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A novel system for the synthesis of nitriles from aldehydes using aqueous ammonia and sodium dichloroiodate

Vikas N. Telvekar *, Kavit N. Patel, Harish S. Kundaikar, Hemchandra K. Chaudhari

Department of Pharmaceutical Sciences and Technology, University Institute of Chemical Technology, Matunga, Mumbai 400 019, India

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Abstract

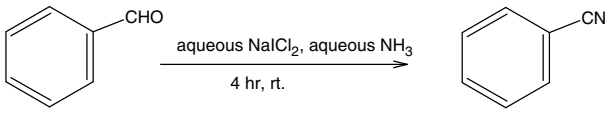
A simple and mild method for the conversion of varieties of aldehydes to the corresponding nitriles using aqueous ammonia and aqueous sodium dichloroiodate reagent at room temperature is discussed. Advantages of this system are short reaction time, easy work-up and moderate to good yields.

Keywords: Sodium dichloroiodate solution; Aqueous ammonia; Aldehydes; Nitriles

A number of methods are known for the conversion of aldehydes into nitriles from the corresponding aldehydes via dehydration of aldoximes or using reagents such as trimethylsilyl azide,[1] triazidochlorosilane,[2] sodium azide and aluminium chloride.[3] There are several methods developed using a combination of ammonia such as $NH_3/O_2/CuCl_2{\cdot}2H_2O$/MeONa in MeOH,[4] $NH_3/Pb(OAc)_4$ in dry benzene,[5] NH_3/I_2 in THF–water,[6] NH_3/NBS in water[7] and recently NH_3/IBX in acetonitrile.[8] Despite these, there is still scope for alternative reagent systems for the preparation of nitriles from aldehydes.

Our group has been working extensively on the development of novel methodologies under mild reaction conditions using various hypervalent iodine reagents.[9] Sodium dichloroiodate is commercially available in 50% water solution,[10] and reported only for the iodination of the aromatic ring at 40–70 °C for 72 h.[11]

We observed that this aqueous reagent could be used in combination with aqueous ammonia at room temperature for the direct conversion of aldehydes to the corresponding nitriles. For our initial studies, benzaldehyde was chosen as model substrate (Scheme 1). A mixture of benzaldehyde, aqueous ammonia and aqueous sodium dichloroiodate solution was stirred at room temperature (25 °C). The starting material was consumed within 4 h as indicated by TLC analysis. After work-up and purification by silica gel column chromatography, benzonitrile was isolated in 90% yield. To the best of our knowledge, there is no report on the use of aqueous $NaICl_2$ solution in aqueous ammonia for the direct conversion of aldehydes to nitriles. No iodination of aromatic ring was observed at room temperature.



Scheme 1. Preparation of nitrile using aq $NaICl_2$ and NH_3.

Encouraged by these results, we subjected various aromatic and aliphatic aldehydes to the reaction conditions and the results are presented in Table 1.[12] The results clearly indicate that ether, acetyl and ester groups are stable to the conditions (Table 1, entries 4–7). Pyridine-3-aldehyde was converted into 3-cyano pyridine in good yield (Table 1, entry 8). Aliphatic aldehydes also underwent this transformation smoothly; however, a slower reaction rate was observed; pentanal (Table 1, entry 12), hexanal (Table

* Corresponding author. Tel.: +91 22 24145616; fax: +91 22 24145614.
E-mail address: vikastelvekar@rediffmail.com (V. N. Telvekar).

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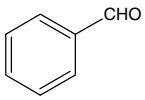
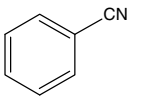
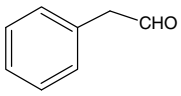
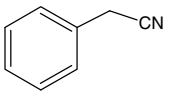
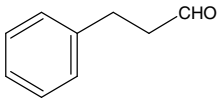
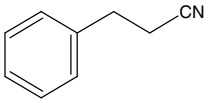
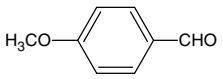
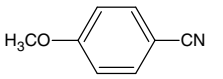
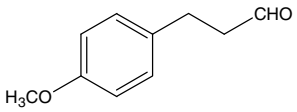
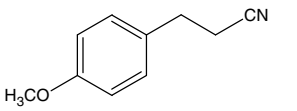
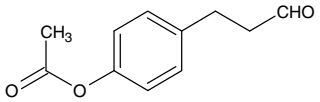
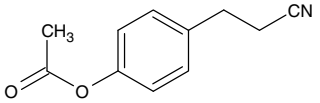
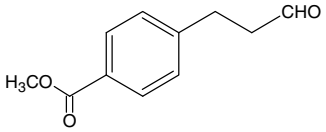
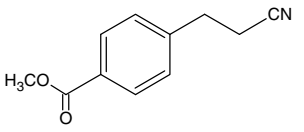
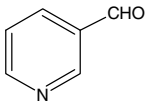
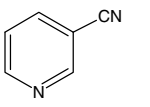
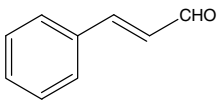
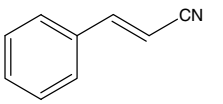
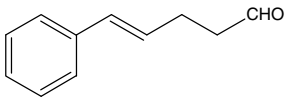
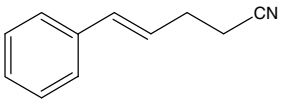
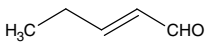
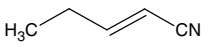
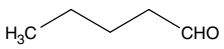
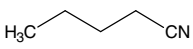
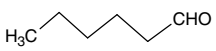
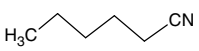
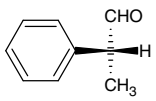
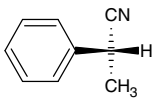
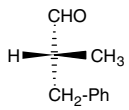
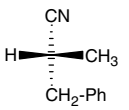
Table 1
Synthesis of nitriles from aldehydes using sodium dichloroiodate solution and aqueous ammonia[a]

Entry	Substrate[b]	Product	Time (h)	Yield[c] (%)
1			4	90
2			6	92
3			6	90
4			5	87
5			7	85
6			7	83
7			7	85
8			5	90
9			6	88
10			9	87
11			9	86
12			9	85
13			9	86
14[d]			6	88
15[d]			6	90

[a] Reaction conditions: substrate (4.7 mmol), aqueous sodium dichloroiodate (2.0 equiv, 2.0 M), aqueous ammonia (15 mL), rt.
[b] Starting compounds were prepared by standard literature procedures.
[c] Isolated yields after column chromatography. Structures confirmed by comparison of IR and ^{1}H NMR with those of authentic materials.
[d] Optical purity confirm by chiral HPLC analysis and optical rotations matches with literature values.[13]

1, entry 13) were converted to the corresponding nitriles in good yields. Double bonds were not affected under these reaction conditions (Table 1, entries 9–11).

Optically active aldehydes, *R*-2-methyl-3-phenylpropanal and *R*-2-phenylpropanal were subjected to reaction conditions, after column purification corresponding optically active *R*-nitriles were obtained, with optical purity >99%, determined by chiral HPLC analysis (Table 1, entries 14 and 15).

In conclusion, a novel method has been developed for the direct conversion of aldehydes to the corresponding nitriles using aqueous sodium dichloroiodate solution in combination with aqueous ammonia at room temperature. The method is mild and gave good to excellent yields of nitriles in the case of both aliphatic and aromatic substrates.

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9. (a) Telvekar, V. N.; Arote, N. D.; Herlekar, O. P. *Synlett* **2005**, 2495; (b) Telvekar, V. N.; Rane, R. M. *Tetrahedron Lett.* **2007**, *48*, 6051.
10. Dark red or brown liquid, stable at room temperature, which has specific gravity 2.26, miscible in acetic acid, light sensitive and cause sensitization by inhalation or through skin contact.
11. (a) William, T.; Einar O. I.; Trygve G.; U.S. Patent RE38,856E, 2005; (b) Bernstein, J.; Kathryn, A. L.; U.S. Patent 3,666,799, 1972.
12. *General experimental procedure*: To a stirred solution of aldehyde (1.0 equiv, 4.7 mmol) in aqueous ammonia (15 mL of a 28–30% solution, Sp. gravity = 0.89) was added the $NaICl_2$ (2.0 equiv, 2.0 M). The resultant mixture was stirred at rt until the starting material had been completely consumed (TLC). The reaction mixture was diluted with water and extracted with chloroform (2 × 20 mL). The combined organic layer was washed successively with 10% aq sodium bisulfite solution (2 × 15 mL), 10% aq $NaHCO_3$ (2 × 15 mL) and finally with H_2O (1 × 20 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue obtained was purified by silica gel column chromatography (10% EtOAc–hexane) to afford pure nitriles.
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