

수중에서 금속 촉매의 니트릴 수화 반응에 의한 환경친화적 아미드 합성

무하마드 아시프 후세인 · 김정원[†]

강원대학교 화학공학과
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Environmentally Friendly Synthesis of Amide by Metal-catalyzed Nitrile Hydration in Aqueous Medium

Muhammad Asif Hussain and Jung Won Kim[†]

Department of Chemical Engineering, Kangwon National University, 346 Joongang-ro, Samcheok, Gangwon-do, 245-711, Korea
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초 록

친환경적 조건에서의 니트릴의 수화 반응은 아미드를 생산하기 위한 가장 경제적이고 매력적인 방법이다. 고체 금속 산화물과 지지체를 이용한 전이 금속 촉매 시스템은 이러한 니트릴 수화 반응을 보다 향상시키기 위한 의미 있는 연구로써 수행되어져 왔다. 이들 촉매들의 중요한 특징은 방향족, 지방족, 이중 원자형, 지방족 고리형 등의 니트릴들을 포함하는 넓은 범위의 다양한 기질들에 적용된다는 것이다. 또한 이들은 높은 촉매적 활성을 유지하면서 여러 번의 재사용성이 가능하고 반응 후 그 혼합물로부터 분리가 용이하다는 장점들을 갖는다. 이 리뷰를 통하여 니트릴 수화 반응을 통한 아미드 합성에 적용되는 금속 산화물과 지지체를 가진 금속 촉매들에 대해 알아본다.

Abstract

Hydration of nitriles in the environmentally benign neutral conditions is the most economical and attractive way to produce amides. Substantial research works have been carried out to apply the solid metal oxides and transition metal supported catalytic systems to promote the hydration of nitriles. The most significant feature of these catalysts is the applicability to a wide range of substrates including aromatic, alicyclic, hetero-atomic, and aliphatic nitriles. These catalysts are also characterized by the easy isolation from the reaction mixture and the reusability while maintaining the high catalytic activity. This review accounts over the detailed survey of the metal oxide and solid supported metal catalysts for preparing amides from the hydration of nitriles.

Keywords: Hydration, nitrile, metal oxide, supported transition metal, catalyst

1. Introduction

Amide bond is one of the most prolific functional groups in the biological, pharmaceutical, and organic chemical industry[1,2]. The amide is the most essential part of life because it makes the peptide bonds in protein[3]. A lot of research has been carried out to synthesize the amide group. In general, amides are synthesized by activating the carboxylic acid and then coupling with the amines[4]. Although these systems have great applicability in industry, they are still struggling from the low efficiency and economically not acceptable because much amount of waste is produced during the reactions[5].

Over the past decades, the focus has been given to cut down the wastes and environmental pollutions to achieve the green chemistry protocols and to develop the environmentally benign synthesis processes[6]. There was no concern previously about the solvent as it has accounted the major part of any chemical reaction in pharmaceutical and fine chemical industry[7]. With the solvent issue, the ultimate solution is to replace the organic solvents with the water for its environmental impact, safety, availability, and cost[8]. In the more simple way, amides can be synthesized by the hydrations of nitriles with atomic economy. However, the conventional methods for hydration of nitriles use strong acidic/basic media and the reactions take place in harsh condition, unfavorable due to further hydrolysis to corresponding carboxylic acids and their incompatibility with various sensitive groups[9].

With these concerns, a considerable effort has been expanded to develop the new transition metal-catalyzed reactions based on heterogeneous protocols recently. These protocols proved to be very efficient

[†] Corresponding Author: Kangwon National University,
Department of Chemical Engineering, 346 Joongang-ro, Samcheok, Gangwon-do,
245-711, Korea
Tel: +82-33-570-6543 e-mail: jwemye@kangwon.ac.kr

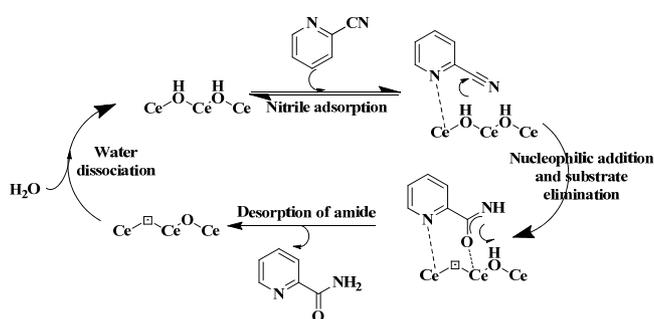


Figure 1. Proposed mechanism for the synthesis of amide from CeO_2 .

and have less environmental impact because isolation of the product and catalyst is very easy. The catalysts are also recyclable for many times without losing their reactivity significantly when they are used for the hydration of the nitriles to produce amides at relatively lower temperatures as compared to previous systems[10-15]. Therefore, the present mini review focuses on the heterogeneous solid oxides and supported transition metal systems to produce the amides under aqueous conditions.

2. Hydration of Nitriles to Amides

2.1. Hydration of nitriles with solid metal oxides

Metal oxides are very stable solid and have some acid-base properties which make them sometimes attractive for heterogeneous catalysis in the organic synthesis. Herein, we discuss few examples of oxides which have been used to synthesize the amide from the hydration of nitriles in the water and amidation from nitriles and amines. Cerium oxide (CeO_2) is one of the solid materials explored for the various organic reactions due to its acid-base and redox character. M. Tamura et al. described a very simple and heterogeneous ceria catalyst to synthesize the amides by hydration of nitrile in aqueous conditions. In the reaction mechanism they proposed that low coordinated CeO_2 sites act as Lewis acid sites and adjacent exposed oxygen atoms as Lewis base sites, which make this reaction to proceed very smoothly as shown in Figure 1[16,17]. They also studied the number of solid oxides for one-pot *N*-alkyl amides formation by the direct reactions of nitriles and amines in the water. Ceria provided the best results for other all oxides studied and gave the amides with very high yields and selectivities[18].

Roy et al. in another work elucidated the hydration process to synthesize the nicotinamide from 3-cyanopyridine with MnO_2 generated by a redox method and also decomposition of $\text{Mn}(\text{NO}_3)_2 \cdot x\text{H}_2\text{O}$. In their work they showed that MnO_2 generated by redox reaction had small particle size with large surface area, showed high catalytic activity[19]. ZrO_2 , TiO_2 and Nb_2O_5 were investigated for the formation of polyamide by the amidation of nitriles and amines[20].

2.2. Hydration of nitriles with metal supported Catalysts

The application of metal supported catalysts has brought great attention because of their activity towards organic reactions. In current, a

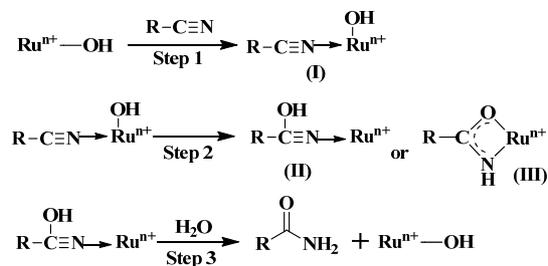


Figure 2. A plausible reaction mechanism to produce amides from nitriles by $\text{Ru}(\text{OH})_x/\text{Al}_2\text{O}_3$ catalyst.

considerable research has been carried out for development and application of ruthenium based catalysts to organic synthesis, owing to its rich coordination chemistry and comparatively cheaper than other palladium group metals. A comprehensive review was published by R. Garcia-Alvarez et al. which explains the application of ruthenium as homogeneous and heterogeneous catalyst for the synthesis of amides[21]. K. More et al. reported the oxidation of primary amines to nitriles with hydroxyapatite-bonded ruthenium complex and further they expanded the applicability of the system to synthesize the primary amides from hydration of nitriles. Although they tested hydration of very few substrates, the system proved to be facile to produce amide with high yield and selectivity under neutral conditions[22]. $\text{Ru}(\text{OH})_x/\text{Al}_2\text{O}_3$ allowed the hydration of the large variety of activated and unactivated nitriles to amides. The conversions and selectivities for the substrates were found to be 91 to > 99% with the selectivities almost 100% in every case. N. Mizuno et al. described a very simple way to isolate the amides from the reaction mixture and the catalyst was reusable for several turns. In their work they reported that reaction rate dependence on the water concentration was of the zero-order, while the dependence on nitrile concentration and amount of catalyst was of the first order. The Mizuno research group suggested the three steps reaction mechanism to catalyze the hydration of nitrile to amides (Figure 2). First step involves the coordination of nitrile substrate to produce intermediate product (I). In the following step hydroxide group attacks on nitrile attached carbon intramolecular, to give ruthenium iminolate (II) or ruthenium 2-amideate (III) species (Step II). In the third step, amide with the hydroxide ruthenium is formed by the ligand exchange between the species (II) or (III) and water[23].

Instead of solid oxides, some polymer resins have also been applied as solid supporting materials to impregnate the ruthenium at their surface. A microwave irradiated hydration of nitriles with supported ruthenium (0) poly styrene resin catalyst was described by S. Kumar et al.[12] and Nafion-Ru catalyst was investigated by G. K. Prakash et al. to synthesize the amide with water[24]. They proposed the reaction mechanism for the process of hydration over catalyst (Figure 3).

A polysaccharide, chitosan has been applied as support for ruthenium to get the amide under neutral conditions with microwave irradiation. Since microwave radiations have been applied to carry out the reaction, the catalyst could give the desirable products in very short time with excellent yields for wide variety of the substrates[10]. Magnetically separable particles have been emerged to use solid sup-

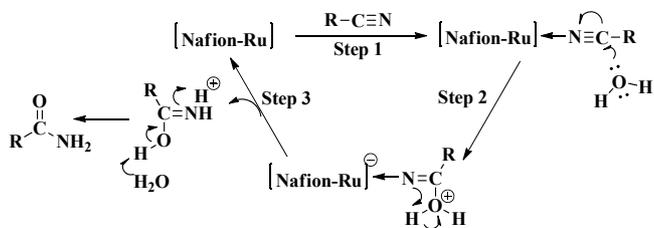


Figure 3. A proposed mechanism to catalyze the nitrile hydration by Nafion-Ru.

port for catalyst, owing to their easy isolation from the reaction mixture at reaction completion. V. polshettwar et al. reported the ruthenium hydroxide supported iron oxide catalyst, which demonstrated a very fast hydration of nitriles to amides and at the end product was easily decanted by collecting the catalyst on the side wall of the reactor tube with a magnet[14]. The Fe_3O_4 -supported silver catalyst was also investigated for the amide production in environmental benign reaction conditions[25]. In two different studies, the activity of silver supported on hydroxyapatite, and silica was estimated for the hydration of the various nitrile substrates[14,26]. These silver supported catalysts showed better catalytic activity for nitriles containing hetero-atoms as compared to benzylic and aliphatic ones contrary to usual behavior of these substrates, where the heteroatoms coordinate with the catalysts or some carboxylic acid is created due to further hydrolysis. Silver supported hydroxyapatite catalyst showed the turnover number (TON) over 10,000, which considered to be the highest value ever reported for the hydration of cyanopyrazine[13]. Moreover, the kinetic studies of the silver supported silica catalyst revealed that surface adsorbed oxygen is indispensable for the hydration of the nitriles to amides as shown in the reaction mechanism (Figure 4(a))[26]. In the similar way, K. Shimizu et al. too observed that surface adsorbed oxygen (O_{ad}) play a major role in the hydration of nitriles with Pd supported carbon catalyst as shown in Figure 4(b)[15]. This system is bifunctional catalytic system, where metal center plays as Lewis acid which activates nitrile molecule, while O_{ad} plays the role of Brønsted base to produce the nucleophile OH-group by breaking the water through hydrogen bonding finally getting the amide by ligand exchange[15].

3. Conclusion

The development of transition and rare earth metals in catalytic systems has opened the doors to synthesize the amides from hydration of nitriles following the green chemistry footsteps. Especially metal supported catalysts have been explored extensively due to their prominent advantages of separation from reaction mixture, reusability, and cost effectiveness as compared to their homogeneous counterparts. Much effort has been made to elaborate the contribution of the solid metal oxides and supported metal catalysts for the amide synthesis in aqueous medium. Metal oxide type such as CeO_2 showed high selectivity and conversion for hydration of nitriles to the corresponding amides as well as MnO_2 catalyst for obtaining the nicotinamide. Several supported metals (Ru and Pd) have an excellent catalytic activity for aromatic,

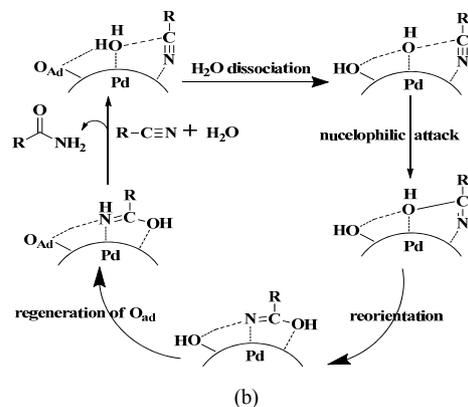
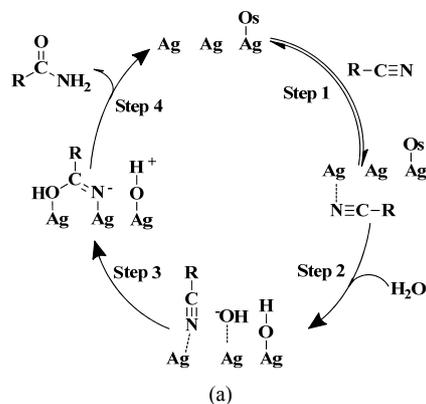


Figure 4. (a) Plausible mechanism to hydrolyze nitrile to amide with Ag/SiO_2 , (b) A catalytic cycle for the hydration of nitriles with Pd nanoparticle supported catalyst.

aliphatic, and alicyclic nitrile hydrations. Most of hydration systems do not fit for the hetero-atomic substrates because of the coordination of active sites with hetero-atoms. But the silver supported hydroxyapatite catalyst showed the highest catalytic performance for nitrile containing hetero-atoms with over 10,000 TON. These metal oxides and supported metal catalysts were very efficient and worked well for several times to hydrolyze the nitriles without losing their catalytic activity significantly. We hope this review article will help researcher to get an ample view about the hydration of nitriles to amides with solid metal oxides and solid supported metal catalysts.

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