Green approach for the regioselective synthesis of β -thiol-1,4-disubstituted-1,2,3-triazoles using $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ as a novel and efficient magnetically recoverable nanocatalyst

Ronak Eisavi (✉ roonak.isavi@gmail.com)

Payame Noor University

Fereshteh Ahmadi

Payame Noor University

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Abstract

The magnetic nanoparticles of Fe_3O_4 were synthesized through a solid-state reaction of hydrated iron (III) chloride, hydrated iron (II) chloride and NaOH, and then purified by calcination at high temperature. To protect ferrite nanoparticles from oxidation and agglomeration, as well as to manufacture a novel catalytic system of anchored copper on the magnetic substrate, the Fe_3O_4 was core-shelled by adding tetraethyl orthosilicate. Next, the prepared $\text{Fe}_3\text{O}_4@\text{SiO}_2$ was supported by phosphomolybdic acid (PMA) as the second layer of nanocomposite at 80 °C after 30 hours. Eventually, the new nanocomposite of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ was successfully synthesized by adding copper (II) chloride solution and solid potassium borohydride. The structure of magnetic nanocatalyst was acknowledged through different techniques such as EDS, VSM, XRD, TEM, FT-IR, and FESEM. The synthesis of β -thiolo/benzyl-1,2,3-triazoles from various thiiranes, terminal alkynes and sodium azide was catalyzed by $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocomposite in aqueous medium. In order to obtain the optimum condition, the effect of reaction time, temperature, catalyst amount and solvent was evaluated. The recycled catalyst was used for several consecutive runs without any loss of activity.

Introduction

Multicomponent reactions (MCRs) are potent synthetic procedures for the convenient formation of complex organic molecules with structural variety and molecular complexity in one-pot and in one-step method, in which all reactants, reagents and catalysts are added simultaneously under the same reaction conditions. From view point of green chemistry, these reactions are of particular importance due to the significant reduction in the amount of solvents and energy required to separate and purify the intermediates. Moreover, MCRs play considerable roles in various research fields such as synthetic organic, biomedical, industrial chemistry, pharmaceutical and drug discovery research ¹⁻⁴.

The Huisgen 1,3-dipolar cycloaddition of azides and terminal alkynes has been identified as click chemistry. Click reactions are fast, simple to use, easy to purify, eco-friendly, and regiospecific which offer high yield products in a short reaction time under mild conditions. The Huisgen 1,3-dipolar cycloaddition has found utilizations in a vast diversity of research areas, including pharmaceutical sciences, organic synthesis, and polymer chemistry ⁵.

1,2,3-Triazoles are a very valuable class of heterocycles that have received special attention in recent decades because of their biological and pharmacological activities such as antimicrobial ^{6,7}, antibacterial ⁸, antitubercular ⁹, analgesic ¹⁰, local anaesthetic ¹¹, anticancer ¹², anti HIV ¹³, antifungal ¹⁴, antiallergic ¹⁵, anticonvulsant ¹⁶, antiproliferative ¹⁷, antiviral, antioxidants ¹⁸, antimalarial ¹⁹ and anti-inflammatory ²⁰.

In recent years, one-pot click synthesis of β -hydroxy-1,2,3-triazoles from azides, epoxides and terminal alkynes has been reported in the presence of different copper catalysts ²¹⁻³⁰. The strained three-

membered heterocycles such as epoxides, thiiranes and aziridines are easily ring opened by various nucleophiles such as azides and amines. However, the synthesis of 1,2,3- triazoles from epoxies using azides and alkynes has been studied in a limited way, and the three-membered thiiranes have not been used except in one case recently reported ³¹.

Recently, ferrite nanoparticles due to recovery and reusability have received great attention in biomedicine ^{32–34} and modern catalysis research ^{35–38}. Compared to the general separation, magnetic separation has appeared as a powerful, efficient, easy and rapid separation method ³⁹.

Although nano-ferrites are promising class of the catalysts, but their surfaces are hydrophobic with very potent magnetic attractions and high surface to volume ratio, and they always suffer from adsorption troubles due to their high potential of self-aggregation. On the other hand, they are involved in other problems such as low quantity of functional groups on the surface, which disrupts their performance ^{40,41}. In order to stabilize them against oxidation, corrosion and aggregation, their surface are modified with organic or inorganic materials. The surface of nano-ferrites could be improved by use of different materials such as polymers, bio molecules, silica, metals, metal oxides, surfactant and etc. ⁴².

Polyoxometalates (POM) are composed of transition metal oxide anions of molybdenum, tungsten and vanadium. This category of compounds bond between small species of metal oxides and bulk solid oxometalates. Their exclusive attributes such as vast physical and chemical adaptability, optical and acidic activities as well as reducing and oxidizing capabilities turn them into the excellent compounds for research on the metal oxide activities ⁴³. phosphomolybdic acid (PMA) is one of the well-known polyoxometalates, which is commercially available and affordable ⁴⁴. But, the use of PMA is restricted because of its disadvantages including small surface area, low stability, dissolution effects ⁴⁵ and destruction in aqueous media ⁴⁶. Moreover, it has a high miscibility in polar solvents, so it is very difficult to separate and recover, which limits its application ⁴⁷.

In order to prevail these obstacles, PMA is embedded on useful support materials such as silica ⁴⁸, positively charged polymer chains ⁴⁹, metal cations (Cs, Co, Fe etc.) ^{50–52}, and carbon ⁵³. The PMA properties such as high solubility, strong acidity and high negative charge, facilitates its anchoring on any support in various solvents ⁵¹.

Considering all these aspects, and in continuation of our previous works ^{54–60}, herein we wish to introduce Fe₃O₄@SiO₂-PMA-Cu nanocomposite as an efficient and novel catalyst, where PMA clusters are found to be anchored on Fe₃O₄@SiO₂ surface and copper nanoparticles are supported on the PMA surface. The new synthesized nanocomposite was utilized in three-component synthesis of β -thiol-1,4-disubstituted-1,2,3 triazoles from sodium azide, thiiranes, and terminal alkynes as a green and recyclable magnetic catalyst (Fig. 1).

Results And Discussions

Synthesis of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$. Immobilization of catalysts on the surface of Fe_3O_4 nanoparticles, compared with nonmagnetic supports, increases the dispersion of effective sites of catalyst, as well as provides the sufficient magnetic properties for easy separation of catalyst from the reaction mixture and thus improves the activity of the surface modified catalyst. To protect the catalyst surface against oxidants and corrosive agents and also to prevent aggregation of its particles, the surface of Fe_3O_4 was coated with silica layer. In addition, the silica layer through its shell thickness, stabilizes the catalyst and controls its particle size and interparticle interactions, as well as improving its surface effects.

Supporting polyoxometalates onto solid materials and decorating them into suitable porous supports such as metal oxides and MNPs is one of the most effective methods for improving their performance, which is achieved by increasing their active centers and reusability of these heterogeneous materials ⁶¹. The heterogenization of phosphomolybdic acid on silica coated nanomagnetic materials enabled us to overcome the limitations involved in the separation and recycling of homogeneous PMA. On the other hand, heteropolyacids such as PMA ($\text{H}_3\text{PMo}_{12}\text{O}_{40}$) have unique structures with a wide range of coordination positions comprising oxygen atoms, which are appropriate for anchoring the single atoms such as copper particles ⁶². Since there are several possible coordination sites on the surface of PMA, it was selected as the support to trap the single metal atoms of copper in this study. The use of atomic catalysts leads to saving the quantity and cost of precious metals, because they increase the efficiency and activity of the catalyst dramatically.

The nanoparticles of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ were synthesized in a four-step procedure (Figure 2). First, Fe_3O_4 was prepared using solid-state reaction of $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, NaOH , and NaCl in an agate mortar. The crude powder was *calcined* at 700 °C, and then Fe_3O_4 particles were acquired with high purity. Coating of silica layer on the surface of Fe_3O_4 nanoparticles was achieved by sonication of a Fe_3O_4 suspension in an alkaline $\text{NH}_3 \cdot \text{H}_2\text{O}$ solution of tetraethyl orthosilicate (TEOS). Then, PMA was added to a suspension of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ in ethanol, while being dispersed by sonication. In order to synthesize $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$, the prepared particles of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA}$ were added to a solution of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ in water and then the KBH_4 powder was gradually added, while the mixture was strongly stirred. Eventually, the dark brick-red sediment of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ was separated magnetically and then washed with distilled water, and dried at room temperature under air atmosphere.

The different techniques such as FT-IR, X-ray diffraction (XRD), energy dispersive X-ray spectrometer (EDS), field emission scanning electron microscope (FESEM), transmission electron microscopy (TEM), vibration sample magnetometer (VSM), and inductively coupled plasma optical emission spectrometry (ICP-OES) analyses were applied for characterization of new synthesized $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocatalyst.

Catalyst characterization

Vibration sample magnetometer (VSM). To confirm magnetic property of the synthesized $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$, VSM analysis was carried out (Fig. 3). As it is revealed in Fig. 1, the saturation magnetization (M_s) of the magnetic catalyst was 2.95 emu g^{-1} and hysteresis phenomenon was not found. The magnetization curve quickly rises without showing any remanence or coercivity, and the sample displays a typical superparamagnetic behavior of soft magnetic materials at room temperature. The superparamagnetic property of these nanoparticles is a vital feature in their application, because it prevents accumulation and aggregation of particles and enables them to re-disperse in the absence of a magnetic field immediately. The saturation magnetization (M_s) amount of the $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ MNPs was appropriate and the separation of the catalyst nanoparticles was easily carried out by using an external magnet.

FT-IR spectrum. Figure 4 shows the FT-IR spectrum of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocatalyst. The absorption peaks at 3449 and 3358 cm^{-1} are assigned to the stretching vibration of H_2O molecules and indicates the OH groups on the surface of the magnetic nanoparticles and hydroxyl groups in PMA structure respectively. The band around 1627 cm^{-1} corresponds to the bending mode of H_2O molecules. The presence of SiO_2 is confirmed by the stretching and bending vibrations of Si-O. The absorption bands at 803 and 1097 cm^{-1} are related to Si-O-Si stretching vibrations, and the band observed at 478 cm^{-1} belongs to the bending vibration of SiO_2 [59]. The peak at 950 cm^{-1} belongs to the Mo-O stretching vibrations, which confirms the existence of phosphomolybdic acid ⁶³. The formation of Fe_3O_4 nanoparticles was confirmed by the absorption band at 561 cm^{-1} which corresponds to the vibration of metal oxide bonds (Fe-O).

X-ray diffraction (XRD). The X-ray diffraction (XRD) pattern of the synthesized $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ magnetic nanocomposite is shown in Fig. 5. As can be seen, the particle structure of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ is amorphous due to the coating of the ferrite surface with layers of silica, phosphomolybdic acid and copper nanoparticles, and the wide peaks confirm the small size of the particles at the nanoscale. In the XRD pattern of nanocomposite, all the peaks of Fe_3O_4 , SiO_2 , PMA and Cu nanoparticles are detectable. The lines (220), (311), (400), (422), (511), (440), (620) and (533) related to $2\theta = 32.88, 35.64^\circ, 44.11^\circ, 53.43^\circ, 57.60^\circ, 64.01^\circ, 71.95^\circ$ and 75.01° respectively, are assigned to the diffraction of Fe_3O_4 crystals. These peaks are compatible with the standard data (JCPDS: 00-43-0317) ⁶⁴. The significant diffraction peaks are observed in case of PMA at $2\theta = 8.95^\circ, 18.49^\circ, 26.43^\circ, 27.65^\circ$ and 28.84° corresponding to (011), (202), (141), (311) and (312) crystallographic planes respectively (JCPDS: 00-043-0317) ⁶⁵. The broad peak at $2\theta = 22.90^\circ$ is related to the amorphous SiO_2 shell on the surface of Fe_3O_4 ⁵⁹. The copper diffraction peaks were compared with the standard sample (JCPDS 04-0836), and peaks appearing at $2\theta = 43.71^\circ, 50.70^\circ$, and 74.32° corresponding to the (111), (200), and (220) planes respectively, revealed the excellent agreement of the synthesized sample with its standard sample ³¹.

TEM, FESEM and EDS of $\text{Fe}_3\text{O}_4 @\text{SiO}_2 \text{-PMA-Cu}$. TEM and FESEM techniques were used to determine the morphology and size distribution of the nanocatalysts. TEM images of the $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$

nanocomposite are shown in Fig. 6. TEM images show that black and spherical Fe_3O_4 nanoparticles were synthesized at the nanoscale and coated with a dark gray silica layer, and the silica layer is entirely coated with phosphomolybdic acid. The PMA layer is visible in light gray. The TEM images also display that very small spherical Cu nanoparticles have been successfully deposited on the PMA layer and completely surround the outer surface of the catalyst.

Figure 7 shows FESEM images of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ that approve the formation of nanocomposite, and small amounts of agglomerates were observed in the $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ surface due to the modification of the catalyst surface with non-magnetic layers and decreased magnetic properties. The information obtained from the FESEM images is consistent with the XRD and TEM data.

The chemical composition and percentage of nanocomposite elements were acknowledged using EDS data (Fig. 8). In this spectrum, Cu, Mg, Fe, and O signals are detectable. The weight percentage of the elements indicates that the expected nanocomposite has been successfully synthesized. In addition, the percentage of copper nanoparticles in the structure of the composite is remarkable. The exact concentration of Fe, Mo, and Cu was also determined by ICP-OES and the resulting amounts were 31.16, 9.2 and 25.84 wt% respectively. These values are consistent with EDS data.

Synthesis of β -thiol-1,2,3-triazoles in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocatalyst. The reaction of styrene episulfide, sodium azide and phenyl acetylene was chosen as model reaction and the synthesis of 2-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethane-1-thiol was optimized under different conditions. The various empirical factors such as temperature, catalyst quantity, solvent, reaction time and the amount of reactants were examined, and the acquired results were provided in Table 1. The desired result in terms of product yield, time and reaction conditions was achieved by use of styrene episulfide (1 mmol), sodium azide (1.2 mmol), phenylacetylene (1 mmol) and $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ (0.1 g) as catalyst in water at 55 °C (Table 1, entry 4). According to the results of experiments, the presence of catalyst was essential to accomplish the reaction and no reaction was performed in the absence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ even after 10 h (entry 1). The catalyst amount was optimized using different quantities of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocomposite (0.05, 0.08, 0.1 and 0.2 g), and 0.1 g of catalyst gave the eligible outcome. The product yield and reaction time were strongly influenced by the concentration of catalyst, so that by increasing the amount of catalyst from 0.05 to 0.1 g, the product yield and reaction rate increased dramatically (entries 2–4). The higher amount of catalyst had no effect on the product yield (entry 5).

The effect of various polar and non-polar solvents on reaction was examined. The polar solvents such as H_2O , CH_3CN , EtOH, MeOH, EtOAc and DMF were efficient and useful whereas non-polar solvents were not appropriate for this purpose (entries 6–13). Water as a green and eco-friendly solvent was the most privileged choice because the yield of the product in water was higher than all other solvents (entry 4).

In order to investigate the effect of temperature, the reaction was tested at different temperatures. The reaction result was not desirable at room temperature (25 °C) and the product yield was low after 9 h (entry 14). As a result of raising the temperature to 45°C, the experimental data improved and the product

yield increased by 72%, and the reaction time was reduced to 4 hours (entry 15). Further raising the temperature to 55 ° C significantly improved the product yield as well as reduced the reaction time (entry 4).

In order to study the catalytic activity of nanocomposite components in the reaction of styrene episulfide, sodium azide and phenylacetylene to give 2-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethane-1-thiol, the reaction was evaluated separately using PMA, Cu and Fe₃O₄ under the optimal conditions. The results of experiments indicated that although the presence of Fe₃O₄ and PMA leads to increase the efficiency and catalytic activity of the nanocomposite, but the fundamental catalytic role is played by copper nanoparticles (entries 16, 17 and 18).

Table 1. Reaction of styrene episulfide with phenylacetylene and sodium azide catalysed by Fe₃O₄@SiO₂-PMA-Cu under different conditions^a

Entry	Fe ₃ O ₄ @SiO ₂ -PMA-Cu (g)	Solvent	Time (h)	Temperature (°C)	Yield (%) ^b
1	-	H ₂ O	10	55	0
2	0.05	H ₂ O	6	55	45
3	0.08	H ₂ O	6	55	75
4	0.1	H₂O	1.5	55	98
5	0.2	H ₂ O	1.5	55	98
6	0.1	CH ₃ CN	4	82	60
7	0.1	EtOH	4	78	65
8	0.1	MeOH	4	65	65
9	0.1	EtOAc	4	77	70
10	0.1	DMF	4	100	60
11	0.1	THF	15	60	0
12	0.1	<i>n</i> -Hexane	15	68	0
13	0.1	CCl ₄	15	77	0
14	0.1	H ₂ O	9	25	40
15	0.1	H ₂ O	4	45	72
16 ^c	0.1	H ₂ O	6	55	Trace
17 ^d	0.1	H ₂ O	6	55	Trace
18 ^e	0.1	H ₂ O	2	55	91
^a All reactions were performed using styrene episulfide (1 mmol), phenylacetylene (1mmol) and sodium azide (1.2 mmol). ^b Isolated yields. ^c Catalysed by Fe ₃ O ₄ nanoparticles. ^d Catalysed by PMA. ^e Catalysed by Cu particles					

To evaluate the generalizability of the proposed synthetic method, the synthesis of 1,2,3-triazoles was examined using different thiiranes with electron donating and withdrawing substituents and cyclic thiiranes in the presence of phenyl acetylene, sodium azide and Fe₃O₄@SiO₂-PMA-Cu nanocatalyst (Table 2, entries 1–8). Moreover, the reactivity of aliphatic terminal alkynes as well as 4-methoxyphenyl acetylene with styrene episulfide was investigated in this reaction and the results were satisfactory (entries 9–11). Different triazole derivatives were synthesized from the corresponding thiiranes in high yields without the formation of any by-products.

Recycling of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$. The catalyst recovery was evaluated under the optimized reaction conditions. The magnetic nanoparticles were first collected with a magnet, then thoroughly washed several times with ethyl acetate and distilled water. After washing, they were dried under air atmosphere and reused several times in successive cycles without losing their activity or magnetic property (Fig. 9). The VSM, XRD, FESEM and TEM techniques were used to confirm the structure of the recycled catalyst (Fig. 10). The data obtained from the recovered catalyst and the freshly prepared sample were compared and the results revealed that the catalyst morphology remained constant after several reuses. The ICP-OES analysis of the supernatant liquid after separating the catalyst was applied to determine the leaching extent of Fe, Mo, and Cu during the reaction, and according to the results, no traces of Fe, Mo and Cu metals were observed in the supernatant liquid.

Hot filtration test. In order to confirm the heterogeneous nature of catalyst, a hot filtration test was carried out for reaction of styrene episulfide under the optimized conditions. For this purpose, the catalyst was filtered after 30 min at 100°C and the filtrate was again transferred back into the reaction vessel and reaction was continued for further 3 h. However, no reaction was performed under these conditions and no triazole product was obtained, indicating the absence of copper particles in the reaction vessel.

Comparison of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ catalytic activity with other catalysts. The synthesis of 1,2,3-triazole from thiiranes has not been reported so far, except in one recent case³¹. The advantages of the presented synthetic method were manifested by comparison of click reaction of styrene episulfide, phenyl acetylene and sodium azide with the other reported procedure in the literature. In viewpoints of temperature, reaction time, recoverability and product yield the present procedure is more preferable. The reaction is performed in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ in a shorter time and the product is obtained with higher yield. In addition, the need for a lower temperature to complete the reaction also indicates the higher efficiency of the new nanocatalyst.

The possible mechanism for the synthesis of β -thiol-1,4-disubstituted-1,2,3-triazoles in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ catalyst. The proposed mechanism for synthesis of β -thiol-1,2,3-triazole is consist of two possible pathways (A and B)^{31,66}. In both paths, $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ plays the role of catalyst (Fig. 11). First, the catalyst facilitates the ring opening of thiirane and then accelerates 1,3-dipolar cycloaddition reaction and formation of triazoles. Pathway A shows that initially, a non-covalent interaction between metal and azide is created, followed by activation of thiirane ring with $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ catalyst. Then, azide is transferred from the catalyst to thiirane and 2-azido-2-arylethanthiol is generated through the ring opening. In this step, the thiirane rings bearing aryl substituents prefer to be opened from the more hindered position because the benzyl carbocation resulting from $\text{S}_{\text{N}}1$ type of mechanism (α -cleavage) is more stable; however, the regioselective ring opening of thiiranes with alkyl and allyl groups is carried out from the less hindered carbon via $\text{S}_{\text{N}}2$ type of mechanism (β -cleavage). In the pathway A, in order to confirm the catalytic role of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ in the preparation of 2-azido-2-arylethanthiol from styrene episulfide and sodium azide, the reaction was performed in the absence of catalyst, and only a very small amount of ring opened product was produced. During the reaction, gas

chromatography (GC) and thin layer chromatography (TLC) runs of the reaction mixture were utilized to monitor the consumption of styrene episulfide and sodium azide and the formation of 2-azido-2-phenylethanthiol intermediate. FT-IR spectrum was used for characterization of 2-azido-2-arylethanthiol through stretching frequency of 2097 cm^{-1} corresponding to the azide (Fig. 12). In pathway B, first, the intermediate (I) is generated by insertion of copper nanoparticles of catalyst into the C-H bonds of phenylacetylene. The intermediate (II) is then obtained from the *in situ* reaction of 2-azido-2-phenylethanthiol produced in pathway A and intermediate (I). Next, The Cu-C-triazole (IV) is formed from the 1,3-dipolar cycloaddition between azide and carbon-carbon triple bond of intermediate (II). The formation of acetylide intermediate (I) was confirmed by mixing phenylacetylene and $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ in a separate vessel and evaluating the pH of the water as solvent. A 0.7 Unit decrease in pH after 15 min showed that the coordination of phenylacetylene to copper led to the formation of acetylide intermediate (I) and release the terminal proton to the water. The consumption of phenylacetylene as well as the vanishing of the 2-azido-2-arylethanthiol intermediate, were controlled through the GC and TLC of the reaction mixture. Finally, the Cu-C bond of intermediate (IV) was protonolyzed by aqueous media to afford the β -thiol-1,2,3-triazole (V).

Conclusions

In this research, the synthesis of novel, efficient, robust and reusable $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ magnetic nanocomposite was described. The new synthesized nanoparticles were characterized using various techniques such as FT-IR, XRD, VSM, EDS, TEM and FESEM. After confirming the structure, it was utilized as a practical catalyst for one-pot synthesis of β -thiol-1,4-disubstituted-1,2,3-triazoles from sodium azide, terminal alkynes, and diverse thiiranes in water. The synthesis of 1,2,3-triazole from thiiranes has not been reported so far, except in one case. The mentioned protocol offers several advantages such as reusability and easy separation of the heterogeneous magnetic catalyst, perfect regioselectivity, short reaction times, high product yields, utilizing the green solvent and simple work-up procedure.

Methods

Instruments and materials. All reagents and substrates were bought from the Aldrich (Gallarate, Milan) and Merck (Darmstadt, Germany) Chemical Companies with high quality without any need for further purification. The prepared nanocatalyst was identified by TEM images recorded using an EM10C-100kV series microscope from the Zeiss Company (Germany). FESEM images were obtained employing FESEM-TESCAN. The elemental composition study was performed using the energy dispersive X-ray spectrometer (EDS) analysis on a MIRA3 FE-SEM microscope (TESCAN, Czech Republic) equipped with an EDS detector (Oxford Instruments, UK). The XRD intensities were measured on a Bruker D8-Advanced diffractometer (Cu-K α radiation, $\lambda = 1.54056\text{ \AA}$). Magnetic property of nanocatalyst was evaluated by VSM (Meghnatis Daghigh Kavir Co., Kashan Kavir, Iran) at room temperature. The amount of copper in the catalyst was measured by Perkin Elmer Optima 7300DV ICP-OES analyzer. IR spectra of catalyst and triazole products were recorded on Thermo Nicolet Nexus 670 FT-IR. $^1\text{H}/^{13}\text{C}$ NMR spectra of products

were recorded on a Bruker 500 MHz spectrometer in deuteriochloroform with tetramethylsilane as internal standard. HRMS analyses were carried out in the electron impact mode (EI) at 70 eV. Melting points were also determined on an Electrothermal IA9100 microscopic digital melting point device.

Catalyst preparation

Synthesis of Fe_3O_4 MNPs. Fe_3O_4 MNPs were prepared by a solid-state method based on the reported research ³¹. In a typical experiment, $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (0.398 g, 2 mmol), $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (1.08 g, 4 mmol), NaOH (0.64 g, 16 mmol), and NaCl (0.232 g, 4 mmol) were blended in a mortar and then were milled for 50 min. The beginning of the reaction was accompanied by the release of heat. After a few minutes, the dark brown paste was obtained. The excess salts of the resulting mixture were removed through repeated rinsing with distilled water. The obtained product was placed in oven at 80°C for 2 h, and then purified by calcination at 700°C for 1.5 h to produce the dark brown powder of Fe_3O_4 MNPs.

Preparation of silica coated MNPs ($\text{Fe}_3\text{O}_4@\text{SiO}_2$). Silica coated MNPs of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ were synthesized through an improved sol-gel method ⁵⁹. In a typical procedure, 0.5 g Fe_3O_4 MNPs was added to a mixed solution of ethanol (50 mL), distilled water (10 mL) and $\text{NH}_3 \cdot \text{H}_2\text{O}$ (2.5 mL, 25%) and dispersed using ultrasonication for 1.5 h. Then 1.5 mL TEOS (tetraethyl orthosilicate) was added dropwise to the above mixture and sonicated for a further 15 min. After ongoing stirring at room temperature for 24 h, the yellow $\text{Fe}_3\text{O}_4@\text{SiO}_2$ MNPs were accumulated, repeatedly washed with double distilled water and dried in an oven at 100°C for 22 h.

Preparation of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -PMA. In order to synthesize the phosphomolybdic acid (PMA) immobilized on the surface of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ nanoparticles, $\text{Fe}_3\text{O}_4@\text{SiO}_2$ (0.5 g) was first suspended in ethanol (20 mL) and then dispersed by ultrasound for 30 min. Next, the solution of PMA (0.5 g) in ethanol (5 mL) was prepared and gently added dropwise to the suspension. The resulting brick-red mixture was stirred for 30 h under inert atmosphere of nitrogen while heating at 80°C. The magnetic nanocomposite of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -PMA was collected by a magnet, washed several times with distilled water and dried at 60°C for 20 h. The $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -PMA nanocomposite was obtained as a soft brick-red powder.

Synthesis of $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -PMA-Cu MNPs. To anchor the copper nanoparticles on the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -PMA, first, $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.68 g, 4 mmol) was dissolved in distilled water (50 mL) and then 1 g $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -PMA was added to it and the mixture was stirred vigorously for 30 min. Next, 0.1 g potassium borohydride powder (KBH_4) was gradually added to the mixture at room temperature and stirred for 1 hour to reduce Cu^{2+} cations to copper nanoparticles. The obtained $\text{Fe}_3\text{O}_4@\text{SiO}_2$ -PMA-Cu nanocomposite was washed three times with double distilled water and after drying under air atmosphere, it was collected as a dark brick-red powder.

Conversion of epoxides to thiiranes using thiourea under solvent-free conditions: general procedure. The different thiiranes bearing electron-donating or -withdrawing substituents were synthesized using

previously reported procedure⁶⁷. In a typical experiment, a mixture of epoxide (1 mmol) and alumina supported thiourea (0.8 g, 25% w/w) was placed in an agate mortar and milled for the required time at room temperature. The reaction completion was tracked by TLC utilizing *n*-hexane/ethylacetate (10:2) eluent. After accomplishing of the reaction, the contents of the mortar were washed with ethylacetate and then filtered. The solvent containing thiirane was evaporated to produce the pure thiirane as a pale yellow oil.

Synthesis of β -thiol-1,2,3- triazoles from thiiranes in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocatalyst: a general procedure. To a prepared mixture of thiirane (1 mmol), terminal alkyne (1 mmol), NaN_3 (0.078 g, 1.2 mmol) and H_2O (5 mL) in a round-bottomed flask equipped with a magnetic stirrer and condenser, 0.1 g of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocomposite was added. The mixture was stirred at 55 °C for an appropriate time (1.5–3.5 h). The reaction process was tracked using TLC and *n*-hexane/ethylacetate (10:2) eluent solvent. After performing the reaction, the $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanoparticles were accumulated utilizing an external magnet and reused in the consecutive cycle. After extraction of the aqueous layer with ethyl acetate and drying over anhydrous sodium sulfate, the organic solvent was evaporated under vacuum and the crude 1,2,3-triazoles were produced. The obtained products were recrystallized with EtOH/ H_2O (1:1) to give the pure β -thiol-1,4-disubstituted-1,2,3-triazoles in 85–98% yield (Table 2). The structure of the products was confirmed using HRMS (EI), ^1H NMR, ^{13}C NMR and FT-IR techniques. The spectra of the products as well as their spectral information are given in the supplementary section.

Recycling of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocatalyst. In order to recycle the catalyst, first, magnetic nanoparticles were collected utilizing an external magnet and washed three times with ethyl acetate and distilled water, and dried under air atmosphere. The dried nanoparticles of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ were reused in the next cycle without any significant loss of catalytic activity or magnetic properties.

Declarations

Data availability

All data from this study are included in the article and the Supplementary Information File.

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Author Contributions

R. Eisavi supervised the study, designed the research framework and carried out the data analysis. F. Ahmadi conducted experiments. The final manuscript has been written by R. Eisavi with contributions from F. Ahmadi.

Additional Information

Supplementary information. The HRMS (EI), ^1H NMR, ^{13}C NMR and FT-IR spectra of the products as well as their spectral information are given in the supplementary section.

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Tables

Tables 2 is available in the Supplementary Files section.

Figures

Figure 1

Preparation of β -thiol-1,2,3-triazoles from various thiiranes in the presence of $Fe_3O_4@SiO_2-PMA-Cu$ nanocatalyst

Figure 2

Four-step synthesis of $Fe_3O_4@SiO_2-PMA-Cu$

Figure 3

Magnetization curve of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$

Figure 4

FT-IR (KBr) spectrum of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$

Figure 5

X-ray diffraction patterns of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$

Figure 6

TEM images of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$

Figure 7

FESEM of Fe₃O₄@SiO₂-PMA-Cu

Figure 8

EDS of Fe₃O₄@SiO₂-PMA-Cu

Figure 9

Recycling of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ in the synthesis of 2-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethane-1-thiol

Figure 10

(a) Magnetization curve, (b) XRD pattern, (c) FESEM and (d) TEM image of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ in the synthesis of 2-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethane-1-thiol after five cycles

Pathway A:

Pathway B:

Figure 11

The proposed mechanism for the synthesis of β -thiol-1,4-disubstituted-1,2,3-triazoles in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PMA-Cu}$ nanocatalyst

Figure 12

FT-IR spectrum of 2-azido-2-phenylethanthiol intermediate

Supplementary Files

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