

A Simple and One-pot Oxidative Conversion of Alcohols or Aldehydes to the Nitriles using NaIO₄/KI in Aqueous NH₃

Mohammad Ali Zolfigol,* Maryam Hajjami, and Arash Ghorbani-Choghamarani^{†,*}

Faculty of Chemistry, Bu-Ali Sina University, P.O. Box 6517838683, Hamadan, Iran

*E-mail: Zolfi@basu.ac.ir or mzolfigol@yahoo.com

[†]Department of Chemistry, Faculty of Science, Ilam University, P.O. Box 69315516, Ilam, Iran

*E-mail: arashghch58@yahoo.com or a.ghorbani@mail.ilam.ac.ir

Received August 30, 2011, Accepted September 27, 2011

Sodium periodate (NaIO₄) and potassium iodide (KI) in aqueous ammonia has been used for the one-pot synthesis of nitriles from the corresponding aldehydes and alcohols in moderate to good yield. This transformation, proceeds *via* an *in situ* oxidation- imination-aldimine oxidation sequence.

Key Words : Nitrile, Sodium periodate, Ammonia, Potassium iodide

Introduction

Transformation of alcohols and aldehydes into nitriles is of interest because of the role of nitriles as starting materials for the synthesis of various functional groups.¹

Classically, nitriles have been synthesized *via* the nucleophilic substitution reaction of alkyl or aryl halides with inorganic cyanides,^{2,3} dehydration of amides and aldoximes,^{4,6} elimination of oxime ethers⁷ and oxime esters,⁸ conversion of alcohols,⁹ aldehydes¹⁰ and oxidative transformation of primary amines.^{11,12} These procedures suffer from some limitations such as prolonged reaction time, low yield, use of toxic solvents, laborious work-up procedures, harsh reaction conditions, expensive or commercially unavailable reagents. However, the synthetic examples of nitriles using alcohols or aldehydes as starting materials in one-pot procedure are convenient and highly desirable. Therefore, the development of new and practical methodologies on this topic is very welcome. The use of ammonia combined with a suitable oxidant is a useful method for the transformation of aldehydes or alcohols to their corresponding nitriles.¹²⁻¹⁶

In this light, as a part of our research program we became interested to report a mild, facile and practical method for the direct conversion of alcohols and aldehydes, to the corresponding nitriles by treatment with sodium periodate (NaIO₄) and potassium iodide (KI) in aqueous ammonia at 60 °C.

In continuation of our efforts to the functionalization of organic compounds, we decided to introduce a new oxidizing system for the one-pot conversion of aldehydes and alcohols to the corresponding nitriles.

In our initial studies, effect of different amount of KI on the outcome of the reaction was considered. For this reason conversion of *p*-methoxybenzyl alcohol to the *p*-methoxybenzyl nitrile, as standard model, was considered. The reaction was performed using mixture containing 1 mmol of *p*-methoxybenzyl alcohol, 2.5 mmol of potassium periodate

Table 1. Conversion of *p*-methoxybenzyl alcohol to *p*-methoxybenzyl nitrile with NaIO₄ (2.5 mmol) and Different Amounts of KI in aqueous ammonia at 60 °C^a

Entry	KI (mmol)	Yield (%) ^b
1	0.2	58
2	0.5	70
3	0.6	74
4	0.8	91
5	1	92
6	1	92 ^c

^aReaction time: 180 min. ^bIsolated yield. ^camount of NaIO₄: 3 mmol.

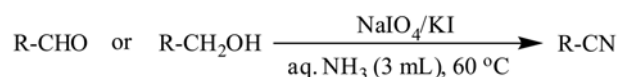
(NaIO₄), and different amounts of KI in aqueous ammonia at 60 °C (Table 1).

The optimal amount of KI to convert *p*-methoxybenzyl alcohol to *p*-methoxybenzyl nitrile is 0.8 mmol, which was used in all oxidation reactions.

Therefore, we report here a very simple procedure for the transformation of a wide range of aldehydes and alcohols into nitriles by their treatment with NaIO₄ and KI in aqueous ammonia at 60 °C (Scheme 1 and Table 2).

All nitrile synthesis reactions were performed in a sealed tube and conversion of aldehydes and alcohols indicated by TLC.

In order to consider the effect of temperature, *p*-methoxybenzaldehyde and *p*-nitrobenzylalcohol were subjected to the oxidative conversion to the corresponding nitriles with aqueous ammonia by addition of NaIO₄ and KI in ambient of temperature (Table 2 entries 3 and 13). In the case of *p*-methoxybenzaldehyde the reaction was not completed and impurity of aldimine was observed and corresponding nitrile obtained in 18% yield. For *p*-nitrobenzylalcohol trace



Scheme 1

Table 2. Oxidative conversion of aldehydes and alcohols to the corresponding nitriles with NaIO₄/KI^a in aqueous NH₃ at 60 °C

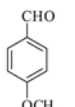
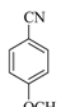
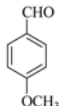
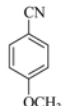
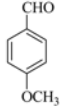
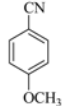
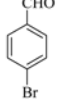
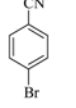
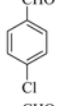
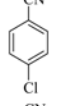
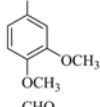
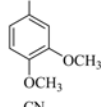
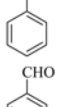
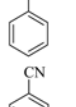
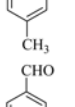
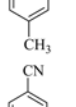
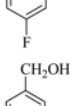
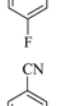
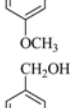
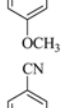
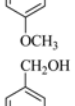
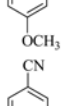
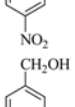
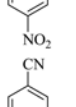
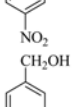
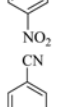
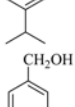
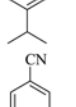


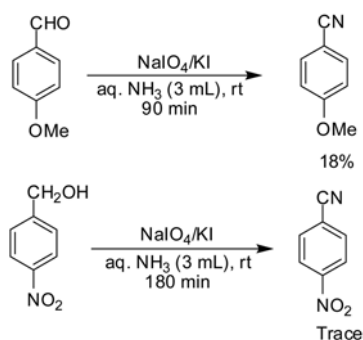
Entry	Substrate	Product	Time (min)	Yield (%) ^b	mp °C (observed)	mp °C (reported)	Ref.
1			90	89	56.5-57.5	59	17
2			90	68 ^{c,d}	-	-	-
3			90	18 ^{e,d}	-	-	-
4			90	87	108-110.5	110-111	16
5			90	88	88-91	94	17
6			90	87	61-63.5	62.5	18
7			90	67	oil	oil	16
8			90	85	27-28	25	19
9			90	73	30-32	33-35	16
10			180	91	57-59	59	17
11			180	5 ^{f,c}	oil	59	17
12			180	84	145.5-148	148-150	20
13			180	Trace ^{g,e}	-	-	-
14			180	77	oil	oil	21
15			180	73	oil	oil	22

Table 2. Continued

Entry	Substrate	Product	Time (min)	Yield (%) ^b	mp °C (observed)	mp °C (reported)	Ref.
16			180	82	104-107	110-111	16
17			180	66	42-43	42	23
18			180	79	31-33	33-35	16
19			180	61	oil	oil	16
20			180	64	47-49	47	23
21			180	12 ^c	oil	-	-

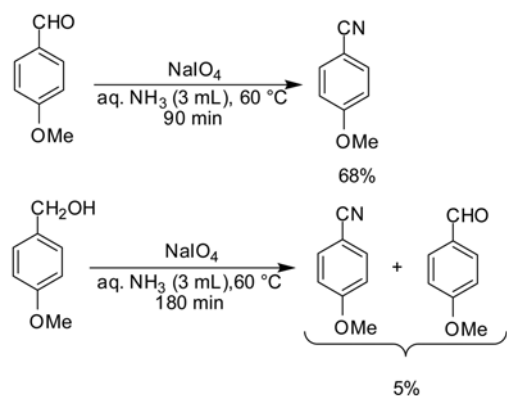
^aAldehyde/NaIO₄/KI = 1:1.5:0.2; alcohol/NaIO₄/KI = 1:2.5:0.8. ^bIsolated yield. ^cIn the absence of KI. ^dYield determined by ¹H NMR. ^eReaction performed at room temperature. ^fYield refer to mixture of aldehyde and nitrile. ^gImpurity was observed.



Scheme 2

conversion was observed. These results have been outlined in Scheme 2.

In order to consider the role of potassium iodide in described transformation, *p*-methoxybenzaldehyde and *p*-methoxybenzyl alcohol were subjected to the oxidative



Scheme 3

conversion to the corresponding nitriles in the absence of KI (entries 2 and 11, Table 1). The results clearly indicate that the reaction of *p*-methoxybenzaldehyde was not completed and in the case of *p*-methoxybenzyl alcohol trace conversion to both aldehyde and nitrile observed (Scheme 3).

Furthermore, the kinetic progress of the described system was investigated by upward trend of time reaction and its influence to amount of conversion. Treatment of *p*-methoxybenzyl alcohol was studied in different periods of reaction time. The results are outlined in Figure 1. As the results show, the *p*-methoxybenzonitrile yield rises gradually and steadily with increasing reaction time.

A plausible reaction pathway for the conversion of alcohol and aldehyde to the corresponding nitrile with NaIO₄/KI in aqueous ammonia at 60 °C is shown in Scheme 4. The initial O-iodination of alcohol with I₂ (which generated *in situ* in the reaction condition) occurred to form O-iodo compound, followed by elimination of HI to form aldehyde. Aldehyde reacts with NH₃ to form aldimine. Then, aldimine treats with

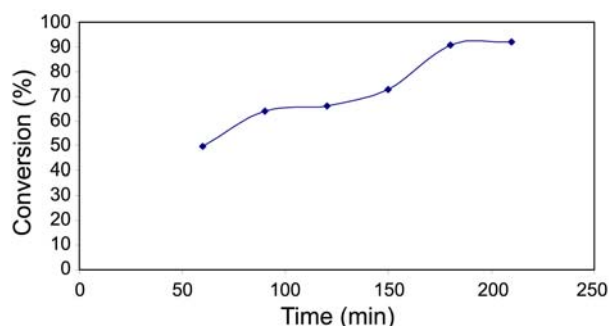
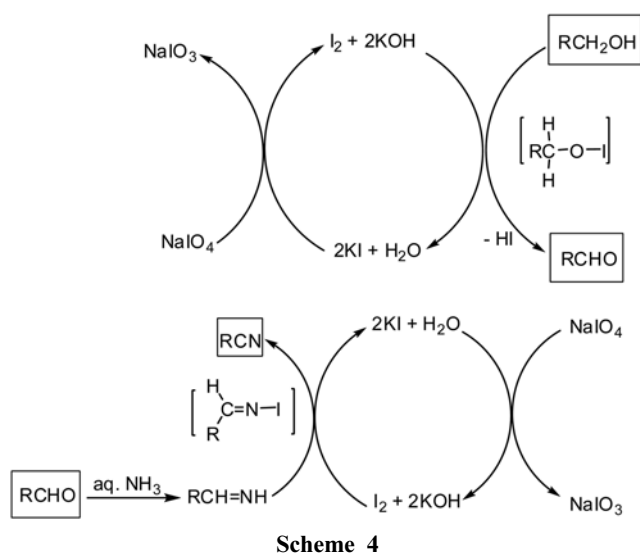


Figure 1. The kinetic progress of the oxidation of *p*-methoxybenzyl alcohol.



in situ generated molecular iodine to form *N*-iodo aldimine, followed by β -elimination of HI by NH_3 to generate the nitrile.

In conclusion, simple, efficient and interesting methodology for the one-pot conversion of aldehydes and alcohols into nitriles has been realized. The method involves the use of sodium periodate (NaIO_4) and KI in aqueous NH_3 at 60 °C. The significant features of the system are as follows: a) good to excellent yields are obtained with both aldehydes and alcohols, b) no special equipment is needed for the reaction, and work up is simple, c) the reagents and chemicals needed are commercial available, they aren't toxic metals and expensive, and d) purification of products is not time consuming.

Experimental

General. The chemicals and solvents were purchased from Fluka, Merck and Aldrich chemical companies without further purifications. The nitrile products were characterized by comparison of their spectral (IR, ^1H NMR, and ^{13}C NMR) and physical data with authentic samples.

One-pot Conversion of *p*-bromobenzaldehyde to the *p*-bromobenzonitrile. NaIO_4 (321 mg, 1.5 mmol) and KI (33.2 mg, 0.2 mmol) was added to a mixture of *p*-bromobenzaldehyde (185 mg, 1 mmol) and aqueous NH_3 (3 mL), at room temperature. The resultant mixture was stirred in sealed tube at 60 °C. Reaction completed after 90 min and suspension was cooled down to room temperature, diluted with water and $\text{Na}_2\text{S}_2\text{O}_3$ (5 mmol) was added. The residue was extracted with dichloromethane (20 mL) and the organic phase dried over anhydrous Na_2SO_4 (3 g) and filtered off after 20 min. *p*-bromobenzonitrile was obtained

after evaporation in 87% yield.

Oxidative Conversion of *p*-nitrobenzylalcohol to *p*-nitrobenzonitrile. In a sealed tube a mixture of *p*-nitrobenzylalcohol (153.13 mg, 1 mmol), NaIO_4 (535 mg, 2.5 mmol) and KI (132.8 mg, 0.8 mmol) in aqueous ammonia (3 mL) was stirred at 60 °C. After 180 min reaction mixture was quenched with water and $\text{Na}_2\text{S}_2\text{O}_3$ (5 mmol). Then the aqueous fraction was extracted with CH_2Cl_2 (20 mL) and the organic layer dried over Na_2SO_4 (3 g). Further purification was carried out by short column chromatography to afford pure *p*-nitrobenzonitrile in 84% yield.

Acknowledgments. The authors acknowledge Bu-Ali Sina University Research Council (Grant Number 32-1716), Center of Excellence in Development of Chemical Methods (CEDCM), National Foundation of Elites (BMN), and Ilam University, Ilam, Iran for financial support of this work.

References

- (a) Bag, S.; Tawari, N. R.; Degani, M. S. *Arkivoc* **2009**, (xiv), 118. (b) Kim, M.; Lee, J.; Lee, H. Y.; Chang, S. *Adv. Synth. Catal.* **2009**, *351*, 1807.
- Iida, S.; Ohmura, R.; Togo, H. *Tetrahedron* **2009**, *65*, 6257.
- Leadbeater, N. E.; Torenius, H. M.; Tye, H. *Tetrahedron* **2003**, *59*, 2253.
- (a) Harrison, C.; Hodge, P.; Rogers, W. *Synthesis* **1977**, 41. (b) Yang, S. H.; Chang, S. *Org. Lett.* **2001**, *3*, 4209.
- Chill, S. T.; Mebane, R. C. *Synth. Commun.* **2009**, *39*, 3601.
- Movassagh, B.; Shokri, S. *Tetrahedron Lett.* **2005**, *46*, 6923.
- Maeyama, K.; Kobayashi, M.; Kato, H.; Yonezawa, N. *Synth. Commun.* **2002**, *32*, 2519.
- Cho, B. R.; Chung, H. S.; Cho, N. S. *J. Org. Chem.* **1998**, *63*, 4685.
- Iranpoor, N.; Firouzabadi, H.; Akhlaghinia, B.; Nowrouzi, N. *J. Org. Chem.* **2004**, *69*, 2562.
- (a) Carmeli, M.; Shefer, N.; Rozen, S. *Tetrahedron Lett.* **2006**, *47*, 8969. (b) Talukdar, S.; Hsu, J. L.; Chou, T. C.; Fang, J. M. *Tetrahedron Lett.* **2001**, *42*, 1103.
- Stevens, T. E. *J. Org. Chem.* **1961**, *26*, 2531.
- Reddy, K. R.; Maheswari, C. U.; Venkateshwar, M.; Prashanthi, S.; Kantam, M. L. *Tetrahedron Lett.* **2009**, *50*, 2050.
- Parameswaram, K. N.; Friedman, O. M. *Chem. Ind. (London)* **1965**, 988.
- Mori, N.; Togo, H. *Synlett* **2005**, 1964.
- Bandgar, B. P.; Makone, S. S. *Synth. Commun.* **2006**, *36*, 1347.
- Arote, N. D.; Bhalerao, D. S.; Akamanchi, K. G. *Tetrahedron Lett.* **2007**, *48*, 3651.
- Movassagh, B.; Fazeli, A. *Synthetic Commun.* **2007**, *37*, 623.
- Dewan, S. K.; Singh, R.; Kumar, A. *Synthetic Commun.* **2004**, *34*, 2025.
- Iida, S.; Togo, H. *Tetrahedron* **2007**, *63*, 8274.
- Chen, F. E.; Li, Y. Y.; Xu, M.; Jia, H. Q. *Synthesis* **2002**, 1804.
- <http://www.chemblink.com/products/4210-32-6.html>.
- <http://www.chemexper.com/chemicals/supplier/cas/78-82-0.html>.
- Sharghi, H.; Sarvari, M. H. *Tetrahedron* **2002**, *58*, 10323.