

## SHORT COMMUNICATION

### EFFICIENT AND CONVENIENT OXIDATION OF BENZYL HALIDES TO CARBONYL COMPOUNDS WITH SODIUM NITRATE AND ACETIC ACID BY PHASE TRANSFER CATALYSIS IN AQUEOUS MEDIA

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**ABSTRACT.** A variety of benzyl halides were converted to the corresponding aldehydes/ketones in good to high yields by phase transfer catalysis combined with sodium nitrate and acetic acid at reflux. As a result, a simple and high yield procedure has been developed.

**KEY WORDS:** Oxidation, Benzyl halides, Phase transfer catalyst, Sodium nitrate

## INTRODUCTION

The oxidation of benzyl halides to the corresponding aldehydes and ketones is a well known transformation in organic synthesis. In many cases, it affords more convenient access to the carbonyl compounds than the oxidation of the corresponding alcohols [1-4]. The oldest method for such a conversion is apparently the Hass-Bender reaction [5] involving O-alkylation of the nitronate anion followed by decomposition of the resulting intermediate, which was reported in 1949. Sommelet reaction [6, 7] is another classic method for this transformation, and involves the use of hexamethylenetetramine to afford the formaldehyde imine derivative of the primary amine, which tautomerized into the methyl imine of the desired carbonyl compound. While each has some limitations, the former method is only satisfied for *para*-substituted substrates, the latter unfortunately has limited substrate scope. Other notable methods to accomplish this conversion include the Krohnke reaction [8], the Kornblum reaction [9-11], the use of various amine N-oxide [12-14], N-alkoxy pyridinium salts [15-18], potassium chromate [19], NaIO<sub>4</sub>-DMF [20], selenium compounds [21], oxodiperoxovanadate [22], etc. [23-26]. All of these procedures, however, are invariably associated with certain limitations in terms of long reaction times, poor yields, harmful to the environment, substrate scope, high temperature, etc.

Phase transfer catalysis (PTC) is a versatile synthetic technique of rate enhancement of a reaction between chemical species located in different phases (immiscible liquids or solid and liquid) by addition of a small quantity of an agent (phase transfer catalyst) that extracts one of the reactants, most commonly an anion, across the interface into the other phase so that reaction can proceed. By using a PTC process, one can achieve faster reactions, obtain higher conversions or yields, make fewer byproducts, eliminate the need for expensive or dangerous solvents which dissolve all the reactants in one phase, eliminate the need for expensive raw materials and/or minimize waste problems. At present, phase-transfer catalysis has been employed in the production of various fine chemicals, pharmaceuticals and so on [27-30]. In this communication, we wish to report an efficient and convenient method for the preparation of aldehydes and ketones from the corresponding halides with sodium nitrate (NaNO<sub>3</sub>) by phase transfer catalysis in aqueous media without any organic solvents.

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## EXPERIMENTAL

*Apparatus and reagents.* All chemicals were obtained commercially and used without further purification. All the products are known compounds and their structures were confirmed by comparing with authentic samples. High performance liquid chromatography (HPLC) experiments were performed on a liquid chromatograph (Dionex Softron GmbH, USA), consisting of a pump (P680) and ultraviolet-visible light detector (UVD) system (170U). The experiments were performed on Diacore C18 column,  $\phi$  4.6  $\times$  150 mm.

*General procedure for the oxidation of benzyl halides to carbonyl compounds using benzyl chloride as an example.* A mixture of benzyl chloride (12.6 g, 0.1 mol), PEG-600 (0.73 g, 1.2 mmol) and AcOH (10 mL) was stirred in 250 mL round flask. Then the solution of NaNO<sub>3</sub> (9.35 g, 0.11 mol) in H<sub>2</sub>O (10 mL) was added drop wise when the mixture was heated at reflux. The reaction progress was monitored by TLC and HPLC. The reaction was completed in 3 h, and then cooled to room temperature, the organic product was extracted with methylene chloride (3  $\times$  30 mL). The combined organic phases were washed with 10% NaHCO<sub>3</sub> solution (3  $\times$  20 mL) and water (3  $\times$  20 mL), then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed and the residue was distilled under vacuum to give the desired product.

## RESULTS AND DISCUSSION

It was found that benzyl chloride could be oxidized to benzaldehyde by sodium nitrate in the presence of polyethylene glycol 600 (PEG-600) and acetic acid (AcOH) at reflux in 3 h [31]. Other nitrates such as potassium nitrate (KNO<sub>3</sub>), calcium nitrate (Ca(NO<sub>3</sub>)<sub>2</sub>), and sodium nitrite (NaNO<sub>2</sub>), although are excellent oxidants for the oxidation of benzyl chloride and the yields were more than 85% under the same reaction conditions, however, the yield was decreased in the order: NaNO<sub>3</sub> > KNO<sub>3</sub> > NaNO<sub>2</sub> > Ca(NO<sub>3</sub>)<sub>2</sub>, the best oxidant is NaNO<sub>3</sub>. Typical results are shown in Figure 1.

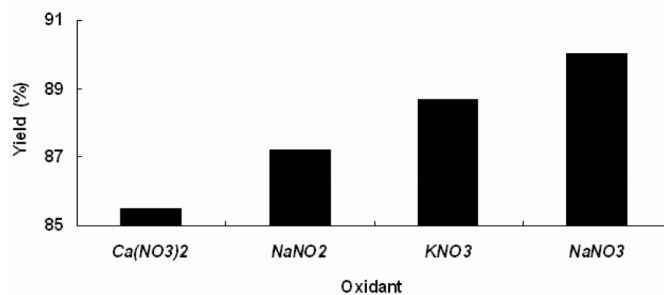
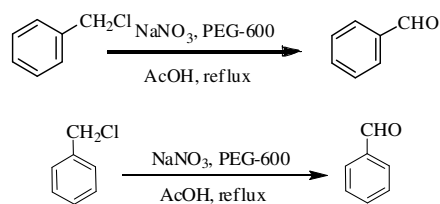


Figure 1. Influence of types of oxidants on the reaction. Reaction conditions: benzyl chloride (0.1 mol), nitrate (0.11 mol), PEG-600 (1.2 mmol), AcOH (10 mL), H<sub>2</sub>O (10 mL), reflux, 3 h.

The oxidation of benzyl chloride (0.1 mol) was then carried out by vigorously stirring the two phase system (benzyl chloride and 10 mL H<sub>2</sub>O) at reflux temperature with NaNO<sub>3</sub> (0.11 mol). The yield was only 15% (Table 1, entry 1) after 10 h. Using PEG-600 (1.2 mmol) as phase transfer catalyst, under the same conditions, benzaldehyde was obtained in a higher yield 52% (Table 1, entry 2). Further addition the amount of PEG-600 had almost no effect on the yield

(Table 1, entries 3 and 5). The color of the reaction mixture varied from colorless to yellow and a red-brown gas as the reaction proceeded. After addition of AcOH 9 mL to the catalytic system, the yield increased to 86% (Table 1, entry 4) within 3 h, which show that AcOH can promote this oxidation reaction to some extent, and the increase in the amount of acetic acid enhance the reaction, the yield reached maximum at 10 mL of the amount (Table 1, entry 5). However, further addition the amount of AcOH, under the same conditions, the yield was not enhanced significantly (Table 1, entries 8 and 9). The results are given in Table 1.

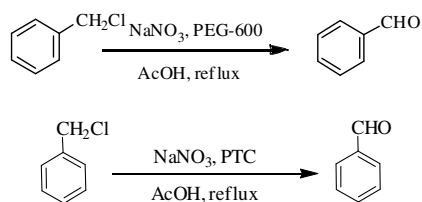
Table 1. PEG-600 catalyzed oxidation of benzyl chloride with NaNO<sub>3</sub> in aqueous media<sup>a</sup>.



Entry	NaNO <sub>3</sub> (mol)	PEG-600 (mmol)	AcOH (mL)	Time (h)	Yield (%) <sup>b</sup>
1	0.11	—	—	10	15
2	0.11	1.2	—	10	52
3	0.11	1.3	—	10	52
4	0.11	1.2	9	3	86
5	0.11	1.2	10	3	90
6	0.11	1.3	10	3	90
7	0.11	—	10	3	64
8	0.11	1.2	12	3	90
9	0.11	1.2	15	3	90

<sup>a</sup>Reaction conditions: benzyl chloride (0.1 mol), NaNO<sub>3</sub> (0.11 mol), H<sub>2</sub>O (10 mL), reflux. <sup>b</sup>Isolated yield.

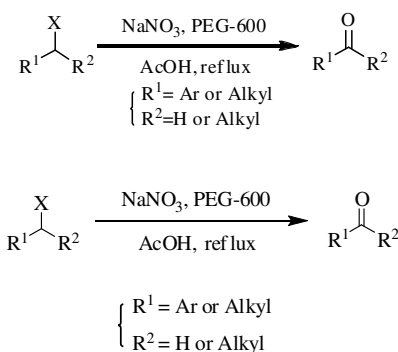
Phase-transfer catalyst and AcOH must coexist in this oxidation system (Table 1, entries 3-8). The yield was raised to 90% in a shorter period (3 h) if both PEG-600 and AcOH were present in the reaction system (Table 1, entry 4). The PEG-600 was also crucial for achieving high yields because the yield decreased to 64% in the absence of PEG-600 (Table 1, entry 6) but increased to 90% in the presence of PEG-600 (1.2 mmol). Using 1.3 mmol of PEG-600, under the same conditions, the yield was not enhanced significantly. Therefore, the optimal reaction conditions were observed in Table 1, entry 4. Besides PEG-600, we also tried to use cetyltrimethylammonium bromide (CTAB), tetraethylammonium bromide (TEAB), tetrabutylammonium bromide (TBAB), dodecyltrimethylammonium bromide (DTAB) and sodium dodecyl sulfonates (SDS) as phase transfer catalysts in this catalytic oxidation system. However, the yields were merely 79%, 67%, 77%, 72% and 74%, respectively (Table 2). The best phase transfer catalyst is PEG-600.

Table 2. PTC catalyzed oxidation of benzyl chloride with NaNO<sub>3</sub> in aqueous media<sup>a</sup>.

Phase transfer catalyst	Time (h)	Yield (%) <sup>b</sup>
PEG-600	3	90
CTAB	5	79
TEAB	6	67
TBAB	4	77
DTAB	7	72
SDS	3	74

<sup>a</sup>Reaction conditions: benzyl chloride (0.1 mol), NaNO<sub>3</sub> (0.11 mol), PTC (1.2 mmol), AcOH (10 mL), H<sub>2</sub>O (10 mL), reflux. <sup>b</sup>Isolated yield.

Under the same conditions, various substituted benzyl halides were readily oxidized to the corresponding aldehydes in high yields in a few hours (Table 3, entries 1-16), while a strong electron-withdrawing nitro group at the para-position resulted in lower conversion, only 12% of the yield was obtained after 12 h (Table 3, entry 17). Under the reaction conditions, further oxidation of benzaldehyde to benzoic acid was not observed. However, on exposure to air, oxidation of benzaldehyde to benzoic acid occurred. Further, alkyl halides such as n-pentyl chloride (Table 3, entry 18) and 2-bromoethyl benzene (Table 3, entry 19) were found inert to this reaction, no product was detected. Secondary bromides such as 1-(1-bromoethyl)-4-fluorobenzene (Table 3, entry 14), benzhydryl bromide (Table 3, entry 15) and 1-bromo-4-(bromo-(phenyl)-methyl) benzene (Table 3, entry 16) were readily oxidized to the corresponding ketones in good yields, and the reaction rates of secondary bromides were obviously faster than that of primary bromides (Table 3, entries 2, 4 and 13). The yield for oxidation of benzyl bromide to aldehydes/ketones was slightly higher than that for benzyl chloride (Table 3, entries 1-4).

Table 3. PEG-600 catalyzed oxidation of benzyl halides with NaNO<sub>3</sub> in aqueous media<sup>a</sup>.

Entry	Substrate	Product	Time (h)	Yield (%) <sup>b</sup>
1	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl	C <sub>6</sub> H <sub>5</sub> CHO	3.0	90
2	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	C <sub>6</sub> H <sub>5</sub> CHO	3.0	91
3	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> CHO	3.0	87
4	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> CHO	3.0	90
5	2- <sup>i</sup> Pr-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	2- <sup>i</sup> Pr-C <sub>6</sub> H <sub>4</sub> CHO	3.5	91
6	4- <sup>t</sup> Bu-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	4- <sup>t</sup> Bu-C <sub>6</sub> H <sub>4</sub> CHO	3.5	90
7	2,4,6-(CH <sub>3</sub> ) <sub>3</sub> -C <sub>6</sub> H <sub>2</sub> CH <sub>2</sub> Cl	2,4,6-(CH <sub>3</sub> ) <sub>3</sub> -C <sub>6</sub> H <sub>2</sub> CHO	8	83
8	2-Cl-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	2-Cl-C <sub>6</sub> H <sub>4</sub> CHO	4.0	90
9	4-Cl-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	4-Cl-C <sub>6</sub> H <sub>4</sub> CHO	4.0	88
10	4-Br-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	4-Br-C <sub>6</sub> H <sub>4</sub> CHO	6.0	83
11	3-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	3-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub> CHO	7.5	81
12	1-C <sub>10</sub> H <sub>7</sub> CH <sub>2</sub> Cl	1-C <sub>10</sub> H <sub>7</sub> CHO	3.0	87
13	2-Naph-CH <sub>2</sub> Br	2-Naph-CHO	3.0	85
14	4-F-PhCHBrCH <sub>3</sub>	4-F-PhCOCH <sub>3</sub>	2.0	79
15	Ph <sub>2</sub> CHBr	PhCOPh	1.5	89
16	4-Br-C <sub>6</sub> H <sub>4</sub> CHBrPh	4-Br-C <sub>6</sub> H <sub>4</sub> COPh	2.0	82
17	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> CHO	12	12 <sup>c</sup>
18	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> Cl	—	12	ND <sup>d</sup>
19	PhCH <sub>2</sub> CH <sub>2</sub> Br	—	12	ND <sup>d</sup>

<sup>a</sup>Reaction conditions: benzyl halide (0.1 mol), NaNO<sub>3</sub> (0.11 mol), PEG-600 (1.2 mmol), AcOH (10 mL), H<sub>2</sub>O (10 mL), reflux. <sup>b</sup>Isolated yield. <sup>c</sup>Some other unknown mixtures detected (80% of starting material was recovered and some other unknowable mixtures detected). <sup>d</sup>No product was detected.

## CONCLUSIONS

In conclusion, we have developed an efficient, convenient method for the transformation of benzyl halides to carbonyl compounds. It provides an easy and eco-safer way to prepare substituted benzaldehydes. Judging from the conditions employed, this oxidation method has great prospects in industrial applications. Efforts to elucidate the scope and limitations of this oxidation system are underway.

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