



J. Serb. Chem. Soc. 86 (11) 1039–1052 (2021)
JSCS–5481

Synthesis and characterization of Fe₃O₄/PEG-400/oxalic acid magnetic nanoparticles as a heterogeneous catalyst for the synthesis of pyrrolin-2-ones derivatives

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(Received 21 May, revised 5 August, accepted 10 August 2021)

Abstract: In this study, oxalic acid was successfully loaded onto Fe₃O₄/PEG-400 under ultrasonic irradiation and Fe₃O₄/PEG/oxalic acid as a new nanomagnetic catalyst was synthesized. The chemical structure of the catalyst was investigated by the FT-IR, XRD, EDX and SEM methods. The catalyst was used for the synthesis of 3-acyl-5-hydroxy-3-pyrrolin-2-one derivatives from the corresponding aldehydes, anilines and dimethyl acetylenedicarboxylate (DMAD) by a one-pot and three-component MCR reaction in the excellent yields (90–95 %) of products within 24 h at room temperature. Fourteen samples are available. The recovered catalyst could be satisfactorily used for a second and third run without regeneration. This method has a green and eco-friendly profile. In addition, this research introduces an improved mechanism for these types of reaction. The chemical structures of new compounds was characterized by their FT-IR, ¹H-NMR, ¹³C-NMR and mass spectra.

Keywords: iron(II), iron(III) oxide; nano-composite catalyst; 2-pyrrolidinone; green chemistry; MCR.

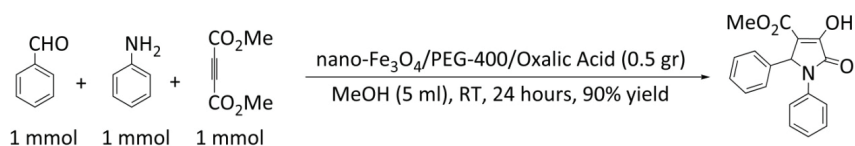
INTRODUCTION

In many catalytic methods, recyclability, recovery, non-toxicity and economical affordability are four valuable characteristics. Magnetic nanoparticle (MNPs) catalysts due to their simple synthesis, easy application, great efficient reusability by magnetic force, low toxicity and economics, are attractive.¹ Such acceptable qualities have caused MNPs to become desirable substitutes for some catalysts.^{2–4} Surface functionalized magnetic Fe₃O₄ nanoparticles have been used in biotechnology and catalysis as a functional substance. There are a variety of different magnetic nanoparticles for the core magnetic support, but Fe₃O₄ nanoparticles have been widely investigated due to their low toxicity, super paramagnetic behavior, large surface areas and especially presenting a great number of OH

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<https://doi.org/10.2298/JSC210521059E>

groups on the exterior of their particles.^{5,6} Therefore, specific shells of different substances can be built to enclose the Fe_3O_4 core, for example: forming proper functional groups for specified different actuators, ligands, and catalysts.⁷ On the other hands, interest in magnetic nanoparticles (MNPs) have been increasing for applications in organic synthesis.^{8,9} The surface of magnetic nanoparticles can be functionalized by surface modifications for performing of a variety of organic reactions.¹⁰

Multicomponent reactions (MCRs) have been of interest in one-pot synthesis of heterocyclic compounds,¹¹ such as pyrrolidinones.¹² The pyrrolin-2-one moiety is important in organic compounds because of its biological activity in some drugs and natural products, for example: cotinine (the predominant metabolite of nicotine in tobacco),¹³ doxapram hydrochloride (a respiratory stimulant),¹⁴ ethosuximide (a succinimide anticonvulsant),¹⁵ lactacystin (synthesized by bacteria of the genus *Streptomyces*),¹⁶ salinosporamide A (produced by the bacteria *Salinispora tropica*),¹⁷ (-)-azaspirene (an angiogenesis inhibitor that is extracted from the fungus *Neosartorya* sp).¹⁸ In view of the importance of these compounds, some synthetic methods have been reported.^{19–24} Moreover, the synthesis of pyrrolin-2-one derivatives, involving the coupling of aromatic aldehydes, arylamines with acylenedicarboxylate derivatives, has been studied, and the development of this procedure under a green profile is attractive and desired, such as: a) using of admicellar catalysis such nano- TiO_2 ,²⁵ b) in water for non-bulky products,²⁶ c) in the presence of *p*-toluensulfonic acid,¹² d) using unconventional energy sources such as ultrasound irradiation²⁷ or microwaves,²⁸ e) with application of ionic liquids²⁹ and f) nano magnetic particles $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{Propyl-ANDSA}$ as a reusable catalyst.³⁰ The study of these methods clarified the development of this procedure under green profile is more attractive and desired. Furthermore, for the extension of green chemistry, several eco-friendly procedures for the synthesis of heterocyclic compounds have been reported.^{11,31} On the other hand, for a synthetic project a series of pyrrolin-2-ones were needed. Encouraged by these results, attention was directed to a new methodology for the room temperature synthesis of 3-acyl-5-hydroxy-3-pyrrolin-2-one derivatives from aldehydes, anilines and dimethyl acylenedicarboxylate (DMAD) catalyzed by $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$ as a novel reusable magnetic nano-catalyst, as shown in Scheme 1.



Scheme 1. The synthesis of 1,5-diphenyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one.

EXPERIMENTAL

Materials

All solvents and reagents were obtained from the Sigma–Aldrich Company. FT-IR, ¹H- and ¹³C-NMR spectra were recorded on a PerkinElmer FT-IR RXI and (250 or 500) MHz Bruker spectrometers, respectively. The products were characterized by their FT-IR, ¹H-NMR, and ¹³C-NMR spectra and comparison with authentic samples for known products. The new compounds characterization has been supported by mass spectrum obtained using Agilent Technology (HP), MS model: 5973 network mass selective detector (ion source: electron impact (EI) 70 eV, ion source and analyzer temperature 230 °C, analyzer: quadrupole). The nanostructures were characterized using a Holland Philips (model: PW1730) Xpert X-ray powder diffraction (XRD) diffractometer (CuK, radiation, λ = 0.154056 nm), Step size 0.05°, time per step, 1 s (2θ 5–80°). Scanning electron microscopy (SEM) of the nanoparticles was performed on a model FESEM: Tescan company (model: Mira III), Czech Republic. Energy dispersive X-ray analysis (EDX) was performed by FESEM: Tescan company (model: Mira II, detector: SAMX, France). Elma (S60H, Germany) with high-performance transducer system with 37 kHz was used.

Preparation of Fe₃O₄ magnetic nanoparticles

The magnetic Fe₃O₄ nanoparticles were prepared by the chemical co-precipitation method.^{8,32} FeCl₂·4H₂O (2.25 g) and FeCl₃·6H₂O (6.11 g) were dissolved into 400 mL deoxygenated water. The reaction was followed by the dropwise addition of 20 mL of concentrated liquid NH₃ under vigorous stirring and N₂ protection at 80 °C. The obtained magnetic nanoparticles were separated from solution by a powerful magnet and were washed with 200 mL deionized water three times. Finally the products were dried at 40 °C overnight to give Fe₃O₄ nanoparticles.

Preparation of Fe₃O₄/PEG-400 magnetic nanoparticles

The magnetic Fe₃O₄/PEG-400 nanoparticles were synthesized by modification of a method known in the literature.^{8,32} The detailed procedure is described as following: Fe₃O₄ nanoparticles (1 g) were dispersed in 60 mL deionized water in an ultrasonic bath for 30 min under nitrogen gas. Then PEG-400 (5 ml) was added, and the mixed solution was irradiated in an ultrasonic bath for 1 h under nitrogen gas at 80–90 °C. After the reaction, the Fe₃O₄/PEG-400 nanoparticles were isolated with a strong magnet and washed with deionized water and dried at 40 °C overnight to give Fe₃O₄/PEG-400.

Preparation of Fe₃O₄/PEG-400/oxalic acid magnetic nanoparticles

The Fe₃O₄/PEG400 nano composite (5 g) was dispersed in ethanol (20 mL) in an ultrasonic bath for 30 min. Subsequently, oxalic acid (0.75 g) was added to the reaction mixture. The mixture was irradiated in an ultrasonic bath for 1 h under nitrogen gas at 80–90 °C. The resulting magnetic nanocomposite was separated from the suspension by a strong external magnet. They were washed with ethanol (2×10 ml) and acetone (2×5 ml), and then dried at 40 °C overnight to give magnetic Fe₃O₄/PEG-400/oxalic acid nano particles.

The synthesis of 1,5-diphenyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one by Fe₃O₄/PEG-400/oxalic acid: A typical procedure

In a round-bottomed flask (25 mL) equipped with a magnetic stirrer, a mixture of benzaldehyde (0.106 g, 1 mmol), aniline (0.093 g, 1 mmol) and Fe₃O₄/PEG-400/oxalic acid (0.5 g) in 5 mL of methanol was prepared and strongly stirred at ambient temperature for 30 min. Then dimethyl acetylenedicarboxylate (DMAD, 0.14 g, 1 mmol) was added to the mixture.

The reaction was completed within 24 h. The reaction was monitored over silica gel 60 F₂₅₄ aluminum sheet (eluent: ethyl acetate/*n*-hexane: 1/1). The catalyst was separated using a strong magnet. The separated catalyst was washed with acetone two times and then dried in oven for reuse in further reactions. The solvent was evaporated under reduced pressure and further purification was achieved by recrystallization from methanol. The white solid was achieved in excellent yield 0.28 g (90 %) with a melting point 173–175 °C. The product was characterized by their ¹H-NMR, ¹³C-NMR and FT-IR spectra.

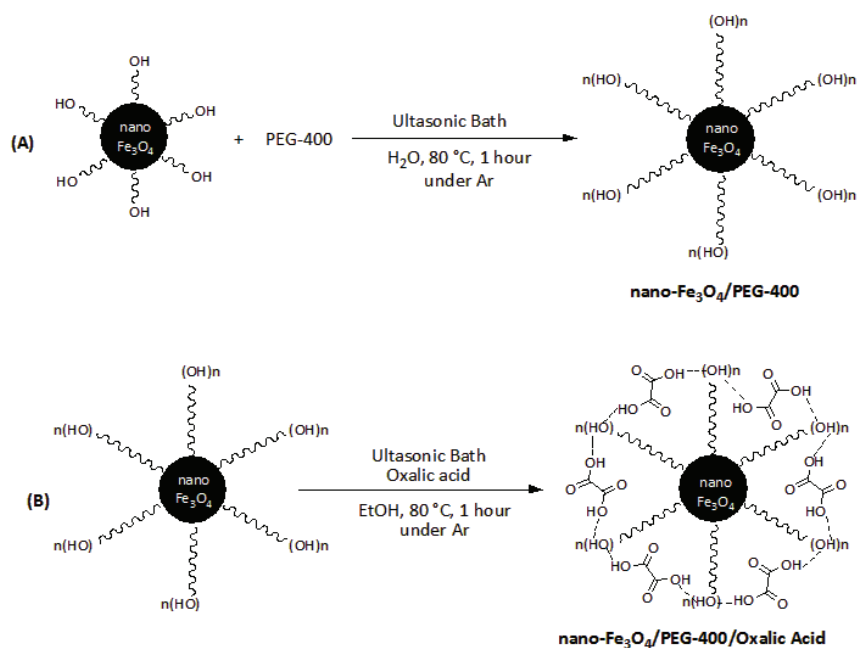
Analytical and spectral data are given in the Supplementary material to this paper.

RESULTS AND DISCUSSION

Oxalic acid is a stronger than acetic acid ($pK_{a1} = 1.27$). It was assumed that by addition of oxalic acid to the mixture of benzaldehyde and aniline, the condensation reaction between them would proceed easily for the preparation of imine as an intermediate. However, the results showed that oxalic acid reacts with aniline and produces oxalate precipitation in many cases. Therefore, many aniline derivatives cannot efficiently react with benzaldehydes derivatives. To avoid the preparation of oxalate precipitation, it was decided to use oxalic acid on Fe₃O₄/PEG-400 magnetic nanoparticles. According to method presented in the literature,^{8,32} Fe₃O₄/PEG-400 magnetic nanoparticles were synthesized by the modified preparation approach. After the synthesis nano-Fe₃O₄/PEG-400, oxalic acid was loaded using ultrasonic irradiation onto this magnetic core. Therefore, the magnetic nanoparticles of Fe₃O₄/PEG-400/oxalic acid were successfully prepared, as shown in Scheme 2. The chemical structure of this catalyst was characterized by different methods, *i.e.*, FT-IR, XRD, EDX and SEM. Furthermore, attempts were made to load other organic acids, such as acetic acid, citric acid, succinic acid, phthalic acid and tartaric acid, onto Fe₃O₄/PEG-400, but these attempts were unsuccessful. It seems Fe₃O₄/PEG-400 has a selectivity for loading oxalic acid, which is because of the chemical structure and the molecular size of oxalic acid. Oxalic acid has two carboxyl groups that make strong hydrogen bonds with the hydroxyl groups of PEG-400 loaded on the Fe₃O₄ magnetic core. In addition, the molecular structure of oxalic has an appropriate size for trapping by PEG-400. On the contrary, although succinic acid, phthalic acid and tartaric acid have two carboxyl groups, the size of the molecular structure of these compounds is greater than that of oxalic acid and they cannot be trapped by Fe₃O₄/PEG-400. Moreover, acetic acid has one carboxylic group which cannot make a strong hydrogen bond with Fe₃O₄/PEG-400. Some interaction for the stabilization of oxalic acid on Fe₃O₄/PEG-400 magnetic nanoparticles are shown in Scheme 2.

The FT-IR spectra of nano-Fe₃O₄, nano-Fe₃O₄/PEG-400 and nano-Fe₃O₄/PEG-400/oxalic acid are shown in Fig. 1 (A, B and C, respectively). The FT-IR spectrum of nano-Fe₃O₄ shows bands at 3367 (assigned to O–H stretching vibrations of absorbed water),³³ 1625 (assigned to O–H bending vibration of water

molecules),³⁴ 1399 (assigned to Fe–O stretching vibration),³⁵ 631 (attributed to some amount of maghemite)³⁶ and 581 cm⁻¹ (assigned to the Fe–O bending vibration).³⁷



Scheme 2. The steps for synthesis of nano magnetic Fe₃O₄/PEG-400 and nano magnetic Fe₃O₄/PEG-400/oxalic acid.

The FT-IR spectrum of Fe₃O₄/PEG-400 shows bands at 3366 (assigned to O–H stretching vibrations of PEG-400), 2867 (assigned to C–H stretching vibrations of PEG-400), 1637 (assigned to O–H bending vibration of the absorbed water), 1449 (assigned to C–H bending vibration of PEG-400), 1349 (assigned to O–H bending vibrations of PEG-400), 1248 (assigned to C–O stretch of PEG-400), 1097 (assigned to C–C–O stretching vibrations of PEG-400), 947 (assigned to O–H bending vibration of PEG-400), 631 (attributed to some amount of maghemite) and 579 cm⁻¹ (assigned to the Fe–O bending vibration). The FT-IR spectrum of Fe₃O₄/PEG-400/oxalic acid shows bands at 3367 (assigned to O–H stretching vibrations of PEG-400 and COOH stretching vibrations of oxalic acid), 2870 (assigned to C–H stretching vibrations of PEG-400), 1712 (assigned to C=O bond stretching of the COOH group), 1624 (assigned to O–H bending vibration of the absorbed water), 1384 (assigned to C–H bending vibration of PEG-400), 1304 (assigned to C–O stretch vibrations of PEG-400), 1087 (assigned to C–C–O stretching vibrations of PEG-400), 1036 (assigned to C–C–O stretching vibrations of COOH group), 940 (assigned to O–H bending

vibration of PEG-400), 805 (assigned to O–H bending vibration of COOH group), 631 (attributed to some amount of maghemite) and 553 cm^{-1} (assigned to the Fe–O bending vibration). The spectrum of nano- Fe_3O_4 (Fig. 1A) shows an absorption at 1399 cm^{-1} , which is assigned to Fe–O stretching bond. This absorption does not appear in the spectrum of $\text{Fe}_3\text{O}_4/\text{PEG-400}$ (Fig. 1B). This could be explained by the covering of PEG-400 layer. The existence of PEG-400 layer in the spectrum of $\text{Fe}_3\text{O}_4/\text{PEG-400}$ can be seen by the C–H stretching vibration at 2867 cm^{-1} as well as the 1449 cm^{-1} C–H bending vibration and 1087 cm^{-1} C–C–O stretching vibrations with strong intensity. The data strongly suggest that the Fe_3O_4 nanoparticles were successfully coated with PEG-400 layer. On the other hands, the spectrum of nano- $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$ (Fig. 1C) in comparison of the spectrum of $\text{Fe}_3\text{O}_4/\text{PEG-400}$ (Fig. 1B) shows a peak at 1712 cm^{-1} for C=O bond stretching, as well as the 1036 cm^{-1} C–C–O stretching vibration, and the 805 cm^{-1} O–H bending vibration of the COOH group. These peaks indicate the existence of oxalic acid in $\text{Fe}_3\text{O}_4/\text{PEG-400}$ nanoparticles. Therefore, the data shows that oxalic acid was successfully loaded on $\text{Fe}_3\text{O}_4/\text{PEG-400}$ nanoparticles for preparation of nano- $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$ catalyst. The Fe–O bending vibration was shifted from 579 to 553 cm^{-1} after addition of oxalic acid to $\text{Fe}_3\text{O}_4/\text{PEG-400}$. This red shift would not have happened after addition of oxalic acid, unless the coverage of the Fe particle with PEG molecules was not completed or oxalic acid causes hydrolysis of some Fe–O–C bonds on $\text{Fe}_3\text{O}_4/\text{PEG-400}$ or other unknown reactions.

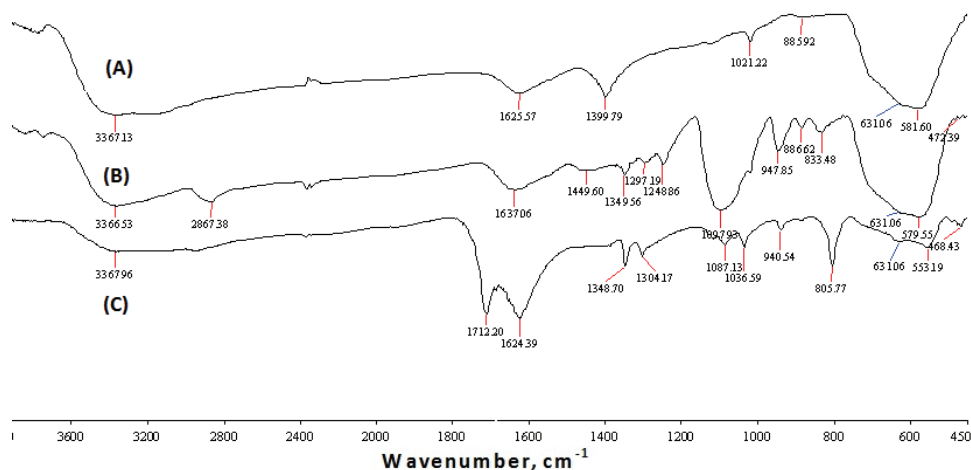


Fig. 1. The FT-IR spectra of the magnetic nano- Fe_3O_4 nanoparticles (A), the magnetic nano- $\text{Fe}_3\text{O}_4/\text{PEG-400}$ nanoparticles (B) and the magnetic nano- $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$ nanoparticles (C).

The XRD patterns of the magnetic nano-Fe₃O₄/PEG/oxalic acid are presented in Fig. 2. In the 2θ range of 20–70°, the peak positions are indexed as (220), (311), (222), (400), (422), (511) and (440). The diffraction peaks suggest the particles are indexed to nano-Fe₃O₄, which is in good agreement with the literature³⁸ and reveals the existence of a magnetic nano-Fe₃O₄ core in the magnetic nano-Fe₃O₄/PEG/oxalic acid.

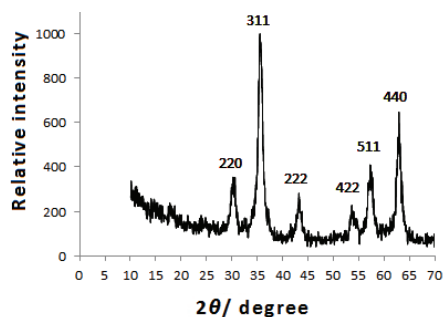


Fig. 2. The XRD patterns of the magnetic Fe₃O₄/PEG-400/oxalic acid nanoparticles.

The SEM images of the nano-magnetic Fe₃O₄/PEG-400 particles Fig. 3A and the nano-magnetic Fe₃O₄/PEG-400/oxalic acid Fig. 3B present particles of size and morphology of nanoparticles. The results show nanoparticles in the range of nanometers of uniform size and spherical shape.

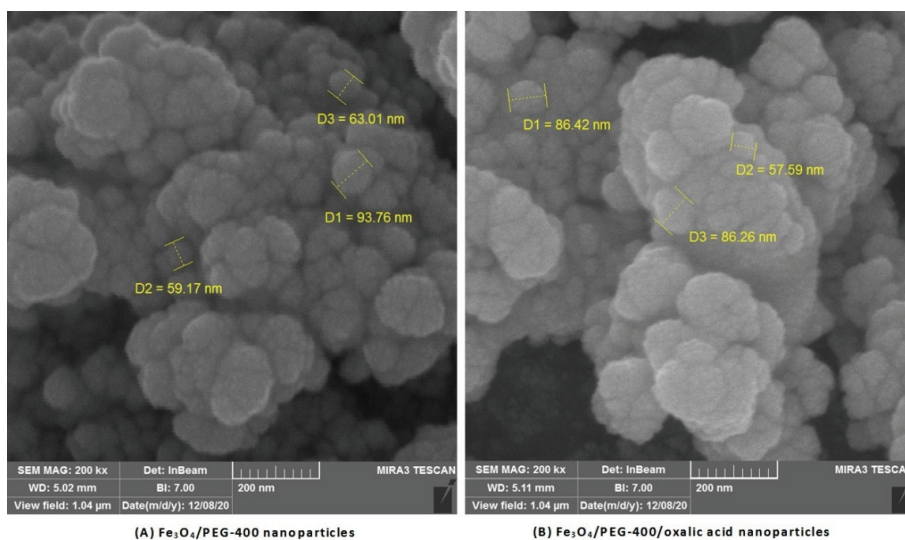


Fig. 3. A) An SEM image of the magnetic Fe₃O₄/PEG-400 nanoparticles and B) an SEM image of magnetic Fe₃O₄/PEG-400/oxalic acid nanoparticles.

The surface chemical composition of magnetic nano-Fe₃O₄/PEG (Fig. 4A) and magnetic nano-Fe₃O₄/PEG/oxalic acid (Fig. 4B) were analyzed by EDX.

The EDX spectrum for nano-Fe₃O₄/PEG shows iron (67.17 wt. %), oxygen (25.71 wt. %) and carbon (7.12 wt. %). It reveals that the iron was from magnetic Fe₃O₄, carbon from PEG-400 and oxygen from Fe₃O₄ and PEG-400. According to these results PEG-400 loaded more than 7 wt.% on the surface of the magnetic Fe₃O₄ nano-particles. Additionally, the EDX spectrum for the magnetic nano-Fe₃O₄/PEG/oxalic acid shows iron (27.04 wt. %) (from Fe₂O₃), oxygen (55.92 wt. %, from Fe₃O₄, PEG-400 and oxalic acid) and carbon (17.03 wt. %, from PEG-400 and oxalic acid). A comparison of the results of the EDX spectra shows that oxalic acid loaded more than 10 wt. % on the surface of the magnetic nano-Fe₃O₄/PEG-400 particles.

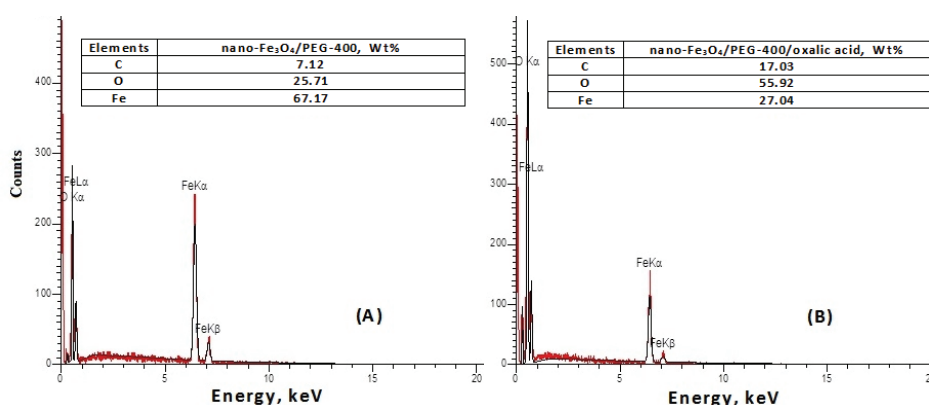


Fig. 4. A) The EDX analysis of the magnetic Fe₃O₄/PEG-400 nanoparticles. B) The EDX analysis of the magnetic Fe₃O₄/PEG-400/oxalic acid nanoparticles.

After characterization of the chemical structure of magnetic nano-Fe₃O₄/PEG/oxalic acid, several reactions for optimum reaction conditions were performed, as shown in Table I. The reaction conditions were carefully examined. It was the best to combine benzaldehyde (1 mmol), aniline (1 mmol), and 0.5 g magnetic Fe₃O₄/PEG/Oxalic acid nano particles as the catalyst in methanol, and the mixture was stirred at room temperature for 30 min. The order of addition components is important to avoid by-products. Then, methyl acetylenedicarboxylate (DMAD) was added, and the reaction was completed after 24 h to give the corresponding pyrrolin-2-ones in 90 % yields as shown in Table I, entry 7–8 and Scheme 1.

The all the new products were characterized by their FT-IR, ¹H-NMR, ¹³C-NMR and mass spectra. The C=O stretching frequency in the FT-IR spectrum of the products appears around 1675–1691 cm⁻¹ (Table II, column 5). The chemical shifts of the CH group in heterocyclic ring (Table II, column 4), which appears at around 5.29 to 6.47 ppm, as a singlet signal. Melting points of the products

(Table II, column 6) were measured and compared with literature data for the known compounds.^{25–30}

TABLE I. Optimization of the reaction conditions for the reaction of benzaldehyde (1 mmol), aniline (1 mmol), DAMD (1 mmol) in the presence of magnetic Fe₃O₄/PEG-400/oxalic acid nano-particles as catalyst at room temperature for the synthesis of 1,5-diphenyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one, as shown in Scheme 1

Entry	Catalyst	Amount	Solvent	<i>t</i> / h	Conversion, % ^a
1	Oxalic acid	1–10 mmol	EtOH	72	30>
2	Oxalic acid	1–10 mmol	MeOH	72	30>
3	Fe ₃ O ₄ /PEG-400	1 g	EtOH	72	0
4	Fe ₃ O ₄ /PEG-400	1 g	MeOH	72	0
5	Fe ₃ O ₄ /PEG-400/Oxalic acid	0.25 g	EtOH	72	50>
6	Fe ₃ O ₄ /PEG-400/Oxalic acid	0.25 g	MeOH	72	50>
7	Fe ₃ O ₄ /PEG-400/Oxalic acid	0.5 g	EtOH	24	90>
8	Fe ₃ O ₄ /PEG-400/Oxalic acid	0.5 g	MeOH	24	100
9	Fe ₃ O ₄ /PEG-400/Oxalic acid	1 g	MeOH	24	100

^aThe conversions were monitored by TLC, eluent: (EtOAc/*n*-hexane:1/1)

The efficiency of this protocol was examined by the reaction of a variety of aromatic aldehydes and arylamines. All the reactions were completed in appropriate times within 24 h in the excellent yields of pure products (90–96 %) as shown in Table II.

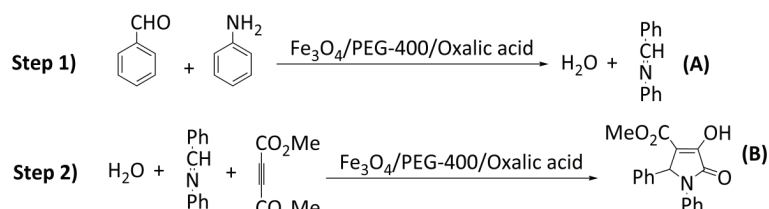
TABLE II. The synthesis of 3-acyl-5-hydroxy-3-pyrrolin-2-one derivatives from aldehydes (Ar), anilines (Ar') and DMAD under the optimized reaction condition (Table 1, entry 2)

Entry	Ar	Ar'	δ_{CH} / ppm	$\nu_{\text{C=O}}$ / cm ⁻¹	m.p., °C	Yield, %
1 ²⁷	Phenyl	phenyl	5.71	1681	173–175	90
2 ²⁵	3-Nitrophenyl	phenyl	5.65	1686	204–206	90
3 ²⁷	2-Chlorophenyl	phenyl	6.47	1686	200–202	92
4 ²⁶	2-Methoxyphenyl	phenyl	5.73	1691	167–169	90
5 ²⁶	2-Bromophenyl	phenyl	6.41	1686	203–205	90
6 ²⁵	4-Bromophenyl	4-bromophenyl	5.29	1684	218–220	95
7 ¹²	Phenyl	4-methoxyphenyl	5.63	1675	170–171	90
8	3-Bromophenyl	4-bromophenyl	5.64	1689	230–231	95
9	4-Methoxyphenyl	4-bromophenyl	5.64	1683	165–167	92
10	2-Methoxyphenyl	4-methoxyphenyl	6.23	1687	210–212	94
11	2-Chlorophenyl	4-bromophenyl	6.38	1683	193–194	95
12	2-Methoxyphenyl	4-methylphenyl	6.25	1686	173–175	90
13	3-Bromophenyl	4-methylphenyl	6.08	1686	184–186	91
14	3-Nitrophenyl	4-bromophenyl	5.69	1679	176–178	91

The magnetic Fe₃O₄/PEG-400/oxalic acid nanoparticles provide a catalyst system that can release hydronium ion smoothly *in situ* to the reaction in the best concentration for the reaction to proceed. The participation of oxalate by this catalyst was not observed during of the reactions. In addition, according to the

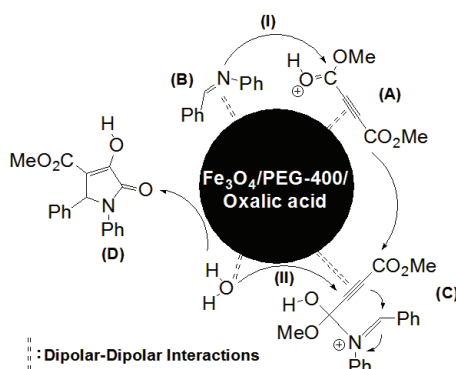
chemical structure of $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$, the OH and CO_2H groups can provide a good polarity on the catalyst surface. On the other hand, all moieties in this reaction are polar. Therefore, they can condense easily on $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$ surface by dipolar–dipolar interactions.

The proposed mechanism is shown in Schemes 3 and 4. The magnetic $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$ nanoparticles catalyst activates aldehyde to produce imine (A) as an intermediate by reaction with aniline (Scheme 3, step 1). Then, the obtained H_2O molecules react with the activated DMAD and the imine moiety to produce the corresponding pyrrolin-2-one (B, Scheme 3, step 2).



Scheme 3. The proposed steps for the synthesis of 1,5-diphenyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one by the magnetic $\text{Fe}_3\text{O}_4/\text{PEG-400}/\text{oxalic acid}$ nanoparticles.

The mechanism for step (1) in Scheme 3 is known. The mechanism for step 2 is shown in Scheme 4. The DMAD is activated by the protonation of the carboxylate group by the catalyst (Scheme 4, A). This process provides the required activation energy for further progress of the reaction. Then, the imine moiety Scheme 4B attacks the protonated carboxylate group of DMAD (Scheme 4, pathway I). Simultaneously, H_2O attacks to β -carbon of the protonated carboxylic acid on DMAD (Scheme 4, pathway II) which produces a stabilized intermediate *via* the intermolecular addition and cyclization (Scheme 4, C). Thereby, the corresponding five-membered heterocyclic compounds (Scheme 4, D) were synthesized by the condensation concerted reaction.



Scheme 4. The modified mechanism of step (2) for the synthesis of pyrrolin-2-ones.

The reusability of nano-Fe₃O₄/PEG-400/oxalic acid catalyst was examined. Recycling of the catalyst is an important characteristic because of environmental and economic concerns. After completion of the reaction, the magnetic nano-catalyst was easily and efficiently separated from the product by an external magnetic field. The nano-Fe₃O₄/PEG/oxalic acid was washed two or three times with acetone and dried at room temperature. It is notable that the recycled catalyst could be used two more times again. For example, in the second and third rounds, the yields of the product (Table II, entry 1) were 87 and 85 %, respectively. However, oxalic acid should be loaded on Fe₃O₄/PEG-400 according to the instruction for the further rounds. Thus the recovered and regenerated catalyst could be useful for reaction with loss of activity.

The efficiency of Fe₃O₄/PEG-400/oxalic acid nonmagnetic catalyst for the synthesis of pyrrolin-2-one derivatives was compared with other reported protocols as shown in Table III. In all cases Fe₃O₄/PEG-400/oxalic acid catalyst has a good potential for the synthesis of this class of compounds.

TABLE III. Comparison of synthesis of 1,5-diphenyl-3-hydroxy-4-methoxycarbonyl-3-pyrrolin-2-one by different reported protocols. All synthesis are green

Entry	Protocol	Yield,%	Time	Reusable cat.	Reference
1	Fe ₃ O ₄ /PEG-400/OA	94	24 h	Yes	This work
2	<i>p</i> -TsOH/EtOH	62	24 h	Non	12
3	TiO ₂ admicelle/H ₂ O	75	18 h	Non	25
4	EtOH/H ₂ O	87	15 h	Non	26
5	Citric acid/US/EtOH	90	20 min	Non	27
6	<i>p</i> -TsOH/MW/EtOH	96	6 min	No	28
7	[bmim]BF ₄ /PEG-400	89	1 h	Yes	29a
8	MW/[BBSI]Cl/Glycol	90	5 min	Yes	29b
9	[BBSI]Cl/ball milling	90	25 min	Yes	29c
10	Fe ₃ O ₄ @SiO ₂ @Propyl-ANDSA/EtOH	87	8 h	Yes	30

CONCLUSIONS

Oxalic acid was have loaded on magnetic Fe₃O₄/PEG-400 for the synthesis of magnetic Fe₃O₄/PEG-400/oxalic acid nanoparticles as a catalyst. The chemical structure of this compound was characterized and approved by different methods (FT-IR, XRD, EDX and SEM). Then, the magnetic Fe₃O₄/PEG-400/oxalic acid nanoparticles were applied for the preparation of a variety of pyrrolin-2-ones, using aromatic aldehydes, anilines and dimethyl acetylenedicarboxylate (DMAD) precursors in one-pot, three-component condensation reaction at room temperature with excellent yields of products (90–95 %). Easy work-up, mild reaction conditions, appropriate catalyst (reusable, economic and eco-friendly), high efficiency and green profile make to this new protocol more attractive for the synthesis of these classes of compounds. Therefore, this new convenient protocol can be added to the list of the currently used methodologies.

SUPPLEMENTARY MATERIAL

Additional data and information are available electronically at the pages of journal website: <https://www.shd-pub.org.rs/index.php/JSCS/article/view/10785>, or from the corresponding author on request.

Acknowledgement. The authors gratefully appreciated the financial support of this work by the research council of Islamic Azad University branch of Mahabad.

ИЗВОД

СИНТЕЗА И КАРАКТЕРИЗАЦИЈА $\text{Fe}_3\text{O}_4/\text{PEG}-400/\text{ОКСАЛНА}$ КИСЕЛИНА МАГНЕТНИХ
НАНОЧЕСТИЦА КАО ХЕТЕРОГЕНОГ КАТАЛИЗАТОРА ЗА СИНТЕЗУ
ПИРОЛИН-2-ОН ДЕРИВАТА

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Наношењем оксалне киселине на $\text{Fe}_3\text{O}_4/\text{PEG}-400$ уз ултразвучно озрачивање успешно је синтетисан нови $\text{Fe}_3\text{O}_4/\text{PEG}/\text{оксална}$ киселина наноманетни катализатор. Применом FT-IR спектроскопије, XRD, EDX и SEM метода испитивана је структура добијеног катализатора. Катализатор је коришћен за синтезу 3-ацил-5-хидрокси-3-пирилин-2-она деривата из одговарајућих алдехида, анилина и диметил ацетилендикарбоксилата (DMAD) у једном реакционом суду и трокомпонентном MCR реакцијом, са високим приносима (90–95 %) током 24 h на собној температури. Добијено је 14 узорака. Једном употребљени катализатор може се са успехом употребити још два пута без регенерације. Описани метод има добар еколошки профил. Поред тога, описана истраживања представљају побољшање механизма за реакције овог типа. Хемијска структура добијених једињења одређена је на бази FT-IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ и масених спектра.

(Примљено 21. маја, ревидирано 5. августа, прихваћено 10. августа 2021)

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