Nanocatalysts for conversion of aldehydes/alcohols/amines to nitriles: A review

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**ABSTRACT**

This review discussed the recent advances and developments on the applications of nanocatalysts in the synthesis of organic nitrile derivatives. The review is divided into three major sections. The first section will cover conversion of aldehydes into nitriles. The second focuses exclusively on conversion of alcohols into nitriles. The third will discuss conversion of amines into nitriles. Literature has been surveyed until the end of 2018.

**Keywords:**
Nanoparticles
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1. Introduction

Organic nitriles represent a versatile motif found in numerous natural products [1], pharmaceuticals [2], and dyes [3, 4]. Interestingly, more than 30 currently marketed drugs contain cyano group, while 20 more are in clinical trials (Figure 1) [5]. In addition, nitriles are one of the most important and versatile intermediates in organic synthesis.

Nitrile containing compounds were successfully transformed into many value-added chemicals including aldehydes, ketones, carboxylic acids, amines, amides, and 1,2,3-triazole derivatives [6-9]. Consequently, significant efforts have been devoted over the last few years in developing efficient synthetic routes to titled compounds. Recently, Yan, Zhang, and Wang published an interesting review paper that covers most of the recent advances in the synthesis of aryl nitrile compounds [10].

However, synthesis of these compounds through nano-sized metal-catalyzed reactions was completely omitted, while these synthetic strategies have recently attracted much attention because of their high efficiency and selectivity [11].

In connection of with our recent reviews in organic synthesis [12-14], we summarize here variety of protocols for the synthesis of organic nitriles catalyzed by metal nanoparticles. It should be mentioned that we have not discussed synthesis of arylnitriles through nano-sized metal-catalyzed cyanation of aryl halides, since it has recently been described in another publication [15].

The review is divided into three major sections. These include: nanocatalysts in conversion of (i) aldehydes; (ii) alcohols; and (ii) amines into nitriles.

2. From Aldehydes

2.1. Silver

In 2016, Das, Harsh, and Karak reported the synthesis of silver nanoparticles (AgNPs-Av) by treatment of silver nitrate with Aloe vera (Av) extract in the presence of poly(ethylene glycol) in water (eq. 1) [16]. The authors characterized the obtained nanoparticles by using various analyses such as UV–visible and FTIR spectroscopy and by UV–visible, FTIR, TEM, XRD, AFM, and EDX.

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The transmission electron microscope (TEM) images of AgNPs illustrated that the particles were spherical in shape with an average diameter of about 25-28 nm (Figure 2).

The synthesized nanoparticles were applied successfully as catalysts for the cyanation of aromatic aldehydes with potassium ferrocyanide (K₄[Fe(CN)₆]) in water at 50 °C (Scheme 1). Under optimized conditions, the reaction tolerated both electron-rich and electron-poor aldehydes and afforded the expected nitriles in good to excellent yields. Interestingly, the catalysts can be separated from the reaction mixture by centrifugation and reused four times with slight loss of their catalytic activity. It should be mentioned that the mechanism of this transformation is not clear.

\[ \text{CHO} + \text{K}_4[\text{Fe(CN)}_6] \rightarrow \text{CN} \]

\[ \text{Cu/RGO/Fe}_3\text{O}_4 \]

Euphorbia bungei Boiss as a reducing and stabilizing agent (Figure 3) [17]. According to the TEM images, Cu and Fe₃O₄ nanoparticles were homogeneously dispersed on the RGO sheets. The biosynthesized nanocomposite was employed for the synthesis of various aromatic and heteroaromatic nitriles via cyanation of the corresponding aldehydes with K₄[Fe(CN)₆] in the absence of any base and additive in refluxing water (Scheme 2). The author studied the reusability of the catalyst and found that it could easily be separated by an external magnet and reused for five reaction runs with no loss of catalytic performance.

\[ \text{Cu/RGO/Fe}_3\text{O}_4 \rightarrow \text{CN} \]

Recently, the same research team reported the in situ synthesis of copper nanoparticles (Cu NPs) via a simple, green and cost effective approach by using an aqueous extract of Plantago asiatica leaf as reductant, stabilizer, natural solvent and reaction biomedia [18]. The UV–Visible spectrum revealed that poly-phenolic compounds in the biomolecules had the most affinity for binding to Cu(II) through π-electrons interaction, and thereby reducing it to Cu(0) and forming of Pd NPs (Scheme 3). The TEM analysis showed that the prepared Cu NPs have a spherical shape with an average size of 7–35 nm. The Cu nanoparticles exhibited highly catalytic activity for the cyanation of (hetero)aryl aldehydes with K₄[Fe(CN)₆] at 80 °C for 30-60 min (Scheme 4). It is noted that the catalyst could be reused to several cycles with slight decrease in catalytic activity.

\[ \text{Cu/RGO/Fe}_3\text{O}_4 \]

2.2. Copper

In 2017, Nasrollahzadeh, Atarod, and Sajadi prepared Cu/reduced graphene oxide/Fe₃O₄ (Cu/RGO/Fe₃O₄) nanocomposite through a green approach by using aqueous extract of leaves of Plantago asiatica leaf.
Very recently, the group of Rai designed a novel cobalt-based photocatalyst [Co@g-C₃N₄] via treatment of graphitic carbon nitride (g-C₃N₄) with cobalt (II) acetate (Co(OAc)₂·4H₂O) in aqueous methanol at room temperature for 6 h, followed by centrifugation and washing with water and methanol [19]. TEM image of Co@g-C₃N₄ is shown in Figure 4. The catalytic activity of Co@g-C₃N₄ was tested for cyanation of aldehydes 11 with NH₂OH·HCl in binary solvent MeOH/H₂O with ratio 1:1 under white LED light irradiation. The expected nitriles 12 were isolated in excellent yields (Scheme 5). Other metal-doped g-C₃N₄ catalysts such as Ni@g-C₃N₄, Cu@g-C₃N₄, and Fe@g-C₃N₄ were also found to promote the reaction, albeit with reduced efficiencies. This photocatalyst could be recycled and reused more than five times without any significant loss of its activity. Furthermore, no significant change in morphology and surface of the catalyst was observed by scanning electron microscopy (SEM) image.

**Scheme 4.** Cu NPs-catalyzed cyanation of aromatic aldehydes 9 with R₃[Fe(CN)₆].

### 2.3. Cobalt

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**Scheme 4.** Cu NPs-catalyzed cyanation of aromatic aldehydes 9 with R₃[Fe(CN)₆].

### 2.4. Iron

In 2016, Ghosh and co-workers designed and synthesized a highly stable and active magnetically retrievable Fe nanocatalyst by coating of Fe₃O₄ NPs with cetyltrimethyl ammonium bromide (CTAB) [20]. The Fe₃O₄-CTAB NPs was employed as an efficient catalyst for the synthesis of nitriles 14 by combination of aldehydes 13 and NH₂OH·HCl in DMF under reflux condition. Various aromatic, heteroaromatic, vinylic as well as aliphatic aldehydes were effectively used to synthesize functionalized nitriles 14 in good to almost quantitative yields (Scheme 6). Beside high yields, simplicity, relatively less toxic nanocatalyst and broad substrate scope were other advantages of this synthetic strategy. The mechanism shown in Scheme 7 was proposed by the authors for Fe₃O₄-CTAB NPs catalyzed one-pot synthesis of nitriles from aldehydes and involves the initial formation of the intermediate A through the nucleophilic attack of hydroxylamine to the activated carbonyl carbon of aldehyde 13. Deprotonation of this intermediate gives the intermediate B, with undergoes dehydration to produce oxime intermediate C. Finally, elimination of a water molecule from this intermediate produces the observed nitriles 14.

**Scheme 5.** Co@g-C₃N₄ catalyzed cyanation of aldehydes 11 with NH₂OH·HCl.

R= aryl, heteroaryl, vinyl

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**Scheme 6.** Fe₃O₄-CTAB NPs catalyzed synthesis of nitriles 14 from aldehydes 13.

R= aryl, heteroaryl, vinyl, alkyl

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synthesis of several nitriles without sacrificing the yield or outcome of the methodology. Additionally, the catalyst could be reused for six reaction runs without a decrease in the catalytic activity and selectivity.

3. From Alcohols

3.1. Cobalt

In 2014, Jagadeesh, Junge, and Beller prepared a series of metal-based catalysts by pyrolysis of the respective metal acetate–phenanthroline complexes on Vulcan at 800 °C under argon [22]. The obtained materials were tested for their catalytic activity for the conversion of primary alcohol to corresponding nitriles in t-amyl alcohol under the oxygen atmosphere at 130 °C. Among the various pyrolyzed metal-phenanthroline materials; (CoO₂-NGr/C; Co-phenanthroline/C-800) was the most efficient as the catalyst. Examination of the scope of the reaction revealed that an array of aromatic, heterocyclic and aliphatic nitriles were successfully produced (Scheme 9). In general, a wide range of functional groups (e.g., F, Cl, NO₂, OH, SMe, SCF₃, SO₂N₂, OMe, COMe, CO₂Me) were tolerated under the optimized conditions. This made possible the further derivatization of the products. It is noted that the catalyst was successfully recycled and reused up to four times without significant deactivation.

Motivated by this work, in 2016, Gao and co-workers developed a novel mesoporous cobalt-coordinated nitrogen-doped carbon catalyst (meso-Co-N/C) catalyst via a four step procedure through coordination of bidppz (11,11’-bis(dipyrido[3,2-a;2’,3’-c]phenazinyl) with cobalt ions (Co(OAc)₄·4H₂O) and subsequent treatment with mesoporous silica SBA-15 as a hard template followed by pyrolyzation under flowing nitrogen with a heating ramp rate of 5 °C/min (700-900 °C) and finally removing of template by treatment with HF (10 wt.%) at room temperature (Figure 6) [23].

![Scheme 8. Fe₂O₃-N/C-catalyzed synthesis of nitriles 16 from aldehydes 15 and ammonia.](image)

![Fig. 5 Synthesis of nitrogen doped graphene activated nanoscale Fe₂O₃-particle supported on carbon (Fe₂O₃-N/C).](image)

![Diagram 1. The plausible mechanism for this amidation reaction is shown in Scheme 11.](image)

The catalyst, meso-Co-N/C was found to be an efficient catalyst in the synthesis of benzonitriles through aerobic amidation of corresponding benzyl alcohols with aqueous NH₃ in t-amyl alcohol at 130 °C (Scheme 10). It is notable that the catalyst can be separated from the final reaction mixture by centrifugation, washing with methanol, and calcination at 400 °C under N₂, and then be reused for at least five successive runs without a significant loss of its catalytic activity. The plausible mechanism for this amidation reaction is shown in Scheme 11. Recently, in a closely related investigation, Huang and co-workers also showed that various functionalized benzonitriles were formed in excellent yields from the corresponding benzyl alcohols through amidation with ammonia employing Co@NC(800-2) as catalyst in t-amyl alcohol as solvent and at 130 °C [24].
for 30 min followed by heating (80 °C) in the presence of NaOH for 12 h) [25]. TEM and SEM analyzes of the synthesized nanoparticles showed that rod shaped lanthanum hydroxides with average diameters of about 50 nm were attached with spherical shape magnetic nanoparticles with average diameters of about 20 nm (Figure 7). The magnetic saturation value (Ms) of the La(OH)₃/Fe₃O₄ is 62 emu/g and exhibit a ferromagnetic behavior at the room temperature. These results demonstrate that the nanoparticles possess magnetic properties and could be separate from the reaction mixture by applying an external magnetic field. The catalytic activity of La(OH)₃/Fe₃O₄ was tested for the oxidative synthesis of nitriles 22 directly from corresponding alcohols 21 with ammonia as nitrogen source and 1.4-dioxane as solvent under an oxygen balloon (Scheme 12). Various benzylid and heterobenzylid alcohols reacted well under the reaction conditions and afforded the corresponding nitriles in excellent yields. However, aliphatic alcohols failed to enter into this reaction.

3.3. Platinum

Very recently, an interesting platinum-catalyzed selective ammoxidation of benzylid alcohols 23 with gaseous ammonia to benzonitrile derivatives 24 was reported by Stahl et al [26]. The carbon-supported Pt nanoparticles/MeCN system was found to be optimal for this reaction, while addition of 1.4 mol% Bi(NO₃)₃ as an additive and 2.8 mol% of K₂CO₃ as a base gave excellent results (Scheme 13). Other Pt and mixed-metal catalysts on various supports such as Pt/Al₂O₃, Pt/SiO₂, PtCoₓ/GO, PtRuₓ₀.₂₅/GO were also found to promote this ammoxidation reaction albeit in lower yields. Unfortunately, the recovery and the recycling of the catalyst was not reported in this study. It should be mentioned that a gram-scale reaction was also successfully performed.

3.2. Lanthanum

In 2018, Ziaee, Gholizadeh, and Seyedi reported the synthesis of magnetically recoverable La(OH)₃/Fe₃O₄ nanoparticles by a facile sol–gel method (sonication of a mixture of Fe₂O₃ and LaCl₃·7H₂O in ethanol/water (1:1)
4. From Amine

Synthesis of nitriles through nano-sized metal-catalyzed oxidation of corresponding amines has been scarcely studied; in fact, only two examples of such reactions were reported in the literature. In 2014, Beller and co-workers reported the first protocol for the nano-metal-catalyzed oxidative conversion of primary amines to the structurally diverse nitriles using (Fe₂O₃/NGr@C) as a reusable and molecular oxygen as a green oxidant [27]. The schematic diagram for the preparation of Fe₂O₃/NGr@C-catalyst is shown in Figure 8. They showed that various aromatic, aliphatic and heterocyclic nitriles could also be synthesized in high to excellent yields through the direct oxidation of primary amines in the presence of a catalytic amount of Fe₂O₃/NGr@C (4 mol% Fe) and 0.5 equiv. of ammonia as an additive in t-amyl alcohol under an oxygen atmosphere (Scheme 14). It is noted that the presence of ammonia was crucial for the selectivity of the reaction. In the absence of NH₃, a mixture of secondary imine, aldehyde and the expected nitrile were formed.

Subsequently, the same research team found that Co₃O₄/NGr@C could also successfully catalyze conversion of primary amines into nitriles [28]. Like previous work, all kinds of structurally diverse aryl, heterocyclic, allylic and aliphatic nitriles were obtained in excellent yields using this highly stable catalyst. Some reported examples are shown in Scheme 15. The authors claimed that this catalyst could be reused at least four times without a decrease in the catalytic activity and selectivity.

Scheme 12. La(OH)₃/Fe₂O₃ NPs-catalyzed conversion of benzylic alcohols 21 into benzonitritiles 22.

Scheme 13. Pt NPs/C-catalyzed ammoxidation of benzylic alcohols 23 with gaseous ammonia developed by Stahl.

Scheme 14. Fe₂O₃/NGr@C-catalyzed oxidative conversion of primary amines 25 to nitriles 26.

allow for rapid conversion of structurally divers aldehydes, alcohols, and amines into corresponding nitriles under mild conditions, with the benefits of high product yield and high selectivity. Interestingly, these catalysts could also be easily separated from the reaction mixture and be used several times without obvious loss in their catalytic activity. We conclude this review by hoping that it will stimulate further research in this domain.

References

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