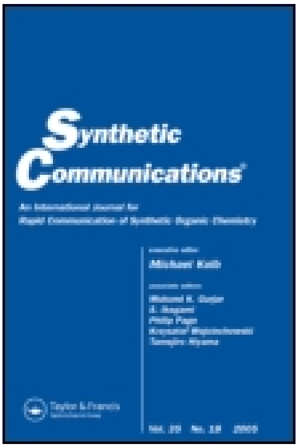

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A Green Procedure for the Oxidation of Benzyl Halides to Aromatic Aldehydes or Ketones in Aqueous Media

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A GREEN PROCEDURE FOR THE OXIDATION OF BENZYL HALIDES TO AROMATIC ALDEHYDES OR KETONES IN AQUEOUS MEDIA

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Green oxidation of benzyl halides to the corresponding aldehydes or ketones was achieved in aqueous media using trimethylamine* N*-oxide generated* in situ *from trimethylamine and H_2O_2. The yield of the reaction was excellent and the workup was simple.

Keywords: Aldehydes; benzyl halides; green oxidation; ketones; trimethylamine N-oxide

INTRODUCTION

The oxidation of benzyl halides to carbonyl compounds is a significant reaction because aromatic aldehydes and ketones are used widely and benzyl halides are easily available. Several oxidations of organic halides to carbonyl compounds are known. These include the Hass-Bender reaction,[1] the Sommelet reaction,[2] the Krohnke reaction,[3] the Kornblum reaction,[4] the Masaki photooxidation,[5] and oxidations using NaOCl,[6] MnO_2,[7] KNO_3,[8] DMSO,[9] Pyridine N-Oxide in the presence of Ag_2O,[10] and transition metal complexes.[11] Our group[12] discovered the first green oxidation of benzyl halides with V_2O_5-H_2O_2 in aqueous media.

Trimethylamine *N*-oxide (TMANO) has been used as an oxidant in the oxidation of benzyl halides to carbonyl compounds.[13] The solvents used include DMF, DMSO, $CHCl_3$, CH_3CN. There has been no oxidation performed in H_2O, that is an environmentally benign solvent. Replacement of organic solvents with water would help to reduce the environment problems associated with the oxidation. For this purpose, we carried out the following investigations. First, we heated benzyl chloride and 1.5 eq. of TMANO in H_2O to reflux. The reaction completed quickly and the conversion of benzyl chloride to benzaldehyde was quantitative. This proved

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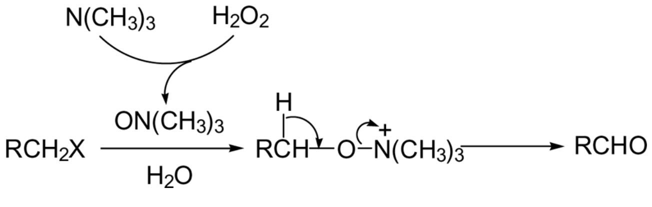
Table 1. Green oxidation of benzyl halides to aldehydes or ketones by TMA/H_2O_2 in aqueous media

Entry	Substrates	Product	Time	Yield (%)[a]
1	$C_6H_5CH_2Cl$	C_6H_5CHO	30 min	82
2	p-$ClC_6H_4CH_2Cl$	p-ClC_6H_4CHO	1 h	85
3	o-$ClC_6H_4CH_2Cl$	o-ClC_6H_4CHO	1 h	93
4	p-$CH_3C_6H_4CH_2Cl$	p-$CH_3C_6H_4CHO$	20 min	92
5	o-$HOC_6H_4CH_2Cl$	o-HOC_6H_4CHO	20 min	93
6	o-$nBuOC_6H_4CH_2Cl$	o-$nBuOC_6H_4CHO$	20 min	92
7	o-$iBuOC_6H_4CH_2Cl$	o-$iBuOC_6H_4CHO$	1 h	88
8	2,6-$Cl_2C_6H_3CH_2Cl$	2,6-$Cl_2C_6H_3CHO$	2 h	94
9	$C_6H_5CHClC_6H_5$	$C_6H_5COC_6H_5$	4 h	87
10	p-$ClC_6H_4CHClC_4H_9$	p-$ClC_6H_4COC_4H_9$	6 h	85
11	p-$NO_2C_6H_4CH_2Cl$	p-$NO_2C_6H_4CHO$	4 h	86
12	$C_6H_5CH_2Br$	C_6H_5CHO	15 min	80
13	1,4-$(BrCH_2)_2C_6H_4$	1,4-$(CHO)_2C_6H_4$	12 h	78

[a] Isolated yield after column chromatography on SiO_2.

that the oxidation can equally be performed in aqueous media. Then, we theorized that TMANO, commercially prepared through oxidation of trimethylamine (TMA) with H_2O_2, could be generated *in situ* from TMA and H_2O_2 and function as an oxidant for benzyl chloride. We refluxed a mixture of benzyl chloride, TMA (1.5 eq.), H_2O_2 (1.5 eq.) in H_2O for 30 min. This led to the formation of benzaldehyde as the only product in 82% yield. When the reaction was conducted at large scales, the product was separated from water layer after cooling to room temperature. We have successfully replaced the TMANO with TMA and H_2O_2 in the oxidation. Altogether 13 halides were similarly oxidized to the corresponding benzaldehydes and aromatic ketones in high yields. As shown in Table 1, electron donating groups such as –OH or –OR on aromatic ring lead to higher reaction rates (entries 4, 5, 6). Electron withdrawing groups such as –NO_2 or –X reduce the reaction rates substantially (entries 2, 3, 11). Bulky groups and *ortho* substituents reduced the reaction rates (entry 7 vs 6, entry 8 vs 3). Generally, primary halides are oxidized faster than secondary halides (entries 1, 2 vs 9, 10). The reaction is faster with benzyl bromide than with benzyl chloride (entry 12 vs 1). All the oxidations produced a single product as determined by TLC and GC. All the products are known compounds and were fully identified by IR and ^1H NMR.

Based on these facts, we put forward the following mechanism (Scheme 1). Under refluxing conditions, TMA and H_2O_2 reacted to form TMANO quickly.



Scheme 1. The mechanism of the oxidation of benzyl halides to aromatic aldehydes or ketones.

The oxygen atom on TMANO is partially negatively charged and can react as a nucleophilic oxidant toward halides that are converted into aldehydes or ketones.

In conclusion, we successfully improved the literature methods from two aspects. One is that the organic solvents was replaced by water. The other is that TMANO could be generated *in situ* from TMA and H_2O_2 during the oxidation. Compared with the known procedure, the new green method we have developed has the following advantages: (1) Environmental friendly water was used as reaction media. Because no organic solvents were used in the whole process, green oxidation of benzyl halides was achieved. (2) TMA and H_2O_2 were used to generate TMANO *in situ* and this avoided the use of TMANO, which simplified the workup procedure. (3) No side products were formed in the oxidation. The reaction rate was high and the yield of the reaction was close to quantitative. The product was easily separated from water and the workup was much simplified.

Typical procedure: A mixture of H_2O (30 mL), benzyl chloride (3.03 g), TMA (33%, 1.5 eq.), H_2O_2 (30%, 1.5 eq.) was refluxed for 30 min. TLC was used to monitor the completion of the reaction. After cooling to room temperature, the oil layer was separated and subsequent isolation by column chromatography on SiO_2 produced 2.08 g of benzaldehyde in 82% yield.

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