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Ruthenium on chitosan: A recyclable heterogeneous catalyst for aqueous hydration of nitriles to amides

R. B. Nasir Baig, Mallikarjuna N. Nadagouda and Rajender S. Varma*

Abstract

Ruthenium has been immobilized over chitosan by simply stirring an aqueous suspension of chitosan in water with ruthenium chloride and has been utilized for the oxidation of nitriles to amides; the hydration of nitriles occurs in high yield and excellent selectivity, which proceeds exclusively in aqueous medium under neutral conditions.

In view of the growing consciousness about the environmental issues, tremendous efforts have been expanded towards the development of new chemical processes that minimize pollution in the synthesis processes. In the catalysis arena, heterogeneous catalysis addresses these challenges and is a prime choice due to ease of catalyst removal, recovery and recycling.[1] The focus, more often, has been on the heterogeneous system developed by the immobilization of active metallic species over inorganic material such as silica and alumina.[2] The petrochemical derived polymer such as polystyrene has also been utilized as a support for the immobilization of transition metals.[3] Thrust for the cleaner and sustainable chemistry has resulted in the shift from petrochemical-based entities to biorenewable materials. There are several reasons to exploit abundant natural polymer macrostructures, and in particular those of polysaccharide origin, to create high-performance and environmentally benign catalysts as they have several functional groups for metal anchoring. They are chemically stable yet can be degraded biologically; an attribute that renders their use as polymeric supports for catalysis all the more attractive. Although there has been a global recognition that natural polysaccharides can be used as feedstocks for the production of large-scale consumer goods, their use as supports for heterogeneous catalysis is also on the rise.[4a] Chitosan is an important amino-polysaccharide used for the catalytic applications and is usually chemically modified for its role as a catalyst support.[4] Chitosan has been useful for the removal of transition metal from it aqueous mixture without any modification of its back bone.[5] A simple experiment to extract ruthenium nano particles from aqueous mixture using chitosan was inspiring as ruthenium could be easily extracted from aqueous solutions with efficiency greater than 99.9%. This prompted us to use the unmodified chitosan as heterogeneous support for the catalytic application in organic synthesis. The hydration of nitriles to amides is an important transformation in the pharmaceutical industry.[6] It has been conventionally achieved using acids and bases, enzymes,[7] and transition metals.[8] However, under these conditions, various by-products, notably carboxylic acids, are

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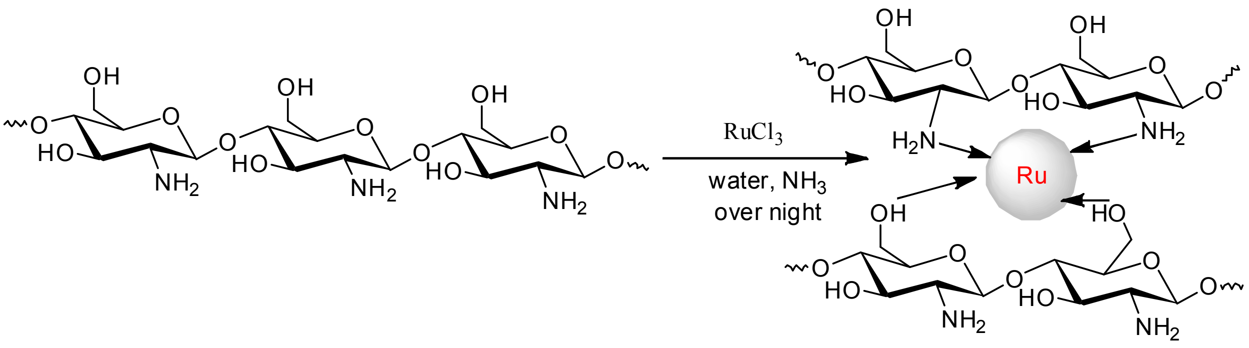
generated by the hydrolysis of the starting nitriles and as well as amides. Several protocols, which predominantly use homogeneous metal complexes, have been reported for the hydration of nitriles.[9] These methods suffer from various drawbacks, especially the difficulty in separation of product and catalyst from the reaction mixture, as well as the use of an inert atmosphere for handling air-sensitive metal catalysts. Many sensitive functional groups do not withstand such harsh conditions, which consequently decrease the selectivity of the reaction protocol.

Heterogeneous catalyst has been utilized, such as alumina,[10] potassium fluoride doped Al_2O_3[11] and phosphates,[12] silica supported manganese oxides,[13] modified hydroxyapatite,[14] and ruthenium hydroxide coated on alumina and ferrites.[15] However, turnover numbers of these protocols are still low and the reusability of the catalyst is difficult. Cadierno and coworkers developed an excellent hydration protocol in pure water under neutral conditions.[16] Although this work paved the way for the advancement of the hydration reaction in aqueous medium, the protocol still needs traditional workup, using organic solvents to isolate the product and exotic ruthenium complexes as catalysts. The magnetically supported ruthenium catalyst works well for the aqueous hydration of nitriles.[17] However, they involve tedious synthesis of magnetic support following by immobilization of ruthenium metal. In our quest for the development of benign and sustainable pathways for organic synthesis,[18] herein, we report the utility of heterogeneous, biodegradable, and reusable chitosan-Ru (ChRu) catalyst for the aqueous hydration of nitrile to amides.

Result and discussion

The first step in the accomplishment of this goal was the immobilization of ruthenium (Ru) over chitosan (Scheme 1). The catalyst was prepared by suspending chitosan in the aqueous mixture of ruthenium chloride overnight at pH, 9 (adjusted using 25% of ammonia). Material with Ru on chitosan was separated using a centrifuge, dried under vacuum at 50 ^{o}C for 12 hours and the ensuing catalyst characterized by SEM (Fig.1 a) and using X-ray diffraction (XRD) (Fig 1b); the signals pertaining to Ru metal were not detected in XRD, possibly due to complexation with chitosan or its low percentage. However, the presence of Ru-metal has been confirmed by Energy Dispersive X-ray Spectroscopy (EDS, Figure 2). XPS analysis of ChRu is performed to analyze the oxidation state of Ru metal.; the binding energy peak for Ru $3d_{5/2}$ at 282.5 eV is in good accordances with Ru(III) (XPS, Figure 3). The weight percentage of Ru was found to be 6.41 % by inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis.



Scheme 1 Synthesis of Chitosan-Ru (ChRu) catalyst

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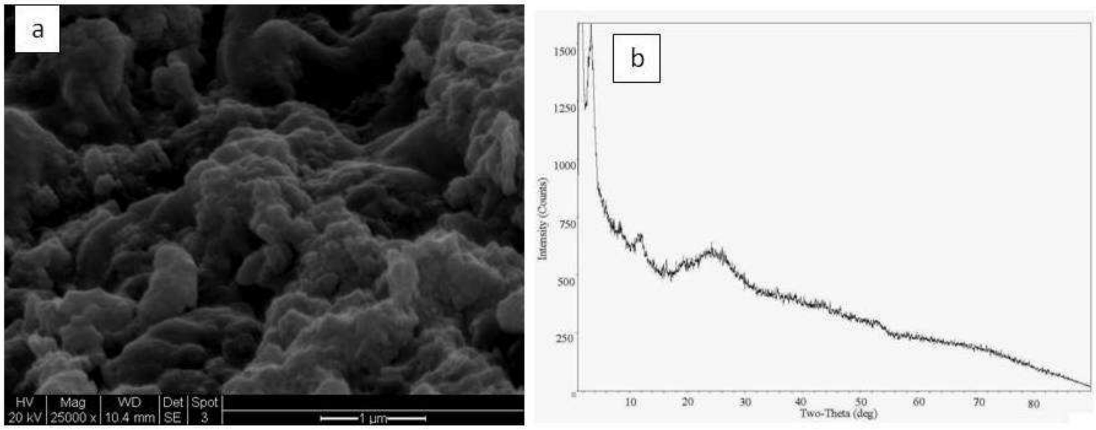

Figure 1 a) SEM image of ChRu Catalyst ; b) X-ray diffraction (XRD) of ChRu

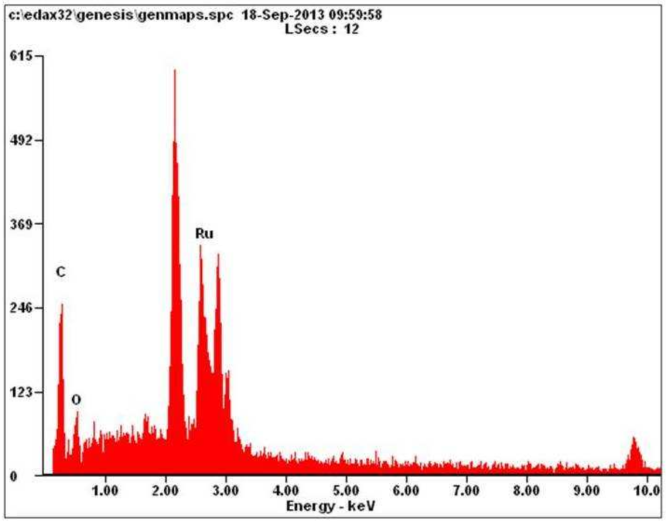

Figure 2 Energy Dispersive Spectra (EDS) of ChRu catalyst

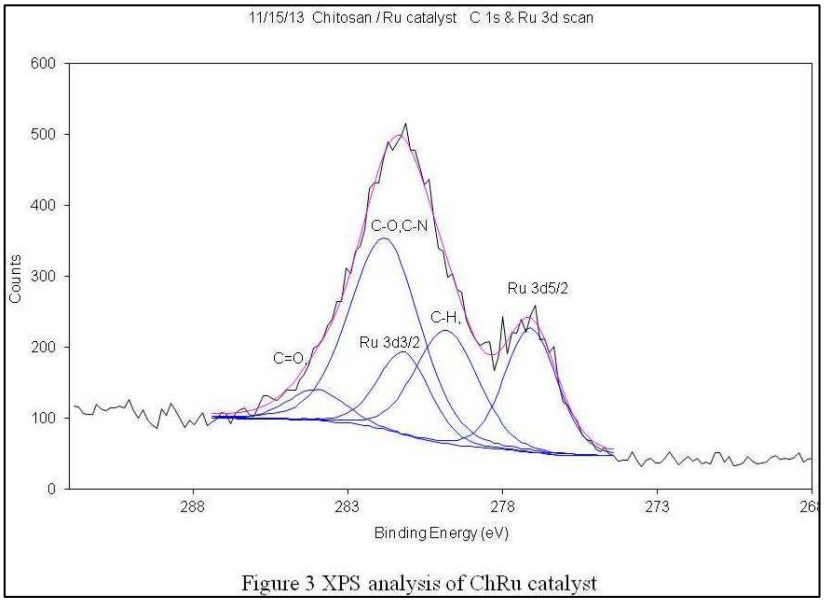

Figure 3 XPS analysis of ChRu catalyst

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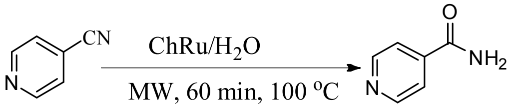
The utility of chitosan supported ruthenium catalyst (ChRu) was then explored in a heterogeneous catalyzed hydration of nitriles in benign aqueous medium under microwave (MW) irradiation conditions (**Scheme 2**). The salient feature of MW-assisted heating is due to the efficiency of the interaction of polar ChRu-catalysts as well as water molecules with microwaves; the reaction mixture is rapidly heated under MW irradiation with the precise control of the reaction temperature.[19] Initially, experiments were performed to optimize the aqueous reaction conditions for the hydration of 4-pyridinecarbonitrile as a substrate (Table 1).



Scheme 2 ChRu-catalyzed hydration of nitriles

Table 1 Optimization of reaction conditions[a]

Entry	Catalyst	Time	Temperature (°C)	Yield[b]
1	Chitosan	30 min	100	-
2	Chitosan	60 min	100	-
3	Chitosan	60 min	120	-
4	ChRu	25 min	100	<30%
5	ChRu	60 min	120	>99%
6	ChRu	12 h	100	trace[c]
7	ChRu	3 h	120	>74.4%[d]

a) Reactions were carried out with 1 mmol of4-pyridinecarbonitrile, 25 mg ChRu-catalyst, in water under MW irradiation; b) Reaction was monitored by GCMS; c) Reaction performed under conventional heating; d) ChRu catalyst with 3.98% Ru loading was used.

First, the reaction was conducted using pure chitosan. The hydration reaction did not proceed at 100 °C or at 120 °C even after 60 min of MW exposure (Table 1, entries 1-3). The chitosan was modified using $RuCl_3$, termed chitosan ruthenium-catalyst **ChRu (Scheme 1)**, and tested for the hydration of 4-pyridinecarbonitrile with **ChRu** at 100 °C for 25 min under MW irradiation. The low conversion of nitrile to amide (monitored by GC-MS) was observed (Table 1, entry 4). However, MW exposure for 60 min at 120 °C leads to the quantitative conversion to the corresponding amide (Table 1, entry 5). However, refluxing the reaction mixture for 12 h under conventional heating resulted in the trace amount of conversion (Table 1 entry 6). Lowering the catalytic loading of Ru metal reduced its catalytic performance. Oxidation of 4-pyridinecarbonitrile to corresponding amide, using 3.98% of ChRu catalyst, did not complete even after 3 h of MW (Table 1, entry 7).

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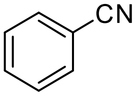
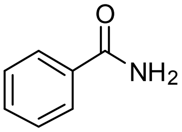
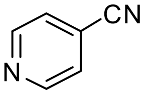
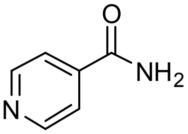
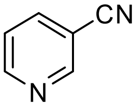
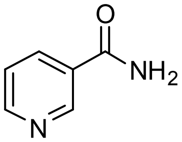
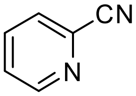
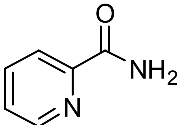
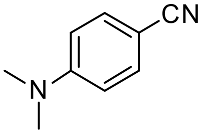
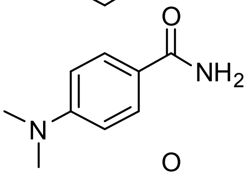
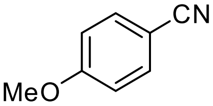
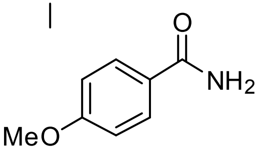
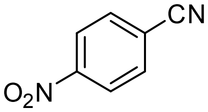
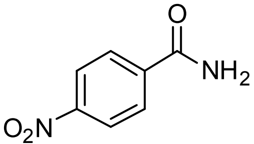
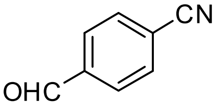
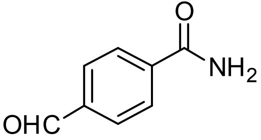
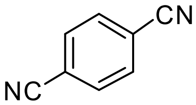
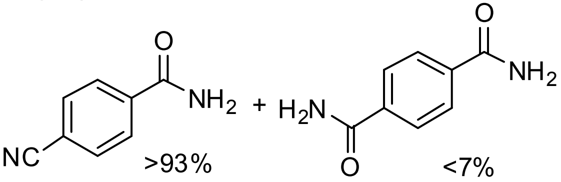
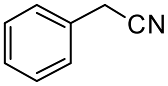
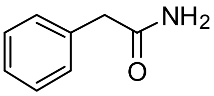
Table 2 Hydration of nitriles catalyzed by ChRu-catalyst[a]

Entry	Substrate	Time	Product	Conversion[b, c]
1		60 min		>99% (89%)
2		60 min		>99% (91%)
3		60 min		>99% (88%)
4		60 min		>99%(88%)
5		75 min		>99% (85%)
6		75 min		>99% (84%)
7		60 min		>99% (85%)
8		60 min		>99% (90%)
9		60 min		
10		90 min		>99% (81%)

a) Reactions were carried out with 1 mmol of nitrile, 25 mg (0.015 mol %) nanocatalyst, in water under MW irradiation; b) Reactions were monitored by GCMS; c) Yield in parentheses represents the isolated yield.

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Using the above-optimized conditions, the scope of chitosan ruthenium-catalyst **ChRu** was then explored for the hydration of a variety of nitriles (Table 2). The catalyst displayed high activity for hydration of activated, inactivated, aliphatic, and heterocyclic nitriles in pure water including a variety of benzonitriles derivatives (Table 2, entries 1 & 9) as well as aliphatic nitriles (Table 2, entries 10) that were smoothly hydrated to the corresponding amides in excellent yield. The rates were slightly influenced by the electronic effects of the substituent's on the aromatic ring of the benzonitriles. Electron donating substituent (Me_2N-, -OMe, Table 2, entry 5 and 6) required little longer time (75 min) for the completion of reaction whereas in case of electron withdrawing substituent (-NO_2, -CN, -CHO, Table 2, entry 7-9) full conversion was observed within 60 min of MW exposure. It was interesting to observe that the selective oxidation of 4-formylbenzonitrile to corresponding amide could be performed without oxidation of the formyl group (Table 2, entry 8). The hydration of 1,4 dicyano benzene was time dependent (Table 2 entry 9); 60 min exposure to MW at 120 ^oC leads to the selective formation of the monohydrated derivative (93%, Table 2 entry 9) whereas exposure for longer time (3 h) resulted in the dihydration of 1,4 dicyano benzene to terephthalamide in quantitative yield.

The separation and recovery of the catalyst is an important step in the synthesis of fine chemicals, which is generally performed either by centrifuge or by filtration with reduced efficiency. In this catalytic system, most of the time catalyst was recovered by simply decantation or centrifuge. Upon completion of the reaction, the mixture turned clear and the catalyst deposited at the bottom, which can be easily separated from reaction mixture by simple decantation or using a centrifuge. After the removal of the catalyst, pure crystals of amides usually appeared in the aqueous layer, which are isolated from the water medium. Thus, synthesis and purification can be carried out in a benign aqueous medium, without the use of organic solvents.

The lifetime of the catalyst and its level of reusability are important considerations for practical application. To clarify this issue, a set of experiments for the hydration of 4-pyridinecarbonitrile using the **ChRu**-catalyst were established. After the completion of the first reaction to afford the corresponding amide, the catalyst was recovered, washed with acetone, and dried at 50 ^oC. A new reaction was then performed with fresh 4-pyridinecarbonitrile under the same conditions. The chitosan supported ruthenium catalyst **ChRu** could be used at least three times without any change in the activity (ESI, Table 1).

Metal leaching was studied by ICP-AES analysis of the catalyst before and after the three reactions. The Ru concentration was found to be 6.41% before the reaction and 6.36 % after the reaction. The TEM image of the catalyst taken after the third cycle of the reaction did not show significant change in the morphology of the catalyst (ESI, Fig. 1 and EDS Fig 2), which indicates the retention of the catalytic activity after recycling. No Ru metal was detected in the reaction solvent (water) after completion of the reaction. This confirms the fact the chitosan held the Ru metal very tightly thus retaining the integrity of the catalyst, minimizing metal leaching, and facilitating efficient catalyst recycling.

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Conclusion

We have developed a novel biopolymer chitosan supported ruthenium catalyst, which can be readily prepared in large scale at ambient condition in aqueous media. The chitosan-ruthenium catalyst catalyzed the hydration of nitriles with high yield and excellent selectivity, which proceeds exclusively in aqueous medium under neutral conditions. After the completion of the reaction, the catalyst could be recovered and reused without affecting the reactivity.

Experimental Section:

Experimental procedure for synthesis of chitosan ruthenium catalyst (ChRu):

Chitosan (3 g, medium molecular weight, Aldrich, CSA # 9012-76-4) was suspended in 100 mL of water. To this suspension, 500 mg of $RuCl_3.3H_2O$ was added, pH, 9 was adjusted using 25% ammonia and stirring was continued overnight. The catalyst was separated using centrifuge (5000 rpm 5 min), dried under vacuum at 50 ^oC. The catalyst was characterized by SEM (Fig.1 a, MS) and using X-ray diffraction (XRD) (Fig 1b, MS). The signals pertaining to ruthenium metal were not detected in XRD; it may be due to complexation with chitosan or low percentage. The weight percentage of ruthenium was found to be 6.41 % by inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis.

Hydration of nitriles to amides

Nitriles (1.0 mmol), and ChRu (25 mg, 0.015, mol %) were placed in a crimp-sealed thick-walled glass tube equipped with a pressure sensor and a magnetic stirrer. Water (5 mL) was added to the reaction mixture. The reaction tube was placed inside the cavity of a CEM Discover focused microwave synthesis system, operated at 120 ^oC (temperature monitored by a built-in infrared sensor), 100 Watts for 60 min-90 min. After completion of the reaction, the catalyst was removed from reaction mixture using a centrifuge. Hydration of nitriles has been monitored using GCMS. The clear liquid was cooled slowly; most of the time analytically pure crystals of corresponding amide were obtained which can be isolated from water medium by simple decantation.

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Ruthenium on chitosan: A recyclable heterogeneous catalyst for aqueous hydration of nitriles to amides

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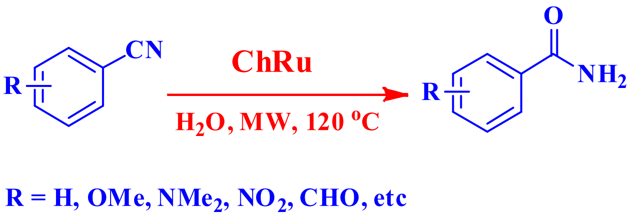
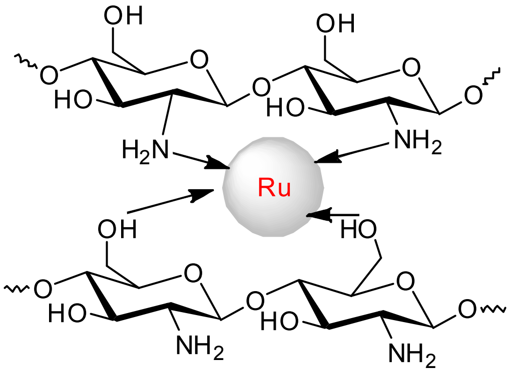
Ruthenium has been immobilized over chitosan by simply stirring an aqueous suspension of chitosan in water with ruthenium chloride and utilized for the oxidation of nitriles to amides; the hydration of nitriles occurs in high yield and excellent selectivity which proceeds exclusively in aqueous medium under neutral conditions.





Chitosan-Ru (ChRu) catalyst