A Novel and Efficient Oxidation of Benzyl Alcohols to Benzaldehydes with DMSO Catalyzed by Acids

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Abstract: Oxidation of benzyl alcohols to the corresponding aldehydes was achieved by an acid catalyzed DMSO oxidation. When the oxidation was catalyzed by HBr, no side products were detected. In most cases, the yields were excellent. The oxidation rate depends on both the nature and the position of the substituents on the aromatic rings. A tentative mechanism is proposed for the oxidation.

Key words: oxidation, DMSO, HBr, benzyl alcohols, benzaldehydes

Oxidation of alcohols to ketones or aldehydes is one of the most useful transformations in organic chemistry.[1] Activated DMSO[2] methods such as the Swern oxidation[3] are often used for this purpose. The disadvantages of the Swern oxidation are the required anhydrous conditions and the low temperatures needed to avoid Pummerer rearrangement. Even under these conditions the formation of side products from Pummerer rearrangement is more than 50% in some cases.[3] In addition, the oxalyl chloride used in the Swern oxidation is moisture sensitive, irritating and toxic. It is therefore desirable to simplify the reaction conditions.

We theorized that benzyl cation formed under acidic conditions would react with DMSO to form a benzyloxydimethylsulfonium salt. Elimination of a benzylic proton and dimethylsulfide would then result in benzaldehyde.[4] To the best of our knowledge, this kind of oxidation is not known although there exist several modifications of the Swern oxidation.[1,3]

In order to investigate our assumption, benzyl alcohols were reacted with DMSO catalyzed by acid at 100 °C. The acids for investigation were H_2SO_4, H_3PO_4, $CeCl_3$, TsOH and aq HBr. All the acid catalyzed reactions led to the formation of aldehydes. But only the reaction catalyzed by aq HBr gave a pure product with excellent yields. Among the acids investigated, Br^- seems to be the best conjugate base to effect the deprotonation of the benzyloxydimethylsulfonium salt. The pathway for the formation of benzyl bromide followed by the DMSO substitution is uncertain according to the report by Kornblum et al.[5] They failed to make benzaldehyde from benzyl bromide and DMSO but succeeded in converting *p*-nitrobenzylbromide into *p*-nitrobenzaldehyde at elevated temperature with acetonitrile as solvent (with 45% yield). It has been reported that DMSO with HBr oxidize the methylene between two carbonyl groups into a third carbonyl group.[6] It is believed that bromine, generated in situ from the oxidation of HBr by DMSO, is the oxidant. But this mechanism is probably not valid here because the hydroxy group of menthol was not oxidized by DMSO with HBr and 1-phenyl-1-pentanol was oxidized into a mixture of pentanophenone and 1-phenyl-1-pentene by DMSO with HBr. Since it is well-documented that bromine oxidizes secondary alcohols faster than it oxidize primary alcohols.[1,7] The oxidation of benzyl alcohols to benzaldehydes with air in refluxing DMSO was reported to take place via radical mechanism by Traynelis et al.[8] We carried out the HBr-catalyzed oxidation under a nitrogen atmosphere and found that air has not affected the acid-catalyzed oxidation at all. Based on these facts, we tentatively put forward the following mechanism (Scheme 1).

Scheme 1

The above facts as well as the reaction rates in Table 1 agreed well with the mechanism proposed above. As shown in Table 1, electron donating groups such as -OH and -OR on aromatic ring lead to higher reaction rates (entries 2, 6, 7). Electron withdrawing groups such as $-NO_2$ or -X reduce the reaction rates substantially (entries 10–12). Additional aq HBr was required to accelerate the latter reactions. Bulky groups and *ortho* substituents reduced the reaction rates (entry 4 vs. entry 5, entries 7 and 8 vs. entry 9). All the oxidations produced a pure product as determined by TLC and GC. All the products are known compounds and were fully identified by IR and ^1H NMR.

In conclusion, we have developed a convenient and efficient method for oxidation of benzyl alcohols to the corresponding aldehydes. It is not necessary to add a weak base such as TEA to the reaction, as required in the Swern oxidation. The products were not contaminated with any side products, such as Pummerer rearrangement products. Exclusion of moisture from the reaction was not necessary and commercial DMSO was adequate. In most cases, the yields were excellent. Its synthetic applications are currently under investigation.

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Table 1 Oxidation of Benzyl Alcohols to Benzaldehydes[9]

Entry	Substrate	T (h)	Product	Yield (%)[a]
1	benzyl alcohol	4	benzaldehyde	95
2	4-methylbenzyl alcohol	3.5	4-methylbenzaldehyde	92
3	1,4-benzenedimethanol[b]	28	1,4-benzenedialdehyde	80
4	2-butyloxybenzyl alcohol	3	2-butyloxybenzaldehyde	95
5	2-(1-methylpropyloxy)benzyl alcohol	14.5	2-(1-methylpropyloxy)benzaldehyde	79
6	4-hydroxy-3-methoxybenzyl alcohol	2	4-hydroxy-3-methoxybenzaldehyde	78
7	4-hydroxybenzyl alcohol	3	4-hydroxybenzaldehyde	96
8	3-hydroxybenzyl alcohol	6	3-hydroxybenzaldehyde	96
9	2-hydroxybenzyl alcohol	11.8	2-hydroxybenzaldehyde	84
10	2-chlorobenzyl alcohol	22	2-chlorobenzaldehyde	86
11	2,5-dibromobenzyl alcohol [b]	12	2,5-dibromobenzaldehyde	93
12	3-nitrobenzyl alcohol [b]	26	3-nitrobenzaldehyde	71
13	diphenylmethanol	8	diphenylmethanone	93

[a] Isolated yields.
[b] 0.3 mL of aq HBr for 0.5 g of alcohol were used.

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(9) Typical procedure: A mixture of 557 mg of benzyl alcohol, 0.15 mL of HBr (48%) and 5 mL of DMSO was stirred in an oil bath at 100 ºC. TLC (petroleum ether/diethyl ether, 1:1) was used to indicate the completion of the reaction (3 h). To the reaction mixture were added 5 mL of brine followed by extraction with 30 mL of diethyl ether. The ether layer was washed with brine (5 mL × 4). Evaporation of ether and subsequent bulb to bulb distillation produced 530 mg of benzaldehyde in 95% yield.