

# Conversion of Benzylic Bromides to Benzaldehydes Using Sodium Nitrate As an Oxidant

K. Kulangiappar, M. Anbu Kulandainathan, and T. Raju\*

*Electro organic Division, Central Electrochemical Research Institute Karaikudi 630 006, India*

A simple and effective approach for the synthesis of benzaldehydes from benzylic bromides is reported using sodium nitrate as an oxidant with 10% sodium hydroxide. Benzyl bromide is oxidized to benzaldehyde in 91% yield with 98% conversion at 120 °C, whereas 82% of benzyl alcohol is obtained at a temperature of 80 °C in 80 min with 20% sodium nitrate solution.

## Introduction

Aromatic aldehydes can be prepared by the direct introduction of a formyl group onto an aromatic nucleus through reactions such as the Gatterman-Koch reaction,<sup>1</sup> the Reimer-Tiemann reaction,<sup>2</sup> and the Vilsmeier reaction.<sup>3</sup> Moreover, the formyl group can be generated from an appropriate precursor group such as a hydroxymethyl, an acid chloride, a halomethyl, or a methyl group, attached the aromatic ring. In preparation of aromatic aldehydes from benzyl alcohols, long reaction times at high temperature may cause undesired autooxidation, which may produce benzoic acid. There are many methods in benzaldehyde preparation from benzyl alcohol to avoid over oxidation.<sup>4–10</sup> One of the most important methods is the oxidation of benzylic halides to benzaldehydes because of its selectivity and lack of formation of benzoic acid. Benzylic halides can be prepared easily through the photohalogenation of the aromatic methyl group<sup>11</sup> or by the Blanc chloromethylation reaction.<sup>12</sup> Benzylic bromides can be simply prepared in very good yield by two-phase electrolysis of 20–50% NaBr as an aqueous phase and chloroform containing alkyl aromatic compound as an organic phase.<sup>13</sup>

Radical bromination<sup>14–16</sup> on benzylic positions has been achieved using bromine and *N*-bromosuccinimide.<sup>17,18</sup> In addition, the bromine complex of the styrene vinylpyridine copolymer<sup>19</sup> and bromotrichloroethane<sup>20,21</sup> and copper(II) bromide<sup>22</sup> have been reported to be effective for benzylic bromination. The majority of brominating agents require the presence of peroxide or another radical initiator. Side-chain bromination using sodium bromate and bromotrimethylsilane has also been reported<sup>23</sup> but in only low yields. By using electrochemical technology, it is possible to carry out a desired reaction via a two-phase electrolytic reaction, resulting in high yields and selectivity. In a two-phase electrolysis system, the reactive species formed by the electrolytic oxidation of a halide ion in the aqueous phase can be taken continuously into the organic layer and then reacted with the substrate to give the products regioselectively either nuclear<sup>24</sup> or side-chain brominated products.<sup>13</sup> After the completion of the electrolysis, separation and concentration of the organic layer affords the product.

By this two-phase electrolysis method using 20–50% sodium bromide solution containing a catalytic amount of HBr, a number of alkyl aromatics and substituted alkyl aromatic compounds gave the corresponding bromo alkyl aromatic compounds in very good yield [60–91%].<sup>13</sup> The reaction proceeds under mild conditions and in an efficient way in the

presence of a less hazardous brominating agent than Br<sub>2</sub>, *N*-bromosuccinimide and pyridinium tribromide.

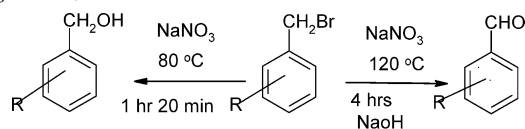
The advantages of the electrochemical bromination process include the in situ generation of bromine, high yield and lower reaction temperature than the conventional chemical method. Hence, the preparation of aromatic aldehydes from benzylic halides, especially from bromides is an attractive route as it involves no special conditions such as very high temperature, pressure, and proceeds smoothly without any special catalyst. Several methods have been developed to carry out this conversion. One such reaction is the Sommelet reaction using hexamine as a reagent.<sup>25</sup> Reagents that convert benzyl halides to benzaldehydes include 2-nitropropane-NaOEt in EtOH,<sup>26</sup> mercury-ethanolic alkali,<sup>27</sup> *p*-nitrosodimethylaniline and water (the Krohnke reaction),<sup>28</sup> NaIO<sub>4</sub>-DMF,<sup>29</sup> IBX,<sup>30</sup> trimethylamine oxide,<sup>31</sup> 4-dimethylaminopyridine-*N*-oxide,<sup>32,33</sup> pyridine *N*-oxide under microwave irradiation,<sup>34</sup> K<sub>2</sub>CrO<sub>4</sub> in HMPA in the presence of a crown ether,<sup>35</sup> and MnO<sub>2</sub><sup>36</sup> polyoxy metalate-hydrogen peroxide.<sup>37</sup> In the Kornblum reaction, benzyl halide is refluxed in DMSO along with sodium bicarbonate to get the corresponding aldehydes.<sup>38</sup> The reaction was recently attempted under microwave irradiation.<sup>39</sup>

Very recently, Lin et al. reported the oxidation of benzyl halides to corresponding benzaldehydes using CTAB as phase transfer catalyst and KNO<sub>3</sub>, KOH as reagents.<sup>40</sup> Major disadvantages of the above-mentioned processes are the use of catalysts, costly reagents, and lengthy reaction time. Even though HNO<sub>3</sub> is used as an oxidant,<sup>41</sup> its sodium salt, NaNO<sub>3</sub>, which is easy to handle has very few reports as an oxidant.<sup>42</sup> To explore the oxidizing capacity of NaNO<sub>3</sub> and to overcome the drawbacks of above-mentioned preparation methods, herein we report the oxidation of benzylic bromides to the corresponding benzaldehydes using sodium nitrate as an oxidizing agent without using an organic solvent (Scheme 1).

## Experimental Section

To a 100 mL two-neck round-bottomed flask fitted with a water condenser and dropping funnel, benzyl bromide (1.71 g,

**Scheme 1. Synthesis of Benzaldehydes from Benzyl Bromides Using NaNO<sub>3</sub><sup>a</sup>**



<sup>a</sup> R = H, Cl, Br, *t*-butyl, CH<sub>3</sub>, CH<sub>2</sub>Br, NO<sub>2</sub>.

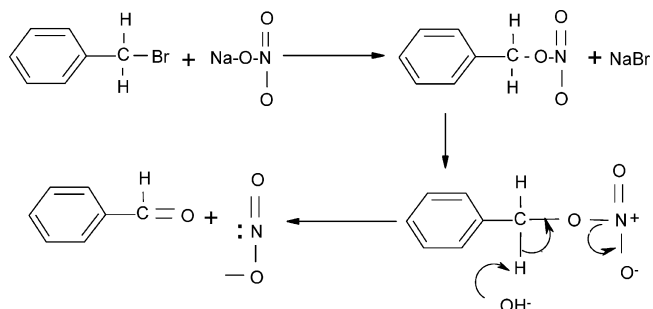
\* To whom correspondence should be addressed. Phone No. 04565-227550. Fax: 04565-227779. E-mail: rajuganic@yahoo.co.in.

10 mmol), sodium nitrate (0.850 g, 11 mmol), and water (1.5 mL) were taken and sodium hydroxide solution (0.440 g, 11 mmol, in 5 mL water) was added dropwise over a period of 4 h at 120 °C with vigorous stirring. The reaction was monitored by HPLC (Shimadzu) using methanol and water (80:20) as eluent. When the reaction is over, then the reaction mixture was cooled and extracted with diethyl ether (3 × 25 mL), washed with cold water to remove any alkalinity, and dried over anhydrous sodium sulfate. The removal of solvent affords 1.0 g benzaldehyde (91% yield).

## Result and Discussions

This protocol demonstrates the direct conversion of benzylic bromides to the corresponding benzaldehydes in good yield. The conversion of benzyl bromide to benzaldehyde was taken as a model reaction for optimization. The reaction was carried out at different temperatures with different concentrations of sodium nitrate. At optimum conditions, benzaldehyde was obtained in 91% yield as a product at 120 °C, while benzyl alcohol, an industrially important compound formed in 82% yield with a minor amount of benzyl nitrate at 80 °C using 20% sodium nitrate solution. Hence, the reaction temperature plays a crucial role in the formation of different products. Among the other nitrate salts used, potassium nitrate performs equally well, but sodium nitrate is preferred due to its low cost. During the reaction, the reaction mixture was stirred well at a stirring rate of 400 rpm.

The oxidation mechanism of the present reaction is well-documented in the literature.<sup>27</sup> The formation of benzyl nitrate followed by the treatment of sodium hydroxide results in the transformation of nitrate esters to the corresponding aldehydes. The reaction takes place in the following manner.



Under optimized conditions, various benzyl bromides were treated with sodium nitrate solution at 120 °C to obtain the corresponding benzaldehydes (Table 1). In the present method, we are using NaNO<sub>3</sub> and sodium hydroxide as cheap reagents and aldehydes are obtained in high yield.

Though there are two phases (organic and aqueous) present at the start of the reaction, it becomes homogeneous at higher temperature and vigorous stirring. After completion of reaction, the phase separation occurs when the reaction mixture attains room temperature. The phase separation has the advantage of isolating the product by simple extraction with organic solvent.

It is observed that the benzyl bromides of unsubstituted, substituted with electron donating groups undergo the reaction in shorter duration with a high yield of benzaldehydes (entry 1,2), while the mild, strong electron withdrawing group substituted benzyl bromides require 2–5-fold reaction time for the same conversion to occur (entry 6,7) along with benzyl nitrate as side product. In all the cases, the conversions are >95%. This process is carried out in organic solvent free conditions and affords high product yield. In the case of

**Table 1. Distribution of Products in the Conversion of Benzylic Bromides with Sodium Nitrate As Oxidant at 120 °C**

S No	Reactant	Product <sup>a</sup>	Time (Hrs)	Yield <sup>b</sup> (%)
1			4.0	91
2			4.5	88
3			4.5	86
4			22 <sup>c</sup>	84
5			6.0	75
6			7.5	80
7			24	50
8			9.0	51
9			6.0	70
10			7.3	68

<sup>a</sup> The structures of the products were established from the spectral data (<sup>1</sup>H NMR, FTIR) and by comparison with the authentic samples by HPLC analysis. <sup>b</sup> Isolated yield. <sup>c</sup> Reaction time is reduced to 4.5 h when 1,4-dioxane is used as solvent.

substrates carrying hydrophobic substituents of large size (Table 1, entry 4), use of polar organic solvent such as 1,4-dioxane reduces the reaction time to 5-fold. The use of cheap sodium nitrate, sodium hydroxide as reagents, and water as solvent makes the process economic and attractive.

In the conversion of benzylic bromides to benzylic alcohols, 20% sodium nitrate solution was used as oxidant and the temperature of the reaction mixture was maintained at 80 °C for a specific time as mentioned in Table 2. Unsubstituted benzyl bromide gave 82% benzyl alcohol, and the other bromides substituted with electron donating or electron withdrawing groups gave only 30–35% benzyl

**Table 2. Synthesis of Benzyl Alcohol from Benzyl Bromide (0.85 g 5 mmol, 25 mL of 20% sodium nitrate at 80 °C)**

S No	Reactant	Product	Time (min)	Yield (%)
1			80	82
2			90	30
3			120	35
4			300	33
5			120	32

alcohols along with an equal amount of benzyl nitrate ester. The formation of benzylic alcohols when the temperature is 80 °C is probably suggesting an initial nucleophilic substitution of the bromine, to form a nitrate which could evolve both by hydrolysis or oxidation depending on the reaction conditions.

## Conclusion

In summary, the oxidation is carried out at 120 °C with sodium nitrate solution under organic solvent free condition. Under optimal reaction conditions a wide range of benzylic bromides can be converted into corresponding aldehyde in high yield. Benzylic alcohols are formed from benzylic bromides using 20% sodium nitrate at 80 °C. This method avoids the usage of harmful organic solvent and the reaction occurs under very mild conditions with simple and clean workup.

## Literature Cited

- (a) Truce, W. E. *Org. React.* **1957**, 9, 37. (b) Tanaka, M.; Fujiwara, M.; Ando, H. Influence of Protonation on Gattermann-Koch Formylation Rate of Alkylbenzene in  $\text{CF}_3\text{SO}_3\text{H-SbF}_5$ . *J. Org. Chem.* **1995**, 60, 2106–2111.
- Wynberg, N.; Meijer, E. W. The Reimer-Tiemann reaction. *Org. React.* **1982**, 28, 1–36.
- Jutz, C. Iminium salts in organic chemistry. Part 1. *Adv. Org. Chem.* **1976**, 9, 225–242.
- Choudary, V. G.; Dumbre, D. K.; Narkhede, V. S.; Jana, S. K. Solvent free selective oxidation of BzOH and BzH by t-Butyl hydroperoxide using  $\text{MnO}_4$ -exchanged Mg-Al hydrotalcite catalysis. *Catal. Lett.* **2003**, 86, 229–233.
- Della, P. C.; Ross, E. F. M. Highly selective oxidation of BzOH for BzH catalysed by bimetallic gold-copper catalyst. *J. Catal.* **2008**, 260 (35), 384–386.
- Chen, Y.; Lim, H.; Tamg, Q.; Gao, Y.; Sun, T.; Qing, Y. y.; Yang, Y. Solvent free aerobic oxidation of BzOH Pd monometallic and Au-Pd bimetallic catalyst supported on SBA-16 mesoporous molecular sieves. *Appl. Catal. A: Gen.*, in press.
- Dmitry, V.; Bavykin, A.; Lapkim, A.; Stan, T.; Kolaczowski, P.; Plucinski, K. Selective oxidation of alcohols in a continuous multi functional reactor. Ruthenium oxide catalysed oxidation of BzOH. *Appl. Catal. A: Gen.* **2005**, 288, 175–184.
- Wang, X.; Kawanami, H.; Sudhir, E. D.; Natarajan, S. V.; Chatterjee, M.; Yokoyama, T.; Kushima, Y. Selective oxidation of alcohols for CHO and ketones over  $\text{TiO}_2$  supported gold nanoparticles in super critical  $\text{CO}_2$  with molecular  $\text{CO}_2$ . *Appl. Catal. A: Gen.* **2008**, 349, 86–90.
- Liosta, L. F.; Venazia, A. M.; Degandalo, G.; Lango, A.; Martorana, A.; Schey, Z.; Guzzi, L. Liquid phase selective oxidation of BzOH over Pd-Ag catalyst supported on pumice. *Catalysis Today* **2001**, 60, 271–276.
- Guo, L.-L.; Hui-zhen. Selective oxidation of BzOH to BzH with  $\text{H}_2\text{O}_2$  over tetraalkyl pyridinium octa molybdate catalysts. *Green Chem.* **2007**, 9, 421–423.
- Poutsma, M. L.; Kochi, J. K. *In Free-Radical*; Wiley: New York, 1973; Vol. 2, 159.
- Belen'Kii, L. I.; Vol'Kenshtein, Y. B.; Karmanova, I. B. New Data on the Chloromethylation of Aromatic and Heteroaromatic Compounds. *Russ. Chem. Rev.* **1977**, 46, 891–903.
- Raju, T.; Kulangiappar, K.; Anbu kulandainathan, M.; Muthukumar, A. A simple and regioselective a-bromination of alkyl aromatic compounds by two-phase electrolysis. *Tetrahedron Lett.* **2005**, 46, 7047–7050.
- Coleman, G. H.; Honeywell, G. E. *p*-Nitrobenzyl bromide. *Org. Synth.* **1943**, 2, 443–445.
- Snell, J. M.; Weissberger, A. Terephthalaldehyde. *Org. Synth.* **1955**, 3, 788–790.
- Stephenson, F. M. *o*-Xylylene dibromide. *Org. Synth.* **1963**, 4, 984–986.
- Pizey, J. S. In *Synthetic Reagents*; Halsted Press: New York, 1974; Vol. 2, pp 1–63.
- Campaign, E.; Tuller, B. F. 3-Thenyl bromide. *Org. Synth.* **1963**, 4, 921–923.
- Sket, B.; Zupan, M. Polymers as reagents and catalysts. Part 12. Side chain bromination of aromatic molecules with a bromine complex of poly(styrene-co-4-vinylpyridine). *J. Org. Chem.* **1986**, 51, 929–931.
- Huysen, F. The Photochemically Induced Reactions of Bromotrichloromethane with Alkyl Aromatics. *J. Am. Chem. Soc.* **1960**, 82, 391–393.
- Baldwin, S. W.; O'Neil, T. H. Benzylic Bromination with Bromotrichloromethane. *Synth. Commun.* **1976**, 6, 109–112.
- Chaintreau, A.; Adrian, G.; Couturier, D. Cupric Bromide as Benzylic Bromination Reagent in Polar Media. *Synth. Commun.* **1981**, 11, 669–672.
- Lee, J. G.; Cha, H. T.; Yoon, U. C.; Suh, Y. S.; Kim, K. C.; Park, J. S. Sodium Halaetes-Halotrimethyl silanes. New reagents for aromatic halogenation reactions. *Bull. Korean Chem. Soc.* **1991**, 1, 4–7.
- Raju, T.; Kulangiappar, K.; Anbu Kulandainathan, M.; Uma, U.; Malini, R.; Muthukumar, A. Site directed nuclear bromination of aromatic compounds by an electrochemical method. *Tetrahedron Lett.* **2006**, 47, 4581–4584.
- Angyal, S. The Sammelet reaction. *J. Org. React.* **1954**, 8, 197–217.
- Hass, H. B.; Bender, M. L. The Reaction of Benzyl Halides with the Sodium Salt of 2-Nitropropane. I A General Synthesis of Substituted Benzaldehydes. *J. Am. Chem. Soc.* **1949**, 71, 1767–1768.
- McKillop, A.; Ford, M. E. An Improved Procedure for the Conversion of Benzyl Halides into Benzaldehydes. *Synth. Commun.* **1974**, 4, 45–50.
- Krohnke, F. Syntheses Using Pyridinium Salts (IV). *Angew. Chem., Int. Ed. Engl.* **1963**, 2, 380–393.
- Das, S.; Panigrahi, A. K.; Maikap, G. C.  $\text{NaIO}_4$ -DMF: a novel reagent for the oxidation of organic halides to carbonyl compounds. *Tetrahedron Lett.* **2003**, 44, 1375–1377.
- Moorthy, J. N.; Singhal, N.; Senapati, K. Oxidations with IBX: benzyl halides to carbonyl compounds, and the one-pot conversion of olefins to 1,2-diketones. *Tetrahedron Lett.* **2006**, 47, 1757–1761.
- Franzen, V.; Otto, S. Eine neue methode zur Darstellung von carbonylverbindungen. *Chem. Ber.* **1961**, 94, 1360–1363.
- Mukaiyama, S.; Inanaga, J.; Yamaguchi, M. 4-Dimethylaminopyridine *N*-Oxide as an Efficient Oxidizing Agent for Alkyl Halides. *Bull. Chem. Soc. Jpn.* **1981**, 54, 2221–2222.
- Suzuki, S.; Onishi, T.; Fujita, Y.; Misawa, H. Otera, A Convenient Method for Conversion of Allylic Chlorides to  $\alpha,\beta$ -Unsaturated Aldehydes. *J. Bull. Chem. Soc. Jpn.* **1986**, 59, 3287–3288.
- Barbry, D.; Champagne, P. Fast synthesis of aromatic aldehydes from benzylic bromides with solvent under microwave irradiation. *Tetrahedron Lett.* **1996**, 37, 7725–7726.

- (35) (a) Cardillo, G.; Orena, M.; Sandri, S. Chromate ion as a synthetically useful nucleophile: a novel synthesis of aldehydes from alkyl halides. *J. Chem. Soc., Chem. Commun.* **1976**, 190. (b) Cardillo, G.; Orena, M.; Sandri, S. Polymer supported reagents. Chromic acid on anion exchange resin synthesis of aldehydes and ketones from allylic and benzylic halides. *Tetrahedron Lett.* **1976**, 17, 3985–86.
- (36) Goswami, S.; Jana, S.; Dey, S.; Adak, A. K. A Simple and Convenient Manganese Dioxide Oxidation of Benzyl Halides to Aromatic Aldehydes under Neutral Condition. *Chem. Lett.* **2005**, 34, 194.
- (37) Mirkhani, V.; Moghadam, M.; Tangestaninejad, S.; Baltork, I. M. P.; Rasouli, N. Investigation of catalytic activity of cobalt-Schiff base complex covalently linked to the polyoxometalate in the alkene and benzyl halide oxidation with hydrogen peroxide. *Catalysis Commun.* **2008**, 9, 219–223.
- (38) (a) Nace, H. R.; Monagle, J. J. Reactions of Sulfoxides with Organic Halides. Preparation of Aldehydes and Ketones. *J. Org. Chem.* **1959**, 24, 1792–1793. (b) Kornblum, N.; Jones, W. J.; Anderson, G. J. A new and selective method of oxidation. The conversion of alkyl halides and alkyl tosylates to aldehydes. *J. Am. Chem. Soc.* **1959**, 81, 4113–4114.
- (39) Xu, G.; Wu, J. P.; Ai, X. M.; Yang, L. R. Chin. Microwave-assisted Kornblum oxidation of organic halides. *Chem. Lett.* **2007**, 18, 643–646.
- (40) Lin, Q.; Lu, M.; Sun, F.; Li, J.; Zhao, Y. Oxidation of Benzyl halides to aldehydes and ketones with potassium nitrate catalysed by Phase-Transfer Catalyst in Aqueous Media. *Syn. Comm.* **2008**, 38, 4188–4197.
- (41) (a) Joshi, S. R.; Kataria, K. L.; Sawwanth, B. S.; Joshi, J. B. Kinetics of Oxidation of Benzyl Alcohol with Dilute Nitric Acid. *Ind. Eng. Chem. Res.* **2005**, 44, 325–333. (b) Lee, J.; Lee, J. N.; Lee, J. M. Facile Oxidation of Benzyl Alcohols with Sodium Nitrate/*p*-TsOH under Microwave Irradiation. *Bull. Kor. Chem. Soc.* **2005**, 26, 1300–1302.
- (42) Putnam, M. E. Method of Making Benzaldehyde. U.S Patent 1,272,522, 1918.

Received for review December 15, 2009

Revised manuscript received June 2, 2010

Accepted June 4, 2010

IE901986G