

**A SIMPLE AND CONVENIENT METHOD FOR THE SYNTHESIS OF
NITRILES BY OXIDATION OF PRIMARY AMINES
WITH NaOCl IN ETHANOL**

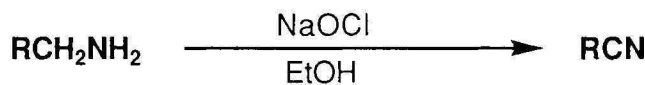
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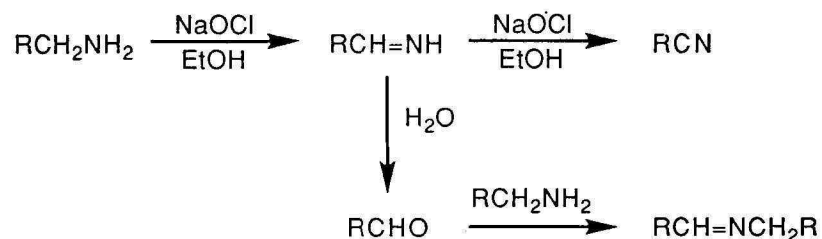
ABSTRACT: The oxidation of aliphatic primary amines having α -methylene on treatment with NaOCl as an oxidant in ethanol has been found to be an effective method for the transformation of primary amines to nitriles.

Selective transformation of functional groups of organic compounds is important in synthetic chemistry. A number of procedures exist for the oxidative transformation of amines to nitriles, although selective and efficient methods are rare. The metal oxidants such as nickel peroxide,¹ copper reagents,² silver reagents,³ cobalt oxide,⁴ and lead tetraacetate⁵ have been known as stoichiometric reagents for the oxidative transformation of amines to nitriles. The use of stoichiometric amount of metal reagents is undesirable from economical and environmental viewpoints. The catalytic oxidations using NiSO₄/K₂S₂O₈,⁶ RuCl₃/O₂,⁷ RuCl₃/K₂S₂O₈,⁸ and ruthenium complex/O₂⁹ have been also reported. Nitriles are also obtained by direct electrochemical oxidation¹⁰ or indirect electrochemical oxidations with mediators.¹¹

Here, we wish to report a simple and convenient method for the oxidation of primary amines to nitriles in good to excellent yields using NaOCl as an oxidant in ethanol.¹²



Benzylamine was smoothly converted to benzonitrile in 92 % yield with 2.2 molar amounts of NaOCl at room temperature within 15 min. A small amount of benzaldehyde and *N*-benzylidenebenzylamine were produced as the by-products. Benzaldehyde must be produced by hydrolysis of the intermediate benzaldimine, while *N*-benzylidenebenzylamine must be produced by condensation of benzaldehyde and benzylamine (Scheme). The use of 1 molar amount of NaOCl with the substrate amine gave a mixture of benzonitrile (18%), benzaldehyde (26%) and *N*-benzylidenebenzylamine (46%). The use of more than 2 molar amounts of NaOCl afforded benzonitrile predominantly. This is because the formation of nitrile from amine requires 2 molar amounts of oxidant as illustrated in Scheme.

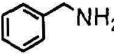

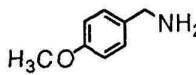
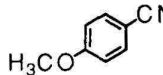
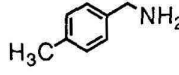
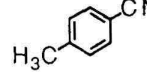
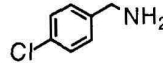
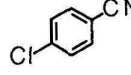
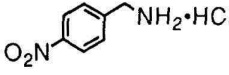
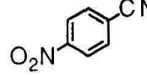
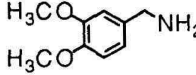
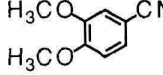
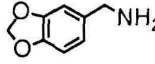
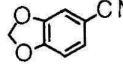
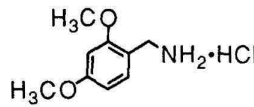
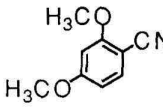
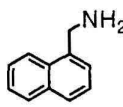
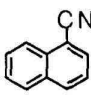
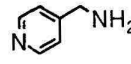



Scheme

Various substituted benzylamines were also converted to the corresponding benzonitriles in good to excellent yield. The results are summarized in Table 1. Not only the amines having electron donating substituents such as methoxy group but also the amines having electron withdrawing groups such as nitro group gave corresponding nitriles in good yields (Entries 2-8). In all cases, no amine remained, and the corresponding benzaldehydes and *N*-benzylidenebenzylamines were produced in a minor amount (generally trace amount to 2-3% by GC) as the by-products. 1-Naphthylmethylamine was oxidized to 1-cyanonaphthalene in 89% yield (Entry 9). 4-(Aminomethyl)pyridine was converted to 4-cyanopyridine in 73% yield at 0 °C (Entry 10).

Aliphatic primary amines were also converted to the corresponding nitriles (Table 2). Linear aliphatic amines such as octyl, decyl, and dodecylamine were smoothly oxidized to the corresponding nitriles in good yields (Entries 1-3). Hexamethylenediamine gave hexanedinitrile in 52% yield (Entry 5). No amine was observed with the use of 2.2 molar amounts of NaOCl. In these cases, the residues after distillation afforded complex GC peaks, which were not identified.







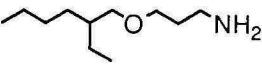
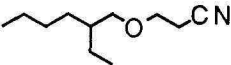
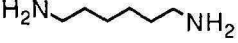
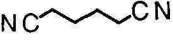
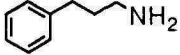
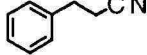
Table 1 Oxidation of Benzylamines with NaOCl in EtOH ^a

Entry	Amine	Nitrile	Yield / % ^b
1			92 ^c
2			80
3			81
4			85
5			72 ^d
6			97
7			95
8			89 ^d
9			89
10			73 ^e

^a Reaction conditions: amine (3.0 mmol), NaOCl (6.6 mmol), in EtOH (10 mL) at room temperature for 15 min. ^b Isolated yield by column chromatography.

^c Determined by GC. ^d NaOH (1 equivalent to amine) was added. ^e At 0°C.

Table 2 Oxidation of Primary Amines with NaOCl in EtOH ^a

Entry	Amine	Nitrile	Yield / % ^b
1			77
2			72
3			78
4			67
5			52
6			96 ^c

^a Reaction conditions: see Table 1. ^b Isolated yield by Kugelrohr distillation. The numbers in parenthesis are the yields determined by GC using internal standard.

^c Isolated yield by column chromatography.

The oxidation of 3-phenylpropylamine gave 3-phenylpropanenitrile in excellent yield (Entry 6). On the other hand, the oxidation of 2-phenylethylamine gave a complex mixture. This is because benzyl cyanide which must be the primary product of the oxidation of 2-phenylethylamine is unstable under the reaction conditions due to the acidity of its benzylic protons. Indeed, the reaction of benzyl cyanide under the same oxidation conditions showed similar GC peaks with that of the reaction mixture from 2-phenylethylamine.

The use of alcoholic solvent is essential for this transformation. Although methanol could be applicable for this reaction, ethanol gave better result than methanol.

In summary, oxidation of primary amines with NaOCl in ethanol provides a simple and convenient method for the transformation of primary amines to nitriles. Although other procedures exist for the oxidation of amines to nitriles, the simplicity and low cost of our procedure provide a practical alternative.

Experimental

Concentration of aqueous NaOCl used for the oxidation was 1-2 M.

A typical procedure is as follows: NaOCl (1.85 M, 3.6 mL, 6.6 mmol) was added to the stirring solution of 3,4-dimethoxybenzylamine (500 mg, 3.0 mmol) in ethanol (10 mL). The mixture was stirred at room temperature for 15 min (exothermic reaction). After the reaction, the reaction mixture was poured into water (50 mL), and was extracted with CH₂Cl₂ (10 mL x 3). The extract was washed with brine, dried over anhydrous Na₂SO₄, and then the solvent was distilled out under a reduced pressure. The obtained yellow oil was separated by silica-gel column chromatography (CH₂Cl₂ as an eluent). 3,4-Dimethoxybenzonitrile was obtained as colorless crystals (472 mg, 97%).

In the cases of Entries 5 and 8 of Table 1, amine and 1 molar amount of NaOH were dissolved in ethanol before the addition of NaOCl.

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