields at  $110^\circ\text{C}$ . This protocol has been successfully employed for a variety of substituted benzyl ethers compiled in Table 1; in all cases, excellent yields of corresponding benzaldehydes were obtained. A noteworthy feature is that the electron-releasing groups like -OH, - $\text{OCH}_3$ , - $\text{CH}_3$  accelerate the reaction considerably (Table 1, entries 4–6), and in contrast electron-withdrawing groups like - $\text{NO}_2$  and -Cl retard the rate of the reaction (Table 1, entries 8–10). Another interesting feature is the presence of an aryl group on the other side of the benzyl ether (Table 1, entry 3) utilized longer duration to give the title compound with the formation of phenol. When dibenzyl ether was subjected to the standard reaction conditions, as expected, the reaction needed a long duration (15 h) with the formation of 2 equivalents of benzaldehyde.

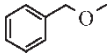
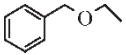
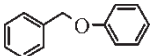
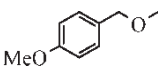
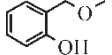
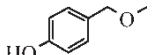
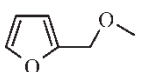
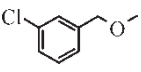
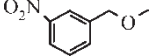
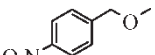
A similar type of mechanism holds good for this protocol as predicted in our previous communication for the oxidation of benzyl amines to benzoic acids<sup>[1]</sup> (Scheme 2).

In conclusion, we have developed a novel protocol for the oxidation of benzyl ethers to the corresponding benzaldehydes in excellent yields.



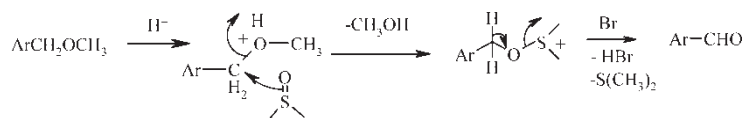
**Scheme 1.** Oxidation of benzyl ethers.

**Table 1.** Oxidation of benzyl ethers into benzaldehydes by DMSO and aq. HBr.

Entry	Ethers	Time (h)	Yield (%) <sup>a</sup>
1		7	85
2		10	80
3		48	78
4		4	92
5		6	86
6		5	94
7		10	86
8		14	88
9		15	89
10		12	84

<sup>a</sup>Isolated yields.**EXPERIMENTAL**

Melting points were determined on a Buchi melting-point apparatus. IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR GC-MS spectra were recorded on Nicolet 400 D FT-IR spectrophotometer, 400-MHz Bruker spectrometer, and Shimadzu GC-MS QP 5050A respectively. Benzyl ethers were prepared by reported methods and purified and characterized thoroughly before use.

**Scheme 2.** Mechanism for the oxidation of benzyl ethers.

### General Procedure for Oxidation of Benzyl Ethers by DMSO Promoted by 49% Aq. HBr

A solution of 4-methoxybenzylmethyl ether (2.0 g, 13.15 mmol), DMSO (10 mL), and 49% HBr (3.0 mL, 17.80 mmol) was heated to 110°C until complete conversion was achieved as monitored by thin-layer chromatography (TLC). Brine (30 mL) was then added, neutralized with saturated NaHCO<sub>3</sub>, and extracted with dichloromethane (3 × 15 mL). The combined DCM extract was again washed with brine (2 × 10 mL), dried over anhyd. Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The resulting crude mixture was purified by silica-gel column chromatography to get 4-methoxybenzaldehyde (1.61 g, 90% yield).

### ACKNOWLEDGMENT

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