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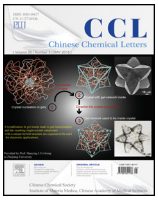

Original article

# Preparation of aromatic nitriles *via* direct oxidative conversion of benzyl alcohols, aldehydes and amines with pentylpyridinium tribromide in aqueous $NH_4OAc$

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ABSTRACT

Pentylpyridinium tribromide and aqueous ammonium acetate was used for the rapid oxidative conversion of benzyl alcohols, benzaldehydes and benzyl amines to the corresponding benzonitriles in good to excellent yields. This simple, mild and one-pot system provides easy workup and separation of the products.

## 1. Introduction

Nitriles are well-known compounds due to their huge potential for applications in synthesis of various bioactive molecules [1–3]. They are viable precursors for preparation of a variety of nitrogen-containing functional compounds [4–7]. In addition, nitriles are versatile and important building blocks of dyes, natural products, herbicides, agrochemicals, pharmaceuticals, and various fine chemicals [8–11]. Therefore, developing a simple and flexible method for the preparation of such compounds is still needful.

Numerous approaches to the synthesis of nitriles are completely reviewed in literature. Conventionally used methods are the nucleophilic substitution reaction of alkyl halides with metal cyanides [12], dehydration of primary amides [13,14] or aldoximes [15–26] and oxidative transformation of primary alcohols [27–32], aldehydes [33–36], alkyl halides [37–40], primary aliphatic amines [37–42] and primary azides [43,44]. In addition Pd and Cu catalyzed cyanation of aryl halides was established for the synthesis of benzonitriles [45–47]. Furthermore transformation of esters to nitriles was reported [48–50]. Recently a mild ammoxidation method, which directly converts methyl arenes into aromatic nitriles, has been developed by using $Pd(OAc)_2$ and *N*-hydroxyphthalimide (NHPI) as the catalysts, and tert-butyl nitrite as the nitrogen source and oxidant [51]. More recently An NBS mediated nitriles synthesis through C═C double bond cleavage has been developed [52].

Undoubtedly, uses of expensive and toxic reagents are some disadvantages of reported methods. Herein an efficient and mild method for mentioned conversion using pentylpyridinium tribromide (PPTB) and aqueous ammonium acetate is reported (Scheme 1). To the best of our knowledge, this is the first report of the application of this reagent for the oxidative conversion of benzyl alcohols, benzyl amines, and benzaldehydes to the corresponding nitriles.

## 2. Experimental

Chemicals were purchased from Fluka, Merck, and Aldrich chemical companies. Pentylpyridinium tribromide is a non-volatile ionic liquid analog of bromine, which play a dual role as solvent and reagent and can be easily prepared from commercially available starting materials [53]. Thin layer chromatography (TLC) was performed on UV-active aluminum-backed plates of silica gel (TLC Silica gel 60 $F_{254}$). Flash chromatography was performed using silica gel (60 Å, 230–400 mesh) with reagent grade solvents. NMR

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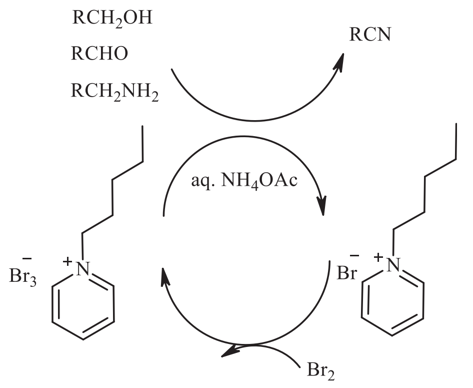

**Scheme 1.** Oxidative conversion of benzylic alcohols, amines and aldehydes to benzonitriles.

spectra were recorded on a Bruker Avance AQS 300 MHz using tetramethylsilane (TMS) as an internal standard. The products were characterized by comparison of their spectral, TLC and physical data with the authentic samples.

*General procedure*: To a mixture of amine, alcohol or aldehyde (1 mmol) and aqueous $NH_4OAc$ (2.0 mL, 45 mmol) in a round-bottomed flask was added pentylpyridinium tribromide (2.2 mmol for alcohols and amines and 1.1 mmol for aldehydes) gradually in several small portions at room temperature. The obtained mixture was stirred at 70 °C for appropriate time. When the reaction was complete (monitored by TLC), it was quenched at this temperature with $H_2O$ (10 mL), aqueous $Na_2SO_3$ at 0 °C, and then it was extracted with $Et_2O$ ($3 \times 5$ mL). The combined organic layers were washed with water, dried ($MgSO_4$) and evaporated under vacuum to give benzonitriles in good yield. If necessary, the product was purified by column chromatography (silica gel, hexane-EtOAc, 4:1).

Benzonitrile (**4a**): Colorless liquid. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.68–7.65 (2H, m), 7.61–7.58 (1H, m), 7.51–7.45 (2H, m); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 112.1, 118.8, 129.1, 132.0, 132.7; Elemental analysis calcd for $C_7H_5N$: C, 81.55; H, 4.85; N, 13.59. Found: C, 81.52; H, 4.87; N, 13.61.

4-Methoxybenzonitrile (**4b**): White solid, mp 59–61 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.53 (d, 2H, $J = 8.4$ Hz), 7.28 (d, 2H, $J = 8.4$ Hz), 2.43 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 162.8, 134.1, 119.2, 114.7, 104.0, 55.4; Elemental analysis calcd. for $C_8H_7NO$: C, 72.18; H, 5.26; N, 10.52. Found: C, 72.17; H, 5.28; N, 10.51.

4-Methylbenzonitirle (**4c**): Colorless oil. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.38 (d, 2H, $J = 8.0$ Hz), 7.15 (d, 2H, $J = 8.0$ Hz), 2.29 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 143.4, 131.7, 129.6, 118.8, 109.0, 21.5; Elemental analysis calcd. for $C_8H_7N$: C, 82.02; H, 6.02; N, 11.96. Found: C, 81.99; H, 6.04; N, 11.97.

4-Chlorobenzonitrile (**4d**): White solid, mp 91–93 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.58 (d, 2H, $J = 8.5$ Hz), 7.46 (d, 2H, $J = 8.5$ Hz); $^{13}C$ NMR (75 MHz; $CDCl_3$): $\delta$ 139.5, 133.4, 129.6, 117.9, 110.8; Elemental analysis calcd. for $C_7H_4ClN$: C, 61.12; H, 2.93; N, 10.18. Found: C, 61.10; H, 2.95; N, 10.16.

3-Nitrobenzonitrile (**4e**): Colorless solid, mp 117–118 °C. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.55–8.54 (m, 1H), 8.53–8.47 (m, 1H), 8.01–7.99 (m, 1H), 7.76–7.74 (m, 1H). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 148.3, 137.6, 130.7, 127.4, 127.2, 116.5, 114.2; Elemental analysis calcd. for $C_7H_4N_2O_2$: C, 56.76; H, 2.72; N, 18.91; O, 21.60. Found: C, 56.73; H, 2.74; N, 18.90; O, 21.62.

4-Bromobenzonitrile (**4f**): White solid, mp 112–115 °C: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.62 (d, 2H, $J = 8.5$ Hz), 7.51 (d, 2H, $J = 8.5$ Hz); $^{13}C$ NMR (75 MHz; $CDCl_3$): $\delta$ 133.3, 132.4, 127.8, 117.9, 111.1. Elemental analysis calcd. for $C_7H_4BrN$: C, 46.19; H, 2.22; N, 7.70. Found: C, 46.12; H, 2.25; N, 7.72.

**Table 1**

Optimization of the amounts of PPTB/aq. $NH_4OAc$ for oxidative conversion of benzyl alcohol to benzonitrile at 70 °C.

| Entry | PPTB/$NH_4OAc$ (eq.) | Time (h) | Yield (%)[a] |
|---|---|---|---|
| 1 | 2/25 | 4 | 15[b] |
| 2 | 2/25 | 4 | 45 |
| 3 | 2.2/25 | 3 | 57 |
| 4 | 2/45 | 2.5 | 80 |
| 5 | 2.2/45 | 2 | 88 |
| 6 | 2.4/45 | 2 | 89 |

[a] Isolated yield.

[b] Room temperature.

## 3. Results and discussion

Pentylpyridinium tribromide is stable ionic liquid at room temperature with high molecular weight (MW = 389.95), less toxic than molecular bromine, nonvolatile, easy to handle and relatively cheap oxidant. Because of these properties, we decided to investigate the oxidative conversion of alcohols, amines and aldehydes to nitrile using this reagent in the presence of aqueous ammonium acetate. It is worthwhile to note that the ionic liquid pentylpyridinium bromide was recycled from the reaction mixture and the reagent was regenerated by the direct action of bromine.

In order to explore the optimum reaction conditions, benzyl alcohol was preferred as the model substrate. A mixture of benzyl alcohol and aqueous ammonium acetate solution was stirred under different conditions (Table 1). The results showed that reactions at room temperature provided low yields of benzonitrile, but increasing the amount of PPTB from 2 mmol to 2.2 mmol and increasing the temperature from room temperature to 70 °C gave a considerable improvement in the conversion. It should be mentioned that during all reactions care must be taken when adding PPTB to the substrate/ammonium acetate solution. Adding the PPTB in one portion would result in a relatively violent reaction. To avoid this problem PPTB was added carefully in several small portions.

The current system was promoted for the direct conversion of aldehydes into nitriles, and the results are summarized in Table 2 (entries 6–11). It should be mentioned that required amount of PPTB for aldehydes is 1.1 mmol. Very good conversion of aldehydes to nitriles was obtained also these reactions were found to be faster compared to the alcohols.

**Table 2**

Oxidative conversion of benzyl alcohols, benzyl amines and benzaldehydes to nitriles with PPTB/aq $NH_4OAc$.

$$\begin{array}{l} ArCH_2OH \\ \text{or } ArCH_2NH_2 \\ \text{or } ArCHO \end{array} \xrightarrow[70\ ^\circ C]{PPTB/aq\ NH_4OAc} Ar\text{-}CN$$

| Entry | Substrate | Time (h) | Yield (%)[a] |
|---|---|---|---|
| 1 | Ph-$CH_2OH$ | 2 | 88 |
| 2 | 4-$CH_3O$Ph-$CH_2OH$ | 2.5 | 90 |
| 3 | 4-Tol-$CH_2OH$ | 2.5 | 89 |
| 4 | 4-ClPh-$CH_2OH$ | 3 | 87 |
| 5 | 3-$O_2N$Ph-$CH_2OH$ | 3 | 90 |
| 6 | Ph-CHO | 2 | 92 |
| 7 | 4-$CH_3O$Ph-CHO | 2 | 83 |
| 8 | 4-Tol-CHO | 1.5 | 90 |
| 9 | 4-ClPh-CHO | 2 | 88 |
| 10 | 3-$O_2N$Ph-CHO | 2.5 | 86 |
| 11 | 4-BrPh-CHO | 2 | 90 |
| 12 | Ph-$CH_2NH_2$ | 1.5 | 95 |
| 13 | 4-$CH_3O$Ph-$CH_2NH_2$ | 1 | 94 |
| 14 | 4-Tol-$CH_2NH_2$ | 1 | 96 |
| 15 | 4-ClPh-$CH_2NH_2$ | 2 | 87 |
| 16 | 3-$O_2N$Ph-$CH_2NH_2$ | 2.5 | 80 |

[a] Isolated yield.