Accepted Manuscript

Title: Cellulose matrix embedded copper decorated magnetic bionanocomposite as a green catalyst in the synthesis of dihydropyridines and polyhydroquinolines



PII: DOI: Reference: S0144-8617(18)31515-7 https://doi.org/10.1016/j.carbpol.2018.12.069 CARP 14423

To appear in:

Received date:20 August 2018Revised date:2 December 2018Accepted date:21 December 2018

Please cite this article as: Maleki A, Eskandarpour V, Rahimi J, Hamidi N, Cellulose matrix embedded copper decorated magnetic bionanocomposite as a green catalyst in the synthesis of dihydropyridines and polyhydroquinolines, *Carbohydrate Polymers* (2018), https://doi.org/10.1016/j.carbpol.2018.12.069

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Cellulose matrix embedded copper decorated magnetic bionanocomposite as a green catalyst in the synthesis of dihydropyridines and polyhydroquinolines

Ali Maleki,* Vahid Eskandarpour, Jamal Rahimi and Negar Hamidi

Catalysts and Organic Synthesis Research Laboratory, Department of Chemistry, Iran University of Science and Technology, Tehran 16846-13114, Iran

* Corresponding author. Tel.: +98 21 77240540; fax: +98 21 73021584. E-mail address: maleki@iust.ac.ir (A. Maleki).

Graphical abstract



Highlights

- *In-situ* preparation and facile modification of a cellulose-based bimetallic nanocomposite.
- Efficient catalytic usage in two important one-pot organic condensation reactions in high yields using simple and readily accessible precursors under solvent-free conditions at room temperature.
- Thermal stability and leaching-free character of the nanocatalyst during the organic reactions enabled sustainability and reusability for several runs.

- Narrow size and uniform distribution of Cu and γ-Fe₂O₃ nanoparticles obtained on cellulose biomatrix in green bionanostructure.
- Short reaction times, simple work-up procedure, high atom economy, high yields and environmentally-benign conditions.

Abstract

A new biopolymer-based magnetic nanocomposite was prepared and characterized by Fourier transform infrared (FT-IR) spectroscopy, energydispersive X-ray (EDX) analysis, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) images, inductivelycoupled plasma atomic emission spectroscopy (ICP-AES) analysis, thermogravimetric/differential thermal (TG/DT) analysis and atomic force microscopy (AFM) image analysis. Then, it was applied as an efficient heterogeneous catalyst in two important three- and four-component one-pot organic condensation reactions for the synthesis of Hantzsch 1,4-dihydropyridine and polyhydroquinoline derivatives in high yields under solvent-free condition at room temperature. The first design and development of a low-leaching bionanostructure, easy separation and reusability of the nanocatalyst, simple work-up procedure, mild, green and environmentally friendly conditions are some important features and advantages of the present work.

Keywords: Biopolymer; Cellulose; Green chemistry; Composite nanocatalyst; Dihydropyridine.

1. Introduction

Carbohydrate polymers due to their natural sources are one of the most interesting substrates for the nanocomposite synthesize (Baran, Baran & Menteş, 2018; Baran, 2018). Cellulose is one of the most available natural polymers on the earth. It is a fibrous and resistant biopolymer consists of monomers joined together by glycosidic oxygen bridges. The repeating unit of this natural polymer is a dimer of glucose, known as cellobiose (Habibi, Lucia, & Rojas, 2010; Klemm et al., 2005). Various advantages of cellulose such as biocompatibility, low toxicity and abundant resources make this polysaccharide as a perfect surface for catalyst preparation. However, cellulose is not soluble in usual solvents and the need for new compounds and appropriate methods to increase the solubility of these polymers should be considered. Forasmuch as, cellulose fibers also have some disadvantages such as moisture absorption, quality variations, low thermal stability, and poor compatibility with the hydrophobic polymer matrix.

Due to the attractiveness of metal nanoparticles in applications such as electronics, optics materials, sensors, biomedicine and catalytic applications. Synthesis of metal and metal oxide nanoparticles in the presence of stabilizing polymers have been intensively developed in the recent years and natural polymers like cellulose due to the mentioned benefits are the best polymer for this purpose and it can be used for biomedical applications (Baran, Baran & Menteş, 2018; Spiridonov et al., 2017). In addition to usual properties of nanoparticles such as high activity level and easy preparation, magnetic nanoparticles are superior to other nanoparticles due to their simple separation from the reaction mixture by an external magnet. The most important known magnetic nanoparticles are Fe₃O₄ and γ -Fe₂O₃. FeO-Fe₂O₃ magnetite, tends to react with oxygen and finally forming non-magnetic oxide/hydroxide iron compounds. Conversely, γ -Fe₂O₃ magnetite is chemically stable (Spiridonov et al., 2017)

Easy recovery of magnetic nanocomposites has made them an excellent choice for the catalysis of organic reactions. A technically possible method for the recycling catalyst is immobilization of the catalytically-active species on the surface of magnetic metal nanoparticles which can be separated from the reaction system by applying an appropriate magnetic field. Moreover, nanocomposites of natural biopolymers have special significance, because of their environmentally-friendly behavior and green chemistry properties.

Multicomponent reactions (MCRs) are one-pot reactions in which three or more than three raw materials react with each other to form a product incorporating essentially all of the starting materials (Zhu, & Bienaymé, 2005; Gunawan et al., 2012; Gunawan et al., 2010; Dömling, Wang & Wang, 2012; Hulme, et al., 1998; Orru, & Greef, 2003). MCRs have opened a revolutionary option in the field of designing methods to create chemical libraries of biologically active compounds (Zhu, & Bienaymé, 2005; Gunawan et al., 2012; Gunawan et al., 2012; Gunawan et al., 2010; Dömling, Wang & Wang, 2012; Hulme, et al., 1998; Orru, & Greef, 2003).

Hantzsch 1,4-dihydropyridines were one of the first heterocyclic compounds that were synthesized via MCRs. They include various medicinal, biological and pharmacological properties such as calcium channel blockers (David, 2007), antitumor (Boer, & Gekeler, 1995), anti-inflammatory (Briukhanov, 1994; Bahekar, & Shinde, 2002) and analgesic (Gullapalli, & Ramarao, 2002) activities. Today, several medicinally important drugs from these class compounds are used. For example: Amlodipine, Nimodipi, Diludine

and Felodipine are driven from these compounds (Bossert, Mayer, & Wehinger, 1981; Gilpin, & Pachla, 1999; Cosconati, et al., 2007) (Fig. 1a).

Due to chemical and biological significance of 1,4-dihydropyridines and polyhydroquinolines, several methods have been reported for the synthesis of their derivatives. The classical Hantzsch's method for the synthesis of 1,4-dihydropyridines is a one-pot condensation reaction of aldehydes with ethyl acetoacetate and ammonia under vigorous conditions (Love, & Snader, 1965). A few methods have been developed to modify the reaction conditions. For instance: conventional heating (Sainani, & Shah, 1994; Sufirez et al., 1999), solar thermal energy (Mekheimer, Hameed, & Sadek, 2008), ionic liquids (Ji et al., 2004; Zhang et al., 2006), metal triflates (Wang et al., 2005; Donelson, Gibbs, & De, 2006), cerium(IV) ammonium nitrate (Reddy, & Raghu, 2008), silica perchloric acid (Maheswara et al., 2006), microwave and ultrasound irradiations (Li et al., 2008; Tu et al., 2001) and Fe₃O₄ magnetic catalyst (Nasr-Esfahani et al., 2014). But, most of them are suffering from various drawbacks such as harsh reaction conditions, expensive catalysts and tedious work-up procedures. Therefore, design and development of new approches for this reaction is of prime importance.

In connection with our previous works on design and development of green protocols, nanocatalysts, biopolymer-based nanocomposite and MCRs (Maleki, Jafari, & Yousefi, 2017; Maleki, Firouzi-Haji, & Hajizadeh, 2018; Maleki et al., 2018; Maleki, A & Paydar, R, 2016; Maleki, & Sarvary, 2015; Maleki, Movahed, & Paydar, 2016; Maleki, Movahed, & Ravaghi, 2017), herein, we are hopefully introducing a new cellulose-based nanocomposite and an efficient approach for the synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives starting from simple and readily accessible of starting materials. Biopolymer-based bimetallic bionanocomposite was prepared *via in situ* synthesis of maghemite (γ -Fe₂O₃) and immobilization of Cu on cellulose. We used this novel nanocomposite for the synthesis of 1,4-dihyropyridines **5a-i** and polyhydroquinolines **6a-s** under solvent-free conditions at room temperature. It showed superb catalytic activity in the organic synthesis (Fig. 1b).



2. Experimental

2.1. General

All solvents, chemicals and reagents were purchased from Merck, Fluka and Aldrich chemical companies. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. FT-IR spectra were recorded as KBr pellets on a Shimadzu FT-IR-8400S spectrometer. Analytical TLC was carried out using Merck 0.2 mm silica gel 60 F-254 Al-plates. NMR spectra were recorded on Bruker DRX-300 Avance spectrometer. The morphology of the nanocatalyst was studied by scanning electron microscopy (SEM, Zeiss-Sigma VP) on gold coated samples. TEM images were obtained on a Zeiss-EM10C-100KV instrument. EDX analysis was recorded on Numerix DXP-X10P. ICP-OES were taken by Shimadzu ICPS-7000 model. TGA/DTA were measured by an STA504. The shell surface was mounted on the AFM stage and the Triboscope recording unit with transducers and leveling device was placed on the top of a NanoScope III E 164 | 164 mm² XY piezo scan base.

2.2. Preparation of γ -Fe₂O₃/Cu@cellulose

A solution of NaOH, urea and H₂O was prepared with material with the ratio of 7:12:81, respectively. Then, its temperature was cooled to -12 $^{\circ}$ C by ice and salt. 4.0 g of microcrystaline cellulose dissolved in it to form a homogeneous solution. Then, 0.5 g of FeCl₂ and 1.0 g of FeCl₃ were dissolved in 50 mL of deionized water was added dropwise into the cellulose mixture with vigorous stirring during 6 h. As a result, γ -Fe₂O₃ nanoparticles were synthesized on cellulose fibers *via in-situ* co-precipitation method. The next step includes CuSO₄.4H₂O solution (1 g CuSO₄.4H₂O dissolved in 20 mL H₂O)adding dropwise to the mixture. Due to the presence of γ -Fe₂O₃ oxidizing nanoparticles, after the addition of copper sulfate, Cu²⁺ can not be reduced to Cu. The final mixture was stirred for 2 h. Finally, the mixture was filtered and washed with H₂O (3×50 mL) and ethanol (3×50 mL) and dried at room temperature to yield the nanocomposite.

2.3. General procedure for the synthesis of 1,4-dihydropyridine derivatives 5a-i

A mixture of ethylacetoacetate (2.0 mmol), 4-chloro-benzaldehyde (1.0 mmol) and ammonium acetate (2.0 mmol) was vigorously stirred in a 5-mL round bottom flask in the presence of γ -Fe₂O₃/Cu@cellulose (3 mg) under solvent-free conditions at room temperature. The progress of the reaction was monitored by TLC (ethyl acetate/*n*-hexane 1/3). After completion of the reaction, the catalyst was removed easily by an external magnet and the residual product was collected by filtration and washed with ethanol and recrystallized to yield pure products. The recycled magnetic nanocomposite was washed, dried and re-used several times in subsequent reactions without further treatments.

2.4. General procedure for synthesis of polyhydroquinoline derivatives 6a-s

At first, 3 mg of γ -Fe₂O₃/Cu@cellulose nanobiocomposite was added to the mixture of an aromatic aldehyde (1.0 mmol), 1,3-cyclohexandione or dimedone (1.0 mmol), ethylacetoacetate (1.0 mmol) and ammonium acetate (2.0 mmol) in a 5-mL round bottom flask. Then, the mixture was homogenized and stirred at room temperature for 20 min. The progress of the reaction was monitored by TLC (ethyl acetate/n-hexane 1/3). After completion of the reaction, 5 mL of ethyl acetate was added and the solid catalyst was separated by an external magnet. The crude products were recrystallized from ethyl acetate/n-hexane to achieve the pure products in high yields. The recycled magnetic nanocomposite was washed, dried and re-used several times in subsequent reactions without further treatments.

2.5. Spectral data of representative compounds

2.5.1. Ethyl 2,7,7-trimethyl-5-oxo-4-p-tolyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (6c)

FT-IR (KBr) (v_{max} , cm⁻¹) = 3276, 3205, 2958, 1701, 1647, 1604, 1492, 1379, 1215, 1033. ¹H NMR (300 MHz, CDCl₃): δ_{H} (ppm) = 0.96 (3H, s, CH₃), 1.08 (3H, s, CH₃), 1.26 (3H, t, J = 7.2 Hz, CH₃), 2.26 (3H, s, CH₃), 2.22-2.34 (4H, m, 2CH₂), 2.38 (3H, s, CH₃), 4.16 (2H, q, J = 7.2 Hz, OCH₂), 5.43 (1H, s, CH), 6.19 (1H, br s, NH); 6.84 (2H, d, J = 7.5 Hz, H-Ar), 7.03 (2H, d, J = 7.5 Hz, H-Ar). Anal. Calcd for C_{22H₂₇NO₃: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.71; H, 7.66; N, 4.03.}

2.5.2. Ethyl 4-(4-chlorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (6d)

FT-IR (KBr) (v_{max} , cm⁻¹) = 3274, 3205, 3076, 2960, 1704, 1647, 1604, 1488, 1380, 1278, 1215, 1070. ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H}$ (ppm) = 0.93 (3H, s, CH₃), 1.08 (3H, s, CH₃), 1.20 (3H, t, J = 7.1 Hz, CH₃), 2.06-2.31 (4H, m, 2CH₂), 2.38 (3H, s, CH₃), 4.06 (2H, q, J = 7.1 Hz, OCH₂), 5.03 (1H, s, CH), 6.23 (1H, br s, NH), 7.16 (2H, d, J = 8.1 Hz, H-Ar), 7.26 (2H, d, J = 8.4 Hz, H-Ar). Anal. Calcd for C₂₁H₂₄ClNO₃: C, 67.46; H, 6.47; N, 3.75. Found: C, 67.32; H, 6.54; N, 3.82.

2.5.2. Ethyl 2,7,7-trimethyl-5-oxo-4-(thiophen-2-yl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (6m)

FT-IR (KBr) (v_{max} , cm⁻¹) = 3274, 3207, 2960, 1701, 1647, 1604, 1492, 1379, 1215, 1072. ¹H NMR (300 MHz, CDCl₃): δ_{H} (ppm) = 1.04 (3H, s, CH₃), 1.10 (3H, s, CH₃), 1.27 (3H, t, J = 7.1 Hz, CH₃), 2.22-2.34 (4H, m, 2CH₂), 2.38 (3H, s, CH₃), 4.16 (2H, q, J = 7.1 Hz, OCH₂), 5.42 (1H, s, CH), 6.19 (1H, br s, NH), 6.84 (2H, d, J = 1.8 Hz, H-Ar), 7.03 (1H, t, J = 2.1 Hz, H-Ar). Anal. Calcd for C₁₉H₂₃NO₃S: C, 66.06; H, 6.71; N, 4.05. Found: C, 67.11; H, 6.63; N, 3.94.

3. Results and discussion

3.1. Catalyst identification

Initially, Cu and magnetic γ -Fe₂O₃ nanoparticles were synthesized by co-precipitation method on microcrystalline cellulose. As indicated in Fig. 2c,d, the size and morphology of the nanocomposite were studied by conventional nanomaterials analysis instruments especially FE-SEM. As can be seen, Spherical nanoparticles are well distributed on the cellulose surface. FE-SEM images showed the homogeneous structure of the catalyst and the cellulose layer was also clearly observed. The nanoparticles were suitably supported by the cellulose. The average size distribution of the nanoparticles was about 25-55 nm. FE-SEM image of the cellulose matrix after its solubilization in NaOH/Urea/H₂O mixture (without modification) is shown in Fig. 2a,b, which have uniform and flat surface before the stabilization of the nanoparticles. To study the elemental composition of γ -Fe₂O₃/Cu@cellulose an EDX analysis was provided. An EDX analysis was provided to approve the presence of C, O, Cu and Fe elements in the nanocomposite structure (Fig. 2e). By comparing Fig. 2e with Fig. 2f, it was confirmed that there is no considerable difference between the values of the elements in the primary catalyst and recycled catalyst. In addition, ICP-AES analysis of the γ -Fe₂O₃/Cu@cellulose nanocomposite indicated that the Cu content in the nanocomposite was about 10%.

The prepared nanocomposite was studied by TEM technique (Fig. 2g,h). It was used to confirm the nanocomposites morphology. TEM proved that γ -Fe₂O₃ and Cu nanoparticles were effectively diffused in cellulose texture by electrostatic forces or chemical interactions. By comparing Fig. 2g,h with Fig. 2i,j, it was proved that there is no considerable difference in the chemical structure of the catalyst between the values of the elements in the primary catalyst and recycled catalyst. Finally, to determine the average size distribution of the nanoparticles, 100 particles were used randomly and the sizes of most of the nanoparticles were less than 30 nm.





Fig. 2. a,b) FE-SEM images of the cellulose matrix after its solubilization in NaOH/Urea/H₂O mixture without adding nanoparticles c,d) FE-SEM images of γ -Fe₂O₃/Cu@cellulose nanostructure with different magnifications, e) EDX analysis of primary γ -Fe₂O₃/Cu@cellulose and f) EDX analysis of recycled γ -Fe₂O₃/Cu@cellulose, g,h,) TEM images of primary γ -Fe₂O₃/Cu@cellulose with different magnifications, i,j) TEM images of recycled γ -Fe₂O₃/Cu@cellulose.

XRD pattern analysis was also used to determine the structure of the nanocatalyst. The XRD pattern of the γ -Fe₂O₃/Cu@cellulose nanocomposite is shown in Fig. 3. The peak in region 2θ = 20 degree, which is a curved peak, represents the cellulose substrate and cellulose XRD. The sharp peaks in the region of 30 to 65 degrees are related to γ -Fe₂O₃ and Cu nanoparticles on its surface and the position of all diffraction peaks match well with those of a lattice cubic system of γ -Fe₂O₃ peaks. This could easily be proven by comparing with the γ -Fe₂O₃ and Cu JCPDS.



Fig. 3. XRD pattern of the γ -Fe₂O₃/Cu@cellulose nanobiocomposite.

FT-IR spectrum indicates the formation of γ -Fe₂O₃/Cu@cellulose. Fig. 4 shows the FT-IR spectra of γ -Fe₂O₃/Cu@cellulose in comparison with γ -Fe₂O₃@cellulose and recycled nanocomposite after 5 times reusing in the organic reactions. A broad peak was observed at about 3350 cm⁻¹ which can be related to stretching mode of OH groups on cellulose of the nanocomposite structure. Hydrogen bonds are the reason of broadness of this peak. In the spectrum of γ -Fe₂O₃/Cu@cellulose, a peak appeared at 460 cm⁻¹ that is possibly originated from Fe–O bonds in γ -Fe₂O₃ nanoparticles and can prove the immobilization of γ -Fe₂O₃ nanoparticles on cellulose surface. Due to addition of nanoparticles on cellulose matrix, all of the peaks were broadened. Furthermore, by addition of Cu and γ -Fe₂O₃ to the cellulose matrix, new peaks were appeared. Furthermore, Fig. 4 shows the catalyst stability and as can be seen from the FT-IR spectrum of the nanocatalyst, it had good chemical stability and there was no considerable happening for its carbohydrate matrix or nanocomposite structure during the chemical reactions.



Fig. 4. FT-IR spectra of γ -Fe₂O₃/Cu@cellulose in comparison to γ -Fe₂O₃@cellulose and recycled γ -Fe₂O₃/Cu@cellulose.

The thermal behavior of the prepared nanocomposite was investigated by TG/DTA analyses over the temperature range of 50-700 °C at air atmosphere (Fig. 5a,b). Thermal analysis identified three separate weight loss regions on the TG curve. As displayed in this figure, γ -Fe₂O₃/Cu@cellulose starts to slight loss of mass upon heating at about 100-200 °C, is due to the removal of volatile elements like water from the nanocomposite. The TGA/DTA results showed that the most mass loss was occurred at about 300–350 °C, that can be associated to the decomposition of functional groups of cellulose and so about 600 °C is due to the decomposition of carbonaceous structure of cellulose linked to nanoparticles. Noteworthy, due of the catalyst's stability of up to 300 °C, this new nanobiocomposite can be used in organic reactions.

Based on AFM analysis, the surface and layers of the nanocatalyst was studied in details. As shown in Fig. 5c, the catalyst level is out of uniformity and surface morphology altered from cellulose and also Fe₂O₃ and Cu. This evidence can be claimed as an important proof for shaping of γ -Fe₂O₃/Cu@cellulose nanostructure as well as its nanostructure dimensions and morphology.







3.2. To study of γ -Fe₂O₃/Cu@cellulose catalytic activity in the synthesis of 1,4-dihydropyridine and polyhydroquinolines

To optimize the reaction conditions for the synthesis of 1,4-dihydropyridine derivatives, the reaction of the 4-chlorobenzaldehyde (1 mmol), ethylacetoacetate (2 mmol) and ammonium acetate (2 mmol) was considered as a model reaction. In the case of polyhydroquinolines, dimedone was used instead of ethylacetoacetate. Both of these reactions were carried out in the presence of various solvents like ethanol, water and acetonitrile and also under solvent-free conditions. The best yield was obtained under solvent-free conditions (Table 1).

To find the optimized catalyst ratio, different amounts of the nanocatalyst were studied (Table 1). At first, this reaction was performed under catalyst-free conditions. But, the yield of the product was low after 1 h. Therefore, the presence of the catalyst was necessary for the completion of the reaction. The best quantity of the catalyst for the synthesis of 1,4-dihydropyridine and polyhydroquinoline was 3 mg. By increasing the amount of the catalyst the reaction yield did not increase.

			Dihydrop	oyridine ^a	Polyhydroquinoline ^b		
Entry	Solvent	Catalyst (g)	Time (min)	Yield (%)	Time (min)	Yield (%)	
1	Solvent-free	· ·	240	25	240	40	
2	Solvent-free	0.002	20	80	15	80	
3	Solvent-free	0.003	20	92	15	95	
4	Solvent-free	0.004	20	92	15	95	
5	Solvent-free	0.008	20	85	15	91	
6	Solvent-free	0.02	20	85	15	87	
7	Ethanol	0.003	40	87	40	90	
8	Water	0.003	80	trace	80	trace	
9	Acetonitrile	0.003	80	60	80	60	

Table 1. Screening of the of γ -Fe₂O₃/Cu@cellulose amounts and solvents effects on the model reactions.

^a Reaction conditions: 1 mmol of 4-chlorobenzaldehyde, 2 mmol of ethyl acetoacetate and 2 mmol of ammonium acetate.

^bReaction conditions: 1 mmol of 4-chlorobenzaldehyde, 1 mmol of ethyl acetoacetate, 1 mmol of dimedone and 2 mmol ammonium acetate.

The scope and generality of the synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives were studied by using various aromatic aldehydes (Tables 2 and 3). Diverse 1,4-dihydropyridine and polyhydroquinolines were synthesized with the aforementioned molar

ratios starting from various aldehydes and 1,3-diketones under optimized solvent-free conditions and easy work-up procedures. Various aldehydes bearing both electron-withdrawing and electron-donating groups were checked out in these reactions. Due to the formation of the imine intermediate in the reaction of aldehydes with electron-withdrawing groups which is an inappropriate factor, these kinds of aldehydes were not reacted so well. But, in the presence of electron-donating groups, the reaction was progressed in short times and high yields. As shown in Table 3, entries 9 and 10, steric hindrance effects were not observed. The results clearly showed that the reaction of various aromatic aldehydes, ethyl acetoacetate, ammonium acetate and dimedone or 1,3-cyclohexandione under solvent-free conditions in the presence of the nanocomposite provided the corresponding products in high yields and appropriate reaction times. Some of the products were synthesized for the first time and were characterized by melting points, IR and NMR spectral data.

Table 2. Synthesis of 1,4-dihydropyridine derivatives 5a-i by using various aldehydes, ammonium acetate and ethyl acetoacetate catalysed by γ -Fe₂O₃/Cu@cellulose.^a

Entry	Aldehvde	Product	Time (min)	Yield (%)	Mp (°C)	Mp (°C, ref.)
1	C ₆ H ₅	5a	25	87	155	154-156 (Maleki et al. 2018)
2	$4-OMeC_6H_4$	5b	15	92	153-154	(Mareki, et al., 2018) 156-158 (Moradi, et al. 2018)
3	$4-MeC_6H_4$	5c	15	91	136-137	141-143 (Moradi, et al., 2018)
4	4-CIC ₆ H ₄	5d	20	92	145-147	144-146 (Maleki, et al., 2018)
5	4-BrC ₆ H ₄	5e	20	82	162-163	160-162 (Maleki, et al., 2018)
6	$4-NO_2C_6H_4$	5f	20	85	134	127-129 (Maleki, et al., 2018)
7	$3-NO_2C_6H_4$	5g	35	80	160-163	163-164 (Maleki, et al., 2018)
8	Thiophene-2-carbaldehyde	5h	20	93	170-171	171-172 (Debache et al., 2009)
9	Furfural	5i	15	90	161-162	162-164 (Debache et al., 2009)

^a Reaction conditions: Aldehyde (1 mmol), ethyl acetoacetate (2 mmol), ammonium acetate (2 mmol) and γ -Fe₂O₃/Cu@cellulose (3 mg), room temperature, solvent-free conditions.

Table 3. Synthesis of polyhydroquinoline derivatives **6a-s** by using various aldehydes, dimedone, ethyl acetoacetate and ammonium acetate in the presence of γ -Fe₂O₃/Cu@cellulose.^a

Entry	Aldehyde	1,3-Diketone	Product	Time (min)	Yield (%)	Mp (°C)	Mp (°C, ref.)
1	C ₆ H ₅	Dimedone	6a	20	87	201	203-205 (Tajbakhsh et al., 2013)
2	4-MeOC ₆ H ₄	Dimedone	6b	10	90	256	256-258 (Moradi, et al.,2018)
3	4-MeC ₆ H ₄	Dimedone	6с	10	91	255	254-256 (Moradi, et al.,2018)
4	$4-ClC_6H_4$	Dimedone	6d	15	95	240	241-243 (Maleki_et al.,_2012)
5	$2-ClC_6H_4$	Dimedone	6e	15	87	201-202	202-205 (Mobinikhaledi_et al.,_2009)
6	4-OHC ₆ H ₄	Dimedone	6f	15	82	230-240	232-234 (Heydari _et al., 2009)
7	2-OHC ₆ H ₄	Dimedone	6g	15	90	214	216-218 (Tajbakhsh et al., 2013)
8	$4-NO_2C_6H_4$	Dimedone	6h	35	80	238-240	238-240 (Moradi, et al.,2018)
9	3-OMe,4-OHC ₆ H ₄	Dimedone	6i	20	95	222-225	225-227 (Kumar, & Maurya, 2007)
10	2,4-OMe,5-OHC ₆ H ₄	Dimedone	6j	20	95	154-157	Not reported
11	$4-BrC_6H_4$	Dimedone	6k	20	87	253-254	259-260 (Davoodnia, Khashi, & Tavakoli <u>-</u> Hoseini, 2013)
12	4-CNC ₆ H ₄	Dimedone	61	30	80	139-142	143-145 (Tajbakhsh et al., 2013)

13	Thiophene-2-carbaldehyde	Dimedone	6m	15	93	225	226-228 (Moradi, et al.,2018)
14	Furfural	Dimedone	6n	15	91	243-244	245-247 (Tajbakhsh et al., 2013)
15	$4-OMeC_6H_4$	1,3-Cyclohexandione	60	9	95	250	248-253 (Ghattali, Saidi, & Khabazzadeh, 2014)
16	$4-MeC_6H_4$	1,3-Cyclohexandione	6р	9	95	244-245	241-243 (Nasr-Esfahani et al., 2014)
17	$4-ClC_6H_4$	1,3-Cyclohexandione	6q	15	98	239	234-236 (Nasr-Esfahani et al., 2014)
18	$4-OHC_6H_4$	1,3-Cyclohexandione	6r	15	90	224-227	222-224 (Nasr-Esfahani et al., 2014)
19	Thiophene-2-carbaldehyde	1,3-Cyclohexandione	6s	10	95	232	232-234 (Nasr-Esfahani et al., 2014)

^a Reaction conditions: Aldehyde (1 mmol), dimedone (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (2 mmol) and γ -Fe₂O₃/Cu@cellulose (3 mg), room temperature, solvent-free conditions.

The reusability of γ -Fe₂O₃/Cu@cellulose nanocatalyst was examined in the model reactions for the synthesis of 1,4-dihydropyridines and polyhydroquinolines (Fig. 6). In both of these reactions, the catalyst was easily recycled at least five times without significant loss of activity. In this regard, after completion of the reaction, the catalyst was separated by an external magnet, washed with hot ethanol and dried at room temperature to be ready for the subsequent runs. To study possible leaching of the nanocomposite components, an ICP-OES analysis was provided after the last recycling. It was found that the percentages of the elements were not changed significantly and the rest of Cu was still about 10%.



To show the efficiency of γ -Fe₂O₃/Cu@cellulose nanocatalyst, it was compared with literature resulted in reports of using various catalysts for the synthesis of 1,4-dihydropyridines and polyhydroquinolines. A few catalysts are reported for these reactions such as MgAl₂-HT, cellulose sulfuric acid, NaHSO₄-SiO₂, [TBA]₂[W₆O₁₉], PPh₃ and Fe₃O₄/SiO₂/Pph₃/[CrO₃Br]⁻. As shown in Table 4, most of them suffer from harsh reaction conditions such as reflux, volatile, hazardous and toxic solvents, long reaction times, low yields, expensive catalysts and tedious workup procedures. While, γ -Fe₂O₃/Cu@cellulose bionanocomposite is safe, green, inexpensive and easily separated from reaction pot. In order to simply separate from the reaction mixture. To compare the role of nanocomposites, the catalytic activity of cellulose, Cu@cellulose and γ -Fe₂O₃@cellulose were also evaluated. As the table illustrates, basic cellulose did not have enough catalytic activity; but, when the nanoparticles were loaded, its activity was considerably increased. In addition, Cu nanoparticle had a more important role than γ -Fe₂O₃. When both of these

components were coated on biopolymer, their synergistic effects were appeared. Furthermore, in the absence of cellulose, despite the increase in the amounts of the nanoparticles, the catalytic activity was not increased significantly.

Table 4. Comparison of the catalytic efficiency of γ -Fe₂O₃/Cu@cellulose with other catalysts for the synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives.

Entry	Catalyst	Reaction conditions	Time (min)	Yield (%)	Literature
1	Mg Al ₂ -HT	Acetonitrile/ r.t.	390	53	(Antonyraj, & Kannan, 2008)
2	Cellulose sulfuric acid	Solvent-free/100 °C	300	78	(Murthy et al., 2012)
3	NaHSO ₄ -SiO ₂	Acetonitrile/r.t.	360	80	(Chari, & Syamasundar, 2005)
4	$[TBA]_{2}[W_{6}O_{19}]$	Solvent-free/110 °C	20	95	(Debache et al., 2009)
5	PPh ₃	EtOH/reflux	120	81	(Davoodnia, Khashi, & Tavakoli-Hoseini, 2013)
6	$Fe_3O_4/SiO_2/PPh_3/[CrO_3Br]^-$	EtOH /r.t.	60	89	(Maleki et al., 2014)
7	γ -Fe ₂ O ₃ /Cu@cellulose	EtOH/r.t.	15	95	Present work
8	γ -Fe ₂ O ₃ nanoparticles	EtOH/r.t.	60	30	Present work

A plausible mechanism for the formation of 1,4-dihydropyridine and polyhydroquinoline derivatives is shown in Fig. 7. γ -Fe₂O₃/Cu@cellulose can activate the reactants and also some intermediates in this reaction. On the basis of the literature and substrates chemistry, the first step is the formation of an intermediate I from the condensation reaction between an aromatic aldehyde 1 and dimedone 3, or 1,3-ketoesters 4 in the presence of γ -Fe₂O₃/Cu@cellulose. Then, the addition of the second mole of 3 or 4 to I produces intermediate II. After that, the reaction between amine part of NH₄OAc and carbonyl group of II yields intermediate III. Finally, it was followed by an imine–enamine tautomerization to afford the final products 5a-i or 6a-s.



Fig. 6. Proposed mechanism for the synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives using γ -Fe₂O₃/Cu@cellulose.

4. Conclusions

In summary, we have prepared and characterized an efficient cellulose-based magnetic bionanocomposite. Biopolymer-based bimetallic bionanocomposite was prepared *via in situ* synthesis of maghemite (γ -Fe₂O₃) and immobilization of Cu on cellulose. Furthermore, the catalytic performance of the bionanocomposite was investigated in two important multicomponent condensation reactions for the synthesis of 1,4dihydropyridine and polyhydroquinoline derivatives starting from simple and readily accessible precursors under solvent-free conditions at room temperature. A large number of unique properties of this novel composite nanocatalyst were observed including short reaction times, simple work-up procedure, reusability of the nanocatalyst, high atom economy, high yields and environmentally-benign reaction conditions. Several analytical methods were used for the characterization of the nanocatalyst. Cu-embedded nanocomposite catalyst was successfully magnetized by γ -Fe₂O₃ nanoparticles and simultaneously immobilized on carbohydrate cellulose matrix to yield γ -Fe₂O₃ nanoparticles which are distributed on the biomatrix as well as uniform morphology. EDX and ICP analysis clearly showed the presence of Fe, Cu, C and O elements in the fresh and recycled nanocomposite. Therefore, leaching was not happened during the organic reactions and reusing of the nanocatalyst after several runs. This finding can be regarded as an important factor in large-scale production. AFM and TGA analyzes were used to further investigate the catalysts' characteristics. AFM image confirmed that the surface and layers of the nanocatalyst was out of uniformity and surface morphology altered from cellulose and also Fe₂O₃ and Cu in γ -Fe₂O₃/Cu@cellulose nanostructure. The appropriate thermal stability behavior of the prepared nanocomposite was approved by TG/DTA analyses over the temperature range of 50-700 °C at air atmosphere.

Acknowledgements

The authors gratefully acknowledge the partial support from the Research Council of the Iran University of Science and Technology.

Notes and references

Catalysts and Organic Synthesis Research Laboratory, Department of Chemistry, Iran University of Science and Technology, Tehran 16846-13114. Iran

*Corresponding author. Tel.: +98 21 77240640-50; Fax: +98 21 73021584. E-mail: maleki@iust.ac.ir (A. Maleki).

- Antonyraj, C. A., & Kannan, S. (2008). Hantzsch pyridine synthesis using hydrotalcites or hydrotalcite-like materials as solid base catalysts. Applied Catalysis A: General, 338, 121-129.
- Baran, N. Y., Baran, T., & Menteş, A. (2018). Production of novel palladium nanocatalyst stabilized with sustainable chitosan/cellulose composite and its catalytic performance in Suzuki-Miyaura coupling reactions. Carbohydrate Polymers, 181, 596-604.
- Baran, T. (2018). Pd (0) nanocatalyst stabilized on a novel agar/pectin composite and its catalytic activity in the synthesis of biphenyl compounds by Suzuki-Miyaura cross coupling reaction and reduction of o-nitroaniline. Carbohydrate Polymers, 195, 45-52.
- Baran, T. (2018). Ultrasound-accelerated synthesis of biphenyl compounds using novel Pd(0) nanoparticles immobilized on biocomposite. Ultrasonics Sonochemistry, 45, 231-237.
- Baran, T., Yılmaz Baran, N., & Menteş, A. (2018). Sustainable chitosan/starch composite material for stabilization of palladium nanoparticles: Synthesis, characterization and investigation of catalytic behaviour of Pd@chitosan/starch nanocomposite in Suzuki–Miyaura reaction. Applied Organometallic Chemistry, 32(2), e4075.
- Boer, R., & Gekeler, V., (1995). Drugs Future, 20, 499.
- Bossert, F., Meyer, H., & Wehinger, E. (1981). 4-Aryldihydropyridines, a new class of highly active calcium antagonists. Angewandte Chemie International Edition in English, 20, 762-769.
- Briukhanov, V. M., (1994). The effect of Ca antagonist on the development of inflammatory edema in rats. Clinical and Experimental Pharmacology, 57, 47–49.
- Chari, M. A., & Syamasundar, K. (2005). Silicagel/NaHSO4 catalyzed one-pot synthesis of Hantzsch 1,4-dihydropyridines at ambient temperature. Catalysis Communications, 6, 624-626.
- Cosconati, S., Marinelli, L., Lavecchia, A., & Novellino, E. (2007). Characterizing the 1, 4-dihydropyridines binding interactions in the L-type Ca²+ channel: model construction and docking calculations. Journal of Medicinal Chemistry, 50, 1504-1513.
- David J. T., (2007). Calcium channel antagonists: Clinical uses-Past, present and future. Biochemical Pharmacology, 74, 1-9.
- Davoodnia, A., Khashi, M., & Tavakoli-Hoseini, N. (2013). Tetrabutylammonium hexatungstate [TBA]₂[W₆O₁₉]: Novel and reusable heterogeneous catalyst for rapid solvent-free synthesis of polyhydroquinoline via unsymmetrical Hantzsch reaction. Chinese Journal of Catalysis, 34, 1173-1178.
- Debache, A., Ghalem, W., Boulcina, R., Belfaitah, A., Rhouati, S., & Carboni, B. (2009). An efficient one-step synthesis of 1,4dihydropyridines via a triphenylphosphine-catalyzed three-component Hantzsch reaction under mild conditions. Tetrahedron Letters, 50, 5248-5250.
- Donelson, J. L., Gibbs, R. A., & De, S. K. (2006). An efficient one-pot synthesis of polyhydroquinoline derivatives through the Hantzsch four component condensation. Journal of Molecular Catalysis A: Chemical, 256, 309-311.
- Gawande, Manoj B., Paula S. Branco, & Rajender S. Varma. (2013). Nano-magnetite (Fe₃O₄) as a support for recyclable catalysts in the development of sustainable methodologies. Chemical Society Reviews, 42, 3371-3393.
- Ghattali, S. N., Saidi, K., & Khabazzadeh, H. (2014). (NH₄)₂.5H0.5PW₁₂O₄₀-catalyzed rapid and efficient one-pot synthesis of dihydropyridines via the Hantzsch reaction under solvent-free conditions. Research on Chemical Intermediates, 40, 281-291.
- Gilpin, R. K., & Pachla, L. A. (1999). Pharmaceuticals and related drugs. Analytical Chemistry, 71, 217-234.
- Gullapalli, S., & Ramarao, P. (2002). L-Type Ca²⁺ channel modulation by dihydropyridines potentiates κ-opioid receptor agonist induced acute analgesia and inhibits development of tolerance in rats. Neuropharmacology, 42, 467-475.
- Gunawan, S., Ayaz, M., De Moliner, F., Frett, B., Kaiser, C., Patrick, N., Xu, Z. & Hulme, C., (2012). Synthesis of tetrazolo-fused benzodiazepines and benzodiazepinones by a two-step protocol using an Ugi-azide reaction for initial diversity generation. Tetrahedron, 68, 5606-5611.
- Habibi, Y., Lucia, L. A., & Rojas, O. J. (2010). Cellulose nanocrystals: chemistry, self-assembly, and applications. Chemical reviews, 110(6), 3479-3500.
- Heydari, A., Khaksar, S., Tajbakhsh, M., & Bijanzadeh, H. R. (2009). One-step, synthesis of Hantzsch esters and polyhydroquinoline derivatives in fluoro alcohols. Journal of Fluorine Chemistry, 130, 609-614.
- Hulme, C., Peng, J., Tang, S. Y., Burns, C. J., Morize, I., & Labaudiniere, R. (1998). Improved procedure for the solution phase preparation of 1,4-benzodiazepine-2,5-dione libraries via Armstrong's convertible isonitrile and the Ugi reaction. The Journal of Organic Chemistry, 63, 8021-8023.
- Klemm, D., Heublein, B., Fink, H. P., & Bohn, A. (2005). Cellulose: fascinating biopolymer and sustainable raw material. Angewandte Chemie International Edition, 44(22), 3358-3393.
- Kumar, A., & Maurya, R. A. (2007). Bakers' yeast catalyzed synthesis of polyhydroquinoline derivatives via an unsymmetrical Hantzsch reaction. Tetrahedron letters, 48, 3887-3890.
- Li, M., Zuo, Z., Wen, L., & Wang, S. (2008). Microwave-assisted combinatorial synthesis of hexa-substituted 1,4-dihydropyridines scaffolds using one-pot two-step multicomponent reaction followed by a S-alkylation. Journal of combinatorial chemistry, 10, 436-441.

- Lian, C., Liu, H., Xiao, C., Yang, W., Zhang, K., Liu, Y., & Wang, Y., (2012). Solvent-free selective hydrogenation of chloronitrobenzene to chloroaniline over a robust Pt/Fe₃O₄ catalyst. Chemical Communications, 48, 3124-3126.
- Maheswara, M., Siddaiah, V., Damu, G. L. V., & Rao, C. V. (2006). An efficient one-pot synthesis of polyhydroquinoline derivatives via Hantzsch condensation using a heterogeneous catalyst under solvent-free conditions. Arkivoc, 2, 201-206.
- Maleki, A., Firouzi-Haji, R., & Hajizadeh, Z. (2018). Magnetic guanidinylated chitosan nanobiocomposite: A green catalyst for the synthesis f 1, 4-dihydropyridines. International Journal of Biological Macromolecules, 116, 320-326.
- Maleki, A., Jafari, A. A., & Yousefi, S. (2017). Green cellulose-based nanocomposite catalyst: design and facile performance in aqueous synthesis of pyranopyrimidines and pyrazolopyranopyrimidines. Carbohydrate Polymers, 175, 409-416.
- Maleki, A., Jafari, A. A., Yousefi, S., & Eskandarpour, V. (2015). An efficient protocol for the one-pot multicomponent synthesis of polysubstituted pyridines by using a biopolymer-based magnetic nanocomposite. Comptes Rendus Chimie, 18, 1307-1312.
- Maleki, A., Movahed, H., & Paydar, R. (2016). Design and development of a novel cellulose/γ-Fe₂O₃/Ag nanocomposite: a potential green catalyst and antibacterial agent. RSC Advances, 6, 13657-13665.
- Maleki, A., Movahed, H., & Ravaghi, P. (2017). Synthesis of magnetic cellulose/Ag as a novel environmentally friendly nanobiocomposite catalyst to achieve chromene-linked 2-amino-4-aryl-nicotinonitrile derivatives. Carbohydrate Polymers, 156, 259-267.
- Maleki, A. & Paydar, R. (2016). Bionanostructure-catalyzed one-pot three-component synthesis of 3, 4-dihydropyrimidin-2 (1H)-one derivatives under solvent-free conditions. Reactive and Functional Polymers, 109, 120-124.
- Maleki, A., Rahimi, J., Demchuk, O. M., Wilczewska, A. Z., & Jasiński, R. (2018). Green in water sonochemical synthesis of tetrazolopyrimidine derivatives by a novel core-shell magnetic nanostructure catalyst. Ultrasonics Sonochemistry, 43, 262-271.
- Maleki, A., Rahimi, R., Maleki, S., & Hamidi, N. (2014). Synthesis and characterization of magnetic bromochromate hybrid nanomaterials with triphenylphosphine surface-modified iron oxide nanoparticles and their catalytic application in multicomponent reactions. RSC Advances, 4, 29765-29771.
- Maleki, A., & Sarvary, A. (2015). Synthesis of tetrazoles via isocyanide-based reactions. RSC Advances, 5, 60938-60955.
- Maleki, A., Zand, P., Mohseni, Z., & Firouzi-Haji, R. (2018). Green composite nanostructure (Fe₃O₄@PEG-SO₃H): Preparation, characterization and catalytic performance in the efficient synthesis of β-amino carbonyl compounds at room temperature. Nano-Structures & Nano-Objects, 16, 31-37.
- Mekheimer, R. A., Hameed, A. A., & Sadek, K. U. (2008). Solar thermochemical reactions: four-component synthesis of polyhydroquinoline derivatives induced by solar thermal energy. Green Chemistry, 10, 592-593.
- Mobinikhaledi, A., Foroughifar, N., Fard, M. A. B., Moghanian, H., Ebrahimi, S., & Kalhor, M. (2009). Efficient one-pot synthesis of polyhydroquinoline derivatives using silica sulfuric acid as a heterogeneous and reusable catalyst under conventional heating and energy-saving microwave irradiation. Synthetic Communications, 39, 1166-1174.
- Moradi, L., & Zare, M. (2018). Ultrasound-promoted green synthesis of 1,4-dihydropyridines using fuctionalized MWCNTs as a highly efficient heterogeneous catalyst. Green Chemistry Letters and Reviews, 11(3), 197-208.
- Murthy, Y. L. N., Rajack, A., Ramji, M. T., Praveen, C., & Lakshmi, K. A. (2012). Design, solvent free synthesis, and antimicrobial evaluation of 1, 4 dihydropyridines. Bioorganic & Medicinal Chemistry Letters, 22, 6016-6023.
- Nasr-Esfahani, M., Hoseini, S. J., Montazerozohori, M., Mehrabi, R., & Nasrabadi, H. (2014). Magnetic Fe₃O₄ nanoparticles: efficient and recoverable nanocatalyst for the synthesis of polyhydroquinolines and Hantzsch 1, 4-dihydropyridines under solvent-free conditions. Journal of Molecular Catalysis A: Chemical, 382, 99-105.
- Orru, R. V., & de Greef, M. (2003). Recent advances in solution-phase multicomponent methodology for the synthesis of heterocyclic compounds.Synthesis, 2003, 1471-1499.
- Pagoti, S., Surana, S., Chauhan, A., Parasar, B., & Dash, J. (2013). Reduction of organic azides to amines using reusable Fe₃O₄ nanoparticles in aqueous medium. Catalysis Science & Technology, 3, 584-588.
- Polshettiwar, V., Baruwati, B., &Varma, R.S. (2009). Nanoparticle-supported and magnetically recoverable nickel catalyst: a robust and economic hydrogenation and transfer hydrogenation protocol. Green Chemistry, 11, 127-131.
- Reddy, C. S., & Raghu, M. (2008). Cerium (IV) ammonium nitrate catalysed facile and efficient synthesis of polyhydroquinoline derivatives through Hantzsch multicomponent condensation. Chinese Chemical Letters, 19, 775-779.
- Rostamnia, S., Lamei, K., Mohammadquli, M., Sheykhan, M., & Heydari, A. (2012). Nanomagnetically modified sulfuric acid (γ-Fe₂O₃@ SiO₂-OSO₃H): an efficient, fast, and reusable green catalyst for the Ugi-like Groebke-Blackburn-Bienaymé three-component reaction under solvent-free conditions. Tetrahedron Letters, 53, 5257-5260.
- Shafiee, M., Khosropour, A. R., Mohammadpoor-Baltork, I., Moghadam, M., Tangestaninejad, S., & Mirkhani, V. (2012). A new green catalyst: 1,3,5-triazine-functionalized bisimidazolium dichloride tethered SPION catalyzed Betti synthesis. Catalysis Science & Technology, 2, 2440-2444.
- Spiridonov, V. V., Panova, I. G., Makarova, L. A., Afanasov, M. I., Zezin, S. B., Sybachin, A. V., & Yaroslavov, A. A. (2017). The one-step synthesis of polymer-based magnetic γ-Fe2O3/carboxymethyl cellulose nanocomposites. Carbohydrate polymers, 177, 269-274.
- Tajbakhsh, M., Alinezhad, H., Norouzi, M., Baghery, S., & Akbari, M. (2013). Protic pyridinium ionic liquid as a green and highly efficient catalyst for the synthesis of polyhydroquinoline derivatives via Hantzsch condensation in water. Journal of Molecular Liquids, 177, 44-48.
- Tu, S. J., Zhou, J. F., Deng, X., Cai, P. J., Wang, H., & Feng, J. C. (2001). One step synthesis of 4-arylpolyhydroquinoline derivatives using microwave irradiation. Chinese Journal of Organic Chemistry, 21(4), 313-316.
- Wang, L. M., Sheng, J., Zhang, L., Han, J. W., Fan, Z. Y., Tian, H., & Qian, C. T. (2005). Facile Yb(OTf)₃ promoted one-pot synthesis of polyhydroquinoline derivatives through Hantzsch reaction. Tetrahedron, 61, 1539-1543.
- Xu, Q., Chen, C., Rosswurm, K., Yao, T., & Janaswamy, S. (2016). A facile route to prepare cellulose-based films. Carbohydrate Polymers, 149, 274–281.

- Yan, J. M., Zhang, X. B., Akita, T., Haruta, M., & Xu, Q. (2010). One-step seeding growth of magnetically recyclable Au@Co core- shell nanoparticles: highly efficient catalyst for hydrolytic dehydrogenation of ammonia borane. Journal of the American Chemical Society, 132, 5326-5327.
- Yu, X., Tong, S., Ge, M., Zuo, J., Cao, C., & Song, W. (2013). One-step synthesis of magnetic composites of cellulose@iron oxide nanoparticles for arsenic removal. Journal of Materials Chemistry, 1(3), 959-965.
- Zhu, J., & Bienaymé, H. (Eds.). (2005). Multicomponent reactions. John Wiley & Sons, Ltd, Weinheim.

17