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Article

Preparation of a Novel Biopolymer Cellulose-Based Nanocomposite by Coating of Gamma-Fe_2O_3/Cu Nanoparticles and Catalytic Application in Chemical Reactions

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Abstract: Hantzsch 1,4-dihyropyridine synthesis is one of the multicomponent reactions that is accomplished with different catalyst and under different conditions. In this work, this one-pot three-component and four-component reactions for the synthesis of 1,4-dihyropyridine and polyhydroquinoline derivatives are described in the presence of biopolymer-based gamma-Fe_2O_3/Cu/cellulose as a nanocatalyst. This magnetic catalyst was very effective for this reaction, and it was carried out by simple work-up procedure under green and environmentally friendly conditions in ethanol at room temperature.

Keywords: Polyhydroquinoline; Hantzsch 1,4-dihyropyridine; Fe_2O_3/Cu/cellulose; Magnetic nanocatalyst.

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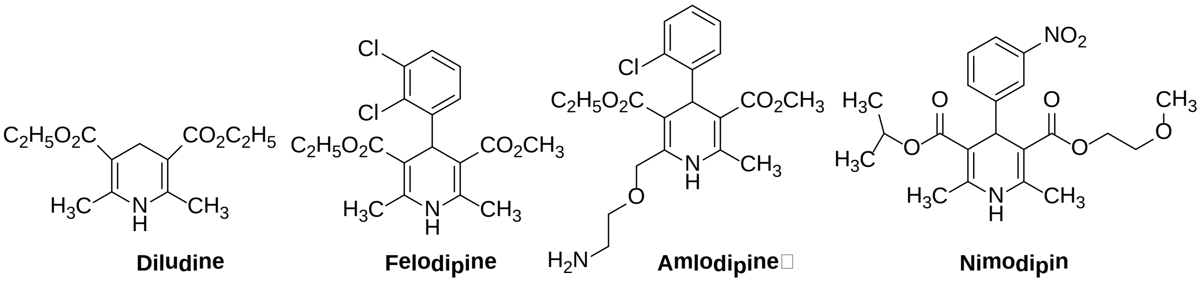
1. Introduction

Multicomponent reactions (MCRs) are one-pot processes in which three or more accessible components react to form a single product that incorporates essentially most or all atoms of the reactants used [1]. MCRs have recently gained a new dimension in the field of designing methods to produce elaborate libraries of biologically active compounds.

Hantzsch 1,4-dihydropyridine synthesis is one of the first synthesis of heterocyclic compounds via MCRs. They include various medicinal, biological and pharmacological activity properties such as calcium channel blockers, antitumor, anti-inflammatory, and analgesic activities. Several medicinally important drugs are now prescribed and used, for example: Diludine, Felodipine, Amlodipine, Nimodipi [2].



Diludine Felodipine Amlodipine Nimodipin

Reports of these reactions were published with solvent or under solvent-free conditions. Different solvents were used but ethanol and water are the best, because of green and environment-friend properties.

In view of the biological, industrial and synthetic importance of 1,4-dihydropyridines and polyhydroquinolines, several methods for their synthesis have been reported. The classical Hantzsch condensation method for the synthesis of 1,4-dihydropyridines is one-pot condensation of aldehydes with ethyl acetoacetate, and ammonia either in acetic acid at room temperature or by refluxing in alcohols for a long time [3]. In this way, the reaction conditions were vigorous and so several impressive methods have been developed for accomplished this reaction under simple conditions. Some of these methods consist of using conventional heating [4,5], solar thermal energy [6], ionic liquid [7], metal triflates [8], cerium(IV) ammonium nitrate [9], silica perchloric acid [10], microwave and ultrasound irradiation [11] and Fe_3O_4 magnetic catalyst [12].

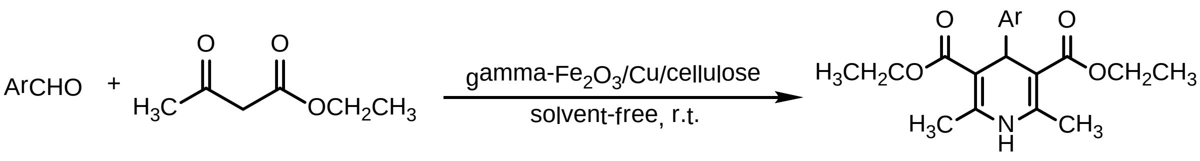
Recently, using of nanoparticles as catalysts of organic reactions has been widely developed. Nanoparticles, because of their great surface area to volume, can operate as efficient heterogeneus catalysts that can be simply seperated from the reaction pot. Magnetic nanoparticles have great superiority than other nanoparticles because of their easier separation with an external magnetic field.

On the other hand, nanocomposites based on the natural biopolymers have special significance because of their environmentally friendly and green chemistry properties. Cellulose, as a naturally abundant biopolymer, can be easily functionalized with various organic groups for desired purposes like applications as a biodegradable support for heterogeneous catalysis, composites matrixes and immobilization processes.

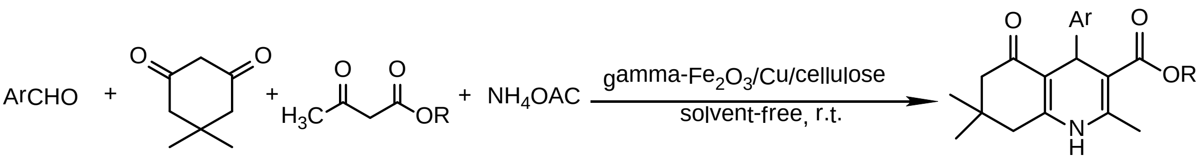
Metal nanocomposites are one of the best catalysts for organic reaction because of their simple recoverable features. They simply can be recovered from reaction pot. A possible method simple separation and recycling of the catalysts is immobilizing catalytically active species in the surface of magnetic metal nanoparticles which can be separated from the reaction system by applying an appropriate magnetic field.

In this study, we have prepared a biopolymer-based bimetallic nanocomposite via in situ synthesis of maghemite (gamma-Fe_2O_3) and Cu on cellulose. It has been proven that this catalyst shows very good activities in organic synthesis. We used this novel nanocomposite for the synthesis of 1,4-dihyropyridine (Scheme 1) and polyhydroquinoline (Scheme 2) synthesis under solvent-free condition at room temperature in high yield and short reaction times.

Scheme 1. Synthesis of 1,4-dihyropyridine derivatives.



Scheme 2. Synthesis of polyhydroquinoline derivatives.



2. Results and discussions

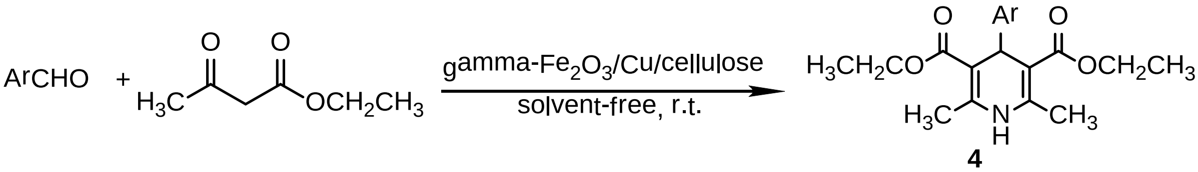
First, to optimize the reaction conditions, we tested the 4-methoxybenzaldehyde (1 mmol), dimedone (1 mmol), ethylacetoacetate (1 mmol) and ammonium acetate (1.5 mmol) under solvent-free condition and also with in ethanol and water as solvents. Reaction analysis showed that solvent-free condition was the optimized and reaction did not proceed in water. For optimization of the catalyst, different amount of catalyst was used (Table 1).

Table 1. Optimization of the solvent and amount of catalyst for the synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives.

Entry	Catalyst (g)	Solvent	Temperature (ºC)	Time (min)	Yield (%)
1	-	-	120	190	Trace
2	0.005	-	r.t	60	58
3	0.01	-	r.t	45	80
4	0.02	-	r.t	20	95
5	0.02	H_2O	-	-	No reaction
6	0.02	EtOH	r.t	30	85

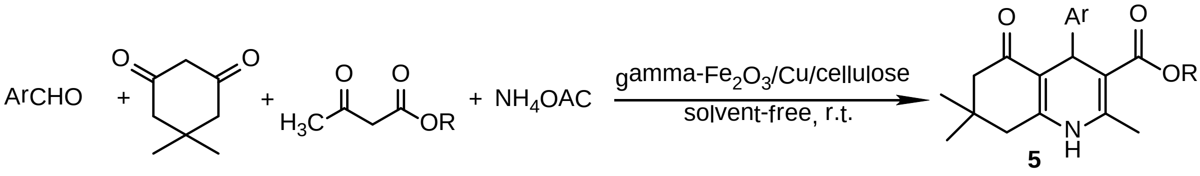
The scope and generality of synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives are well showed with structurally diverse aromatic aldehydes. The results are summarized in Tables 2 and 3 for 1,4-dihydropyridines and polyhydroquinolines, respectively.

Table 2. Synthesis of 1,4-dihydropyridine derivatives using gamma-Fe_2O_3/Cu/cellulose.



Ar	Product	Time (min)	Yield (%)	Melting point (°C)	
				Found	Reported
4-MeO-C_6H_4	**4a**	30	88	153-154	161-163[13]
4-Me-C_6H_4	**4b**	30	91	136-137	135-137[14]
4-C-C_6H_4	**4c**	20	90	145-147	147-148[13]
3-O_2N-C_6H_4	**4d**	35	80	157-160	162-164[13]

Table 3. Synthesis of polyhydroquinoline derivatives using gamma-Fe_2O_3/Cu/cellulose.



Ar	Product	Time (min)	Yield (%)	Melting point (°C)	
				Found	Reported
4-MeO-C_6H_4	**5a**	20	93	256-257	258-260[15]
4-Me-C_6H_4	**5b**	15	90	253-255	258-260[16]
4-Cl-C_6H_4	**5c**	25	95	244-245	241-243[17]
2-Cl-C_6H_4	**5d**	22	88	208-210	202-205[18]
3-OH-C_6H_4	**5e**	30	85	238-239	232-234[19]

3. Experimental

3.1. Materials and methods

All chemicals were purchased from Merck, Fluka and Sigma-Aldrich companies and were used without further purification. All reactions and the purity of 1,4-dihydropyridine and polyhydroquinoline derivatives were monitored by thin-layer chromatography (TLC) and using ethyl acetate and *n*-hexane as eluents. Melting points were determined in open capillaries using an Electro thermal 9100 instrument.

3.2. Synthesis of gamma-Fe_2O_3/Cu/cellulose nanocomposite.

A solution of NaOH, urea and H_2O is prepared with material ratio of 7:12:81, respectively. Its temperature is cooled to -12 ^{0}C by ice and salt, and then 4.0 g micro crystaline cellulose dissolved directly in it. 0.5 g $FeCl_2$ and 1.0 g $FeCl_3$ was dissolved in 50 mL deionized water, and then added dropwise to the first cellulose solution. As a result, gamma-Fe_2O_3 was synthesised in situ on cellulose fiber and then $CuSO_4.4H_2O$ was added dropwise to mixture and Cu is coated on cellulose too, and the mixture was stirred for 2 h. Fionally, the mixture was filtered and washed with H_2O (3*50 mL) and dried at room temperature.

3.3. General procedure for the synthesis of 1,4-dihydropyridines.

First, ethylacetoacetate (2 mmol), benzaldehyde (1 mmol) and ammonium acetate (1.5 mmol) was added to the reaction pot in the presence of gamma-Fe_2O_3/Cu/cellulose (0.02 g), and the reaction was completed after 20 minutes. After completion of reaction, as indicated by TLC (ethyl acetate/n-hexane 1/3), 5 mL ethyl acetate was added and solid catalyst was separated by a magnet. The crude product was recrystallized from ethyl acetate/n-hexane to give the pure products in 85–95% yields.

3.4. General procedure for synthesis of polyhydroquinolines.

First, 0.02 g of gamma-Fe_2O_3/Cu/cellulose was added to the mixture of an aromatic aldehyde (1 mmol), dimedone (1 mmol), ethylacetoacetate (1 mmol) and ammonium acetate (1.5 mmol) in a 10 mL round bottom flask. The mixture was homogenized and stirred at room temperature for 20 min and the reaction was monitored with TLC. After completion of the reaction, 5 mL of ethyl acetate was added and then solid catalyst was separated by a magnet. The crude product was recrystallized from ethyl acetate/n-hexane to give the pure products in high yields.

4. Conclusion

In summary, we have introduced a new nanocomposite system based on cellulose which due to the presence of two metal nanoparticles, it can catalyzes organic reactions. In present work, we used this system for the synthesis of 1,4-dihydropyridine and polyhydroquinoline derivatives in high yields and very mild conditions. Meanwhile, because of magnetic properties of this system (gamma-Fe_2O_3) the separation of catalyst from reaction pot was very simple.

Acknowledgements

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Conflicts of Interest

The authors declare no conflict of interest.

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