A Simple and Convenient Manganese Dioxide Oxidation of Benzyl Halides to Aromatic Aldehydes under Neutral Condition

Shyamaprosad Goswami,* Subrata Jana, Swapan Dey, and Avijit Kumar Adak
Department of Chemistry, Bengal Engineering and Science University Shibpur[†]*, Howrah -711 103, West Bengal, India*

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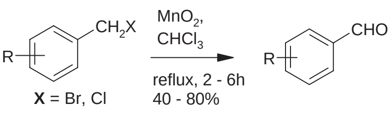
A simple, convenient and inexpensive benzylic oxidation reaction of arylmethylhalides under neutral conditions by manganese dioxide to the corresponding aldehydes has been described.

Since the discovery of the Sommelet reaction[1] in 1913, the oxidation of benzyl halides to the carbonyl compounds represents one of the important fundamental reactions in organic synthesis.[2] Several other reaction procedures have been reported for this transformation which include the Hass Bender reaction,[3] pyridine followed by *p*-nitrosodimethylaniline,[4] dimethyl sulfoxide,[5] dimethylselenoxide-dipotassium hydrogen phosphate,[6] bis(tetrabutylammonium)dichromate,[7a] potassium chromate-HMPT in presence of crown ether,[7b] certain amine *N*-oxides,[8] and also photooxidation[9] of organic halides to the corresponding carbonyl compounds. Recently, sodium periodate in refluxing dimethylformamide,[10] 3,6-bis(triphenylphosphonium)cyclohexene in refluxing acetonitrile-water,[11] H_2O_2 catalyzed by V_2O_5 and Aliquat 336 in boiling water,[12] and also microwave-expedited solvent free synthesis using pyridine-*N*-oxide[13a] and montmorillonite K10-HIO_3[13b] have been used for such conversion. However, most of these procedures suffer from strong oxidizing conditions, longer reaction time, high reaction temperature, and also the cost of the reagents used. Therefore, the need for a convenient and mild reaction procedure still stimulate a continuous research effort.

In our previous study,[14] we showed that $Co(I)(PPh_3)_3Cl$ is an effective and versatile catalyst for the synthesis of aromatic aldehydes from arylmethyl bromides in the presence of aerial oxygen under very mild conditions. Manganese dioxide in chlorinated hydrocarbons has been widely applied for the oxidation of α,β-unsaturated alcohols (e.g. allylic, benzylic alcohols), and also been employed in a variety of other organic reactions.[15] Manganese dioxide is a readily available and inexpensive oxidizing agent, however, its use in the conversion of benzyl halides to the carbonyl compounds remains relatively unexplored.

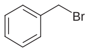
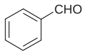
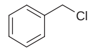
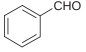
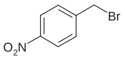
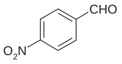
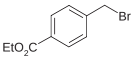
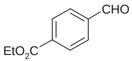
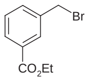
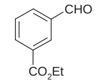
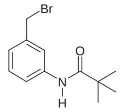
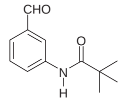
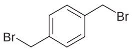
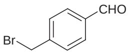
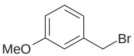
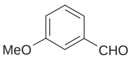
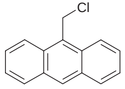
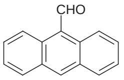
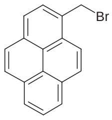
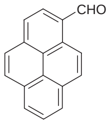
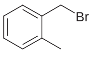
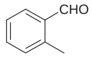
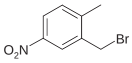
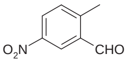
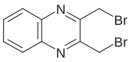
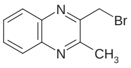
In continuation of our work for the synthesis of aromatic and heteroaromatic benzyl bromides,[16] herein, we wish to describe a convenient and inexpensive method for the oxidation of benzylic halides to the aromatic aldehydes in moderate to good yields under mild reaction conditions (manganese dioxide in chloroform, reflux, 2–6 h) (Scheme 1).

The results of our investigation are presented in the Table 1. As can be seen from this Table, it is clear that our method works well for a wide variety of benzyl bromides (Entries 1–12), which can be directly converted to the corresponding aldehydes where a number of different functional groups like nitro, carbethoxy, pivaloyl, methoxy, etc. survived. This method is also efficient for the synthesis of polynuclear aromatic aldehydes (Entries 9 and 10).



Scheme 1. Oxidation of benzyl halides to aldehydes.

Table 1. Yield and products of MnO_2 oxidation of benzyl halides

Entry	Substrate	Time (/h)	Products	Yield (/%)[a]
1		2		80
2		6		40
3		4		74
4		4		70
5		4		75
6		4		60
7		4		60
8		4		48
9		4		60
10		5		40
11		6		58
12		6		48
13		6		40

[a] Isolated yields are of chromatographically pure material.

However, under identical condition, 2,3-bis(bromomethyl)-quinoxaline (Entry 13) surprisingly gave 2-bromomethyl-3-methylquinoxaline in 40% yield with the recovery of some unreacted starting material, although attempts to oxidize 2,6-bis(bromomethyl)pyridine, 2-*N*-acetylamino-6-bromomethyl-

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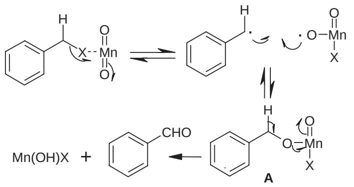

Scheme 2. A plausible reaction mechanism for the MnO2 oxidation of benzyl halides.

pyridine, 2-pivaloyl-6-bromomethylpyridine, and 2-*N*-phthalimido-6-bromomethylpyridine were unsuccessful. Interestingly, in the case of 1,4-bis(bromomethyl)benzene (Entry 7) only one bromomethyl group got oxidized while the other remained unaffected under the same conditions.

Although, at this point, no rigorous mechanistic studies have been done, a working hypothesis may be suggested on the basis of the observation of the products (Scheme 2). The labile benzyl halide is probably displaced thermally to form a benzyl radical by activated interaction with MnO_2 under refluxing conditions, which immediately couples with the oxygen radical of •OMn(X)(O) to form a possible intermediate (A). This undergoes subsequent loss of acidic benzylic hydrogen followed by reductive cleavage of oxygen–manganese bond in (A) with loss of oxomanganese halide resulting in the formation of aromatic aldehydes and probably MnO as a salt Mn(OH)X as the oxide in reduced Mn^{II} state is basic.[17]

The reason for the formation of 2-bromomethyl-3-methylquinoxaline (Table 1, Entry 13), as an exception to the normal benzylic oxidation to aldehyde, may possibly be that the benzyl radical gets quenched by hydrogen capture from solvent chloroform giving the observed product. We are currently extending this methodology onto other heterocyclic as well as other aromatic systems having poly(bromomethyl) substituents.

Representative procedure for the oxidation of 4-nitrobenzyl bromide: A mixture of 4-nitrobenzyl bromide (216 mg, 1 mmol) and activated manganese dioxide (480 mg, 5 mmol, Aldrich 21,764-6) in chloroform (10 mL) was refluxed for 4 h at 60 °C. The progress of the reaction was monitored by TLC using petroleum ether–dichloromethane (3:1) as eluent. The reaction mixture was filtered and washed with chloroform. The combined filtrates after evaporation and silica gel (60–120 mesh) purification afforded 4-nitrobenzaldehyde (112 mg, 74%) along with recovery of unreacted (15%) starting material.[18]

In conclusion, we have developed a very simple, efficient, mild, and inexpensive procedure for the oxidation of benzyl halides to the aromatic aldehydes. We have found that this procedure (MnO_2 in refluxing chloroform) is even more controlled at least in the case of oxidation of simple benzylbromide itself than our previous one (aerial oxygen, $Co(I)(PPh_3)_3Cl$),[14] though it required lower temperature (Co(I), aerial oxygen is thus more reactive). In the latter case, benzoic acid was obtained appreciably from benzyl bromide itself (benzaldehyde was further oxidized) unlike the present case where the yield of benzaldehyde is excellent.

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References and Notes

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18 All products are characterized by FT-IR, 1H NMR and also comparison of the melting points with authentic samples when available.

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