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Direct oxidative conversion of aldehydes to nitriles using IBX in aqueous ammonia

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Abstract—A mild, simple, chemoselective and high yielding procedure for the direct oxidative conversion of aldehydes to nitriles has been developed using IBX in aqueous ammonia.

Hypervalent iodine reagents are well known for their selective, efficient and mild properties as oxidizing agents.[1] Although *o*-iodoxybenzoic acid (IBX) and Dess–Martin periodinane (DMP) are two important reagents that are suitable for a wide range of chemical transformations, IBX has become a reagent of choice.

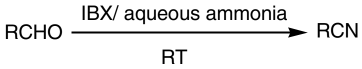
Nitriles are useful precursors for the synthesis of amines, amides, amidines, ketones, carboxylic acids and esters. Preparation of nitriles from the corresponding aldehydes is an important functional group transformation in organic synthesis.[2] Several methods are known for the transformation of aldehydes to nitriles via dehydration of aldoximes[3] or using reagents such as trimethylsilyl azide,[4] triazidochlorosilane,[5] sodium azide and aluminium chloride.[6]

The use of ammonia combined with an appropriate oxidant is an expedient method for the transformation of aliphatic and aromatic aldehydes to their corresponding nitriles. Reagents developed to effect this conversion are $NH_3/O_2/CuCl_2{\cdot}2H_2O/MeONa$ in MeOH,[7a] $NH_3/Pb(OAc)_4$ in dry benzene,[7b] $NH_3/I_2/MeONa$ in MeOH,[7c] $NH_3/S_8/NaNO_2$,[7d] $NH_3/H_2O_2/CuCl$ in 2-propanol,[7e] NH_3/I_2 in THF–water,[7f] and NH_3/NBS in water.[7g] Despite these, additional methods for this conversion are still valuable.

The development of reaction methodologies using hypervalent iodine reagents is of interest. To the best of our knowledge, there is no report on the use of IBX in aqueous ammonia for any organic transformations. In continuation of our efforts to develop newer applications of hypervalent iodine (λ^5) compounds,[8] we explored the combination of IBX and aqueous ammonia for direct conversion of aldehydes to nitriles (Scheme 1). IBX is highly soluble in aqueous ammonia.

The reaction conditions were established using benzaldehyde as substrate. Addition of benzaldehyde to a solution of IBX in aqueous ammonia resulted in oxidation to benzonitrile. However, addition of acetonitrile as a co-solvent to dissolve the aldehyde in the reaction medium was advantageous; the reaction was complete within 2 h at room temperature and the nitrile obtained was practically pure with no need for further purification.

A variety of aldehydes[9] including aromatic, hetero-aromatic, α,β-unsaturated and aliphatic were transformed to nitriles smoothly via this protocol in high yields (Table 1). This methodology is chemoselective and functionalities such as phenolic, *tert*-amine, allyl ethers and alkenes were unaffected (entries 5–7, and 12). Thiophene and furan rings were also stable (entries 10 and 11) under the present reaction conditions. Aliphatic aldehydes also underwent this transformation smoothly, however, the reactions took longer time for completion (entries 13–15).



Scheme 1.

Keywords: IBX; Oxidation; Aldehyde; Nitrile; Ammonia water.

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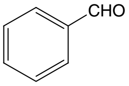
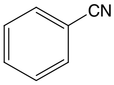
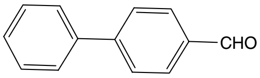
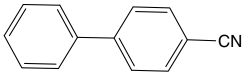
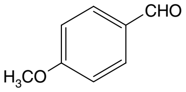
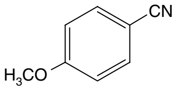
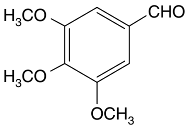
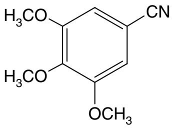
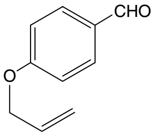
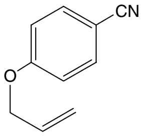
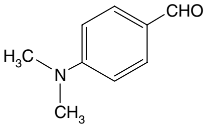
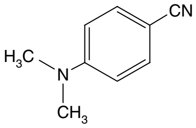
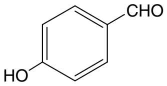
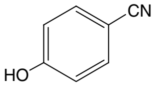
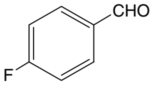
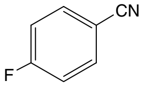
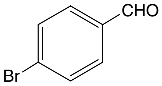
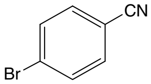
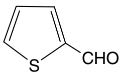
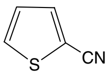
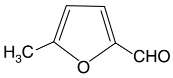
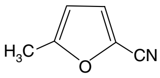
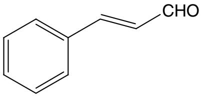
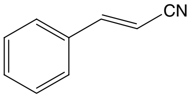
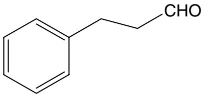
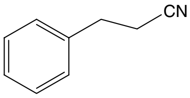
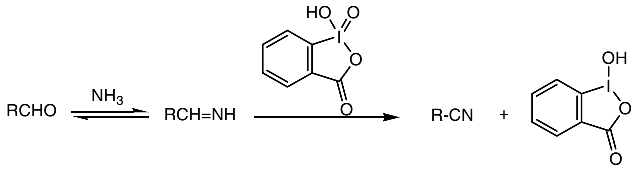
Table 1. Oxidative conversion of aldehydes to nitriles with IBX/aqueous ammonia

Entry	Substrate	Product[a]	Time (h)	Yield[b] (%)
1			2	90
2			2	92
3			2	95
4			2	93
5			3	92
6			3	95
7			2	90
8			6	92
9			8	89
10			2	92
11			2	93
12			2.5	91
13			10	88
14	$CH_3–(CH_2)_3–CHO$	$CH_3–(CH_2)_3–CN$	10	90
15	$CH_3–(CH_2)_2–CHO$	$CH_3–(CH_2)_2–CN$	10	88

[a] Structures were confirmed from their spectral (NMR and IR) analysis data.

[b] Isolated yield.

A plausible reaction pathway is shown in Scheme 2. We suggest that the reaction proceeds via formation of an intermediate aldimine, which then undergoes oxidation by IBX to afford the nitrile. Iodosobenzoic acid (IBA)



Scheme 2. A plausible reaction pathway.

obtained from the reduction of IBX has been recycled by oxidation.[10]

In summary, a simple, chemoselective, efficient and mild method has been developed for direct conversion of aldehydes into nitriles.

Acknowledgement

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Supplementary data

Spectral data for the compounds in Table 1 can be found, in the online version. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.03.137.

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9. Aldehyde (5 mmol) was added to a stirred solution of IBX (7.5 mmol) in aqueous ammonia (20 ml of a 28–30% solution, Sp. gravity = 0.89) and acetonitrile (3 ml) at room temperature. The resultant clear solution became turbid as the reaction proceeded. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate (2 × 25 ml). The combined organic layer was washed successively with water (2 × 25 ml), and brine (25 ml), dried over sodium sulfate and concentrated under vacuo to afford practically pure nitrile.
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