International Journal of Heterocyclic Chemistry, Vol. 1, No. 3, pp. 23-34 © Ahvaz Branch, Islamic Azad University

Polyethyleneimine-modified super paramagnetic Fe_3O_4 nanoparticles: An efficient, reusable and water tolerance nanocatalyst.

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Abstract- A novel magnetically immobilized polyethyleneimine (PEI) fabricated by covalently anchoring on silica coated Fe_3O_4 nanoparticles (PEI@Si-MNPs) was prepared. The synthesized catalyst was characterized by Fourier transform infrared (FT-IR), thermogravimetric analysis (TGA), X-ray powder diffraction (XRD), transmission electron microscopy (TEM) and vibrating sample magnetometry (VSM). The immobilized PEI was shown to be an efficient heterogeneous catalyst for the synthesis of spiro-oxindole, benzopyranes and chromene derivatives *via* multi-component reaction (MCR), in water as a green solvent. The catalyst is readily recovered by simple magnetic decantation and can be recycled several times with no significant loss of catalytic activity.

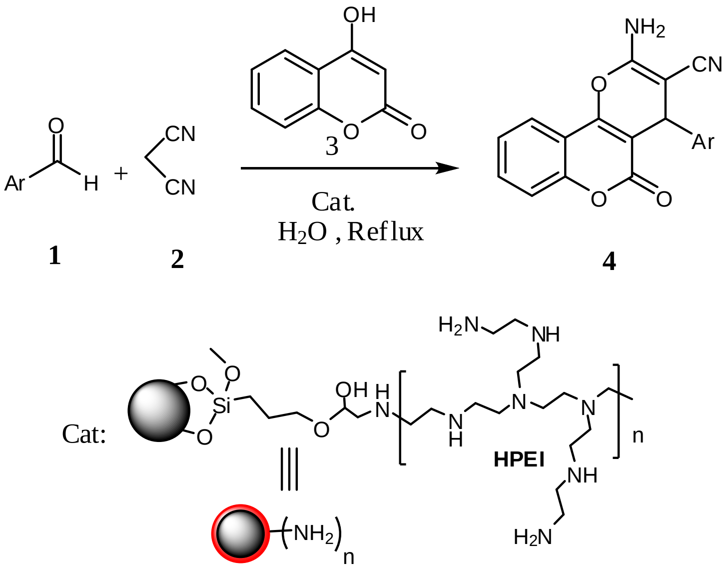
Keywords: Polyethyleneimine (PEI), Magnetic Nanoparticle, benzopyranes, Surface functionalization

Introduction:

Immobilization of homogeneous catalysts on heterogeneous support materials specially nano materials have opened a new hatch on the catalyst science to combines the positive aspects of a homogeneous catalyst (e.g. high activity and selectivity) with those of a heterogeneous catalyst (e.g. stability and ease of isolation and recovery)[1,2]. The introduction of magnetic nanoparticles (MNPs) in a variety of solid matrices allows the combination of well-known procedures for catalyst heterogenization with techniques for magnetic separation. Among various nano materials, magnetite (Fe_3O_4) as vastly powerful and clean recoverable catalyst has attracted considerable interest due to its biocompatibility, non-toxicity, ease of synthesis as well as easy and successive recovery cycles by applying an external magnetic field [3]. Magnetite nanoparticles have been used in various hybrid systems such as magnetite–polypeptide hybrid materials or polymeric shell decorated with catalyst in recent years as a versatile support for diverse classes of organic transformations [4-9].

PEI is a readily available synthetic polycation which have been widely used for drug/gene delivery [10-12], CO_2 adsorption [13], nucleic acid precipitation, protein coagulation/flocculation [14], nucleotide, cell and enzyme immobilization as well as modified surface agent of nanoparticles [15-18]. It was used as a good capping and reducing agent which cause to stabilize the nanoparticles [19]. Several groups have reported various methods for preparation of PEI-coated magnetic particles (PEI-MPs) which were demonstrated to act as efficient transfection agents [20-22]. Although many procedures have been performed to immobilize PEI on solid materials, only a few reports have been recently appeared in the literature about PEI supported magnetic nanoparticles (PEI-MNPs). The first example of non-covalent immobilization of PEI on MNPs was reported by Wang et.al [23]. They have prepared PEI-MNPs via electrostatic adsorption of PEI to negatively charged magnetic particles. The aggregate size of as-prepared PEI-MNPs was adjusted by changing the ratio of PEI to magnetic particles. In the other hand only a few reports have been published on PEI application as a catalyst [24-27]. Amali et al have reported Pd entrapped by highly branched PEI on the surface of Fe_3O_4 as successful catalyst in hydrogenation and ligand-free Suzuki–Miyaura reactions [24]. Gonsalves et al have reported silica grafted polyethylenimine as heterogeneous catalyst for condensation reactions [25]. Recently, gold nanoparticles immobilized in PEI modified polyacrylonitrile fiber show good efficiency in reduction of 4-nitrophenol by $NaBH_4$ [28].

Bearing in mind the important properties of different 2-amino-3-cyano-4H-pyran derivatives in biological and pharmacological areas as well as their potential applications in laser dyes, pigments, cosmetics, optical fluorescence markers, brighteners [29] and the efficiency of PEI as a water soluble and cationic polymer consisting of large number of terminal amino groups, in connection of our previous works [30], we decided to explore on novel magnetically immobilized PEI fabricated by covalently anchoring (PEI@Si-MNPs) for the preparation of chromene derivatives (see Scheme 1).



Scheme1. PEI@Si-MNPs catalyzed one-pot synthesis of benzopyrane derivatives

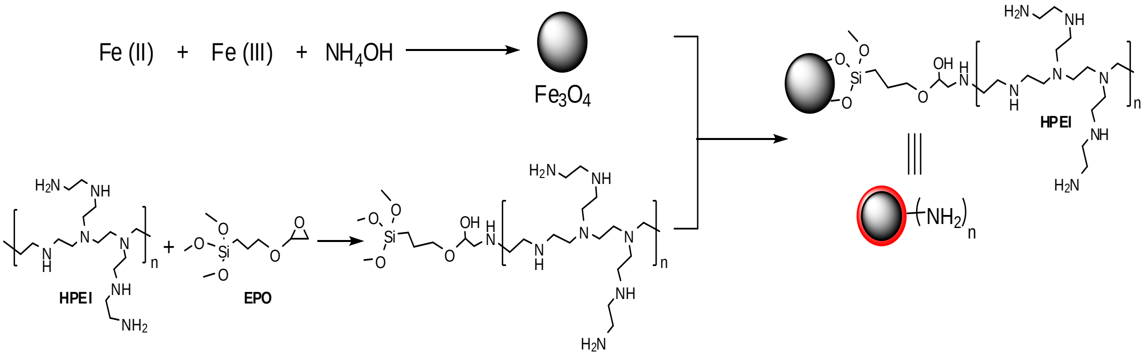
Experimental

General

All chemicals were purchased from Merck (Darmstadt, Germany). Hyper branched PEI (Mw=60,000) were purchased from Sigma-Aldrich (St. Louis, MO, USA). X-ray diffraction (XRD) patterns were recorded with a XPert MPD advanced diffractometer. The magnetic properties of the samples were detected at room temperature using a vibrating sample magnetometer (VSM, Meghnatis Kavir Kashan Co., Kashan, Iran). FT-IR spectra were obtained using Nicolet FT-IR Magna 550 spectrographs (KBr disks) spectrometer. Melting points were measured on a Kofler hot stage apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ on a Bruker 500 MHz spectrometer.

Synthesis of PEI@Si-MNPs

Fe_3O_4 MNPs were synthesized using the chemical coprecipitation method [31]. In order to graft of PEI onto Fe_3O_4 MNPs, EPO (1 mmol) was added to a stirred solution of 150 mL dry toluene containing 1.5 gr of PEI. The resultant mixture was allowed to react at 80 °C for 24 h. To this solution, 2.5 g of Fe_3O_4 MNPs and 25 mL of ethanol were added, and the solution was stirred at 80 °C for 24 h. PEI@Si-MNPs was magnetically isolated by an external magnet and repeatedly washed with ethanol (Scheme 2). Subsequently, it was Soxhleted with ethanol for 24 h to remove un reacted substrates and byproducts, subjected to another round of magnetic separation, and dried at 40 °C for several days [25].



Scheme 2. Schematic representation of the formation of PEI@Si-MNPs

General procedure for Catalytic synthesis of compounds 4

A stirring mixture of an active carbonyl compound (aldehyde, 1 mmol), malononitrile (1.2 mmol), magnetic catalytic system ([PEI@Si-MNPs], 5 mg) and ethylene glycol/water (EG/H_2O 20/80, 2 mL) were sonicated for one minute. To this stirred mixture, 4-hydroxycoumarin (1 mmol) was added. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was allowed to cool at room temperature and diluted with ethyl acetate and the catalyst was easily separated from the reaction mixture with an external magnet and washed twice with ethyl acetate. The combined organic layers were concentrated in vacuum and the residue was purified by recrystallization from ethanol. All compounds gave satisfactory spectral data and they were identical with those reported in the literature [30, 32-38].

Results and discussion:

Characterization of PEI@ Si-MNPs

The as-synthesized PEI@Si-MNPs catalyst was characterized by various techniques. The FT-IR spectrum of PEI@Si-MNPs, shows bands at 1581 and 1457 cm^{-1} assigned to the stretching vibration of C–N and bending vibration of C-H bonds of PEI macromolecular chains respectively, which are chemically linked on the surfaces of MNPs and the bands at around 2924 and 2831 cm^{-1} are attributed to stretching vibration of the aliphatic C-H bands. In addition, the characteristic peaks of Fe-O at 584 cm^{-1} and strong adsorption band at 1029–1023 cm^{-1} of Si-O-Si and Si-OH were also observed (Fig. 1).

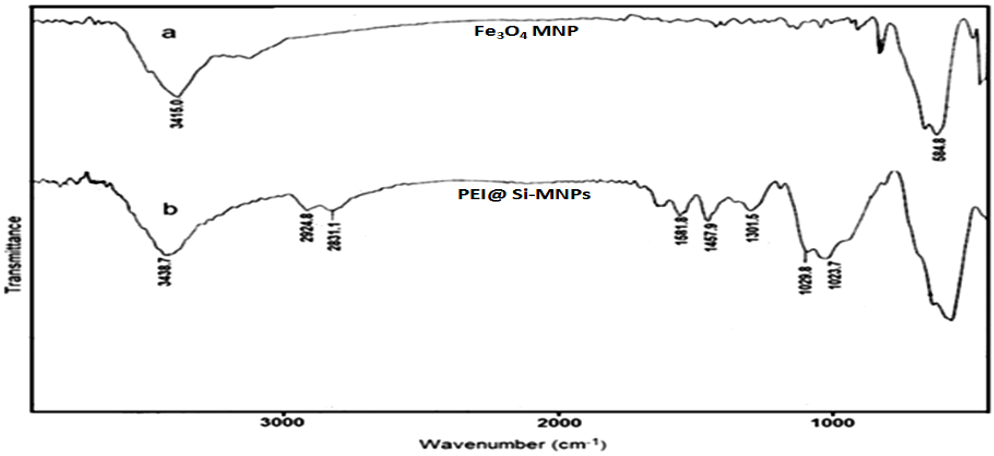


Fig.1. FT-IR spectrum of Fe_3O_4 MNPs and PEI@Si-MNPs

The X-ray diffraction patterns of MNPs and PEI@Si-MNPs are shown in Fig. 2. The position and relative intensity of all the diffraction peaks suitably matched those of standard Fe_3O_4 [39]. The MNPs are in the form of inverse spinel Fe_3O_4 with a face-centered cubic structure, suggesting that the sample has a cubic crystal system. Moreover, no characteristic peaks of impurities were observed in the XRD spectrum. The comparison of the diffraction patterns of MNPs and PEI@Si-MNPs shows that the broadening of these diffraction peaks is reflective of polycrystalline as-prepared MNPs. The Bragg diffraction angles are nearly identical, indicating that the structures of the MNPs are preserved after PEI loading.

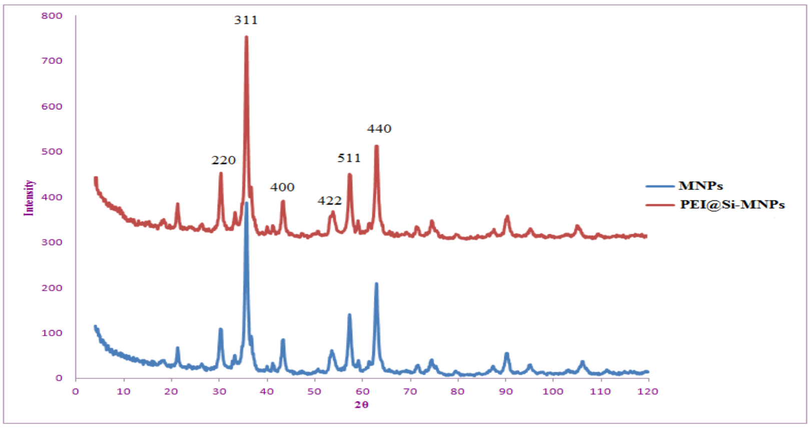


Fig. 2. XRD patterns of Fe_3O_4 MNPs and PEI@ Si-MNPs

The SEM and TEM image of MNPs and PEI@Si-MNPs is presented in Fig. 3, showing that most of the particles have quasi-spherical shape. The average size of MNPs is less than 100 nm and they present uniform particles. These results are in good agreement with the XRD analysis (Fig. 2).

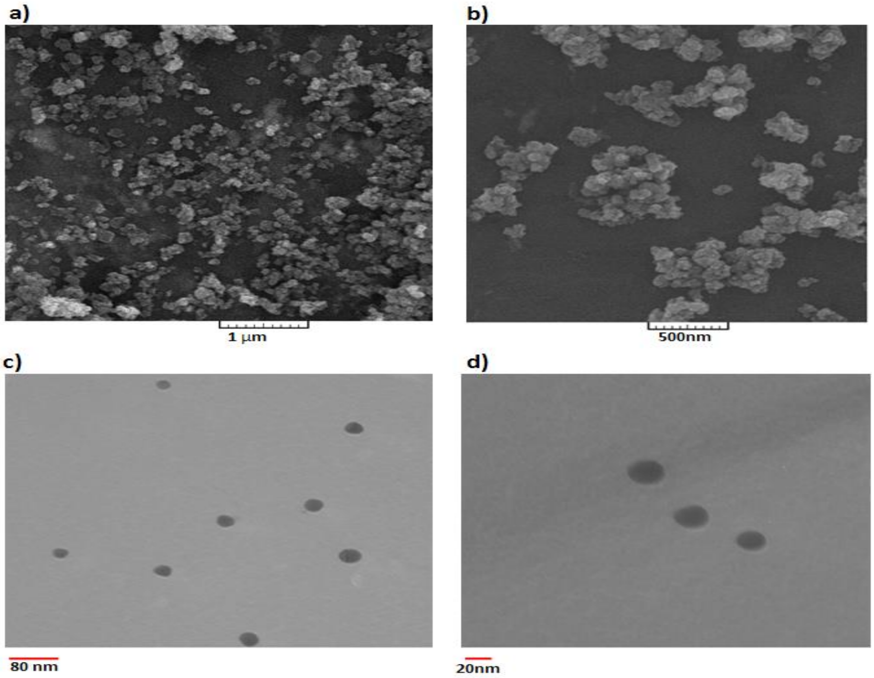


Fig. 3. SEM image of a) Fe_3O_4 MNPs, b) PEI@Si-MNPs and c) and d) TEM image of PEI@ Si-MNPs

There are two weight loss steps in TGA curve of PEI@Si-MNPs (Fig.4a). The first mass loss between 60 to 250 ˚C may be due to removal of surface adsorbed water of the catalyst. The loss of weight at temperatures higher than 250 ˚C can be ascribed to the slow decomposition of the higher-molecular-weight species present in the magnetic nanospheres; EPO and PEI groups. Comparison between the TGA results of Fe_3O_4 MNPs and PEI@Si-MNPs show the percentage of EPO and PEI grafting density is about 20%.

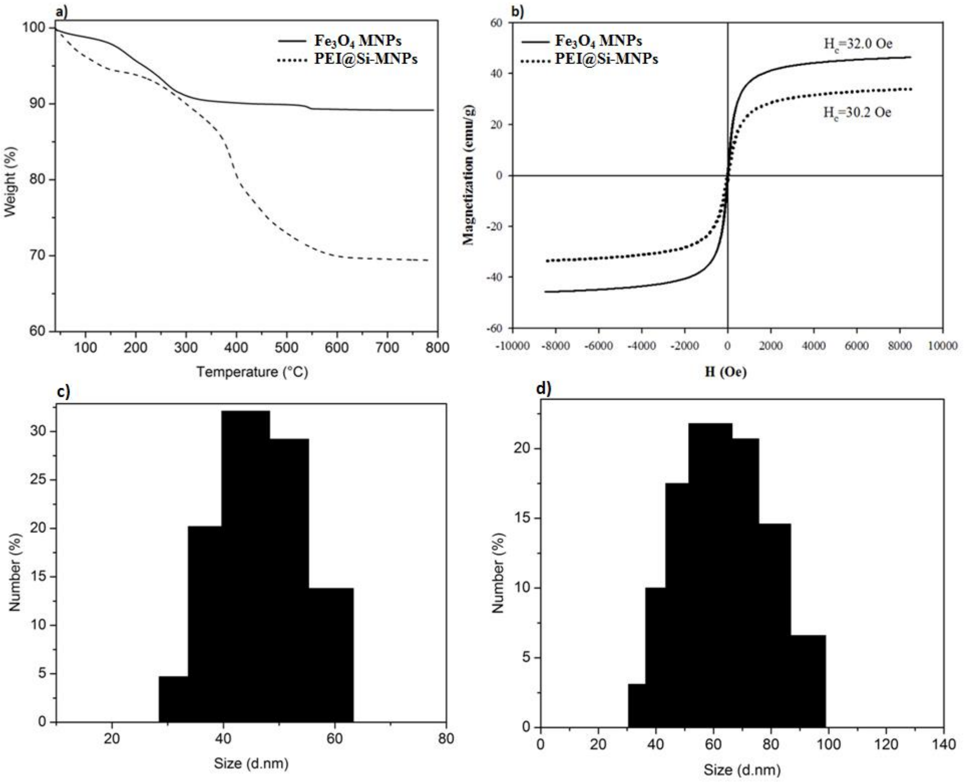


Fig. 4. a) TGA of Fe_3O_4 MNPs and PEI@Si-MNPs, b) Hysteresis loops of MNPs and PEI@ Si-MNPs, c) HDs sizes of Fe_3O_4 MNPs and d) PEI@Si-MNPs

Magnetic measurements for Fe_3O_4 MNPs and PEI@Si-MNPs were performed using a vibrating sample magnetometer (VSM) with a peak field of 8 kOe and their hysteresis curves are presented in Fig. 4b. It could be seen from the loops in Fig. 4b that the specific saturation magnetization (σ_s) and the coercive field (H_c), which represents the force required to rotate the magnetization vector of a magnet out of its equilibrium direction, for the Fe_3O_4 MNPs are 46.4 emu g^{-1} and 32 Oe, respectively. While, those for PEI@Si-MNPs are 30.2 Oe and 33.8 emu g^{-1}, respectively. The decrease in mass saturation magnetization can be ascribed to the contribution of the non-magnetic silica and PEI shell. Although the σ_s values of the PEI@Si-MNPs have decreased; they still could be efficiently separated from solution with a permanent magnet. The HDs sizes of Fe_3O_4 MNPs and PEI@Si-MNPs are obtained in the range of 30–65 and 40–100 nm, respectively (shown in Fig. 4c and 4d). This increase in HD size of aqueous dispersion of MNPs@PEI could be attributed to higher surface positively charged PEI.

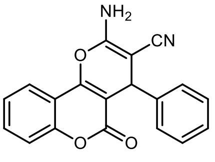
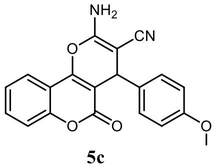
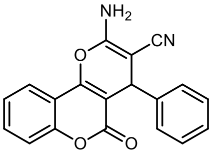
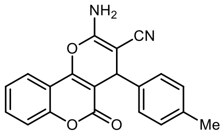
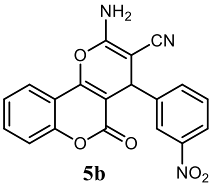
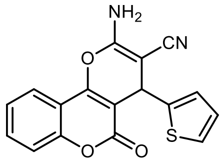
Catalytic synthesis of benzopyranes derivatives

The catalytic activity of PEI@Si-MNPs was investigated for the synthesis of different 2-amino-3-cyano-4H-pyran derivatives using a MCR approach. For a model reaction, the reaction between benzaldehyde, malononitrile, and 4-hydroxycoumarin was chosen in the presence of innocuous solvents. The results confirmed the crucial role of solvent in the dispersion of the nano catalyst and adsorption of reactants on the surface of the nano catalyst which cause to increase the local concentration of reactants around the active sites of the catalyst.

With this result in hand, same procedure was used for the preparation of derivatives in excellent yields by means of three-component reactions of 4-hydroxycoumarin, malononitrile, and various aldehyde catalyzed by mentioned magnetic catalytic system in EG/water at 40 ºC and very short reaction times.

In order to explore the scope and the limitations of this catalytic method, we investigated various aldehydes containing either electron withdrawing or electron donating functional groups under the optimized reaction conditions. The results show that this one pot, three component condensations completed within 50-120 min, with good isolated yields. The results clearly indicate that reactions can tolerate a wide range of differently substituted aldehydes. In addition, it was observed that the reaction of 4-hydroxycoumarin was completed under reflux condition.

Table 1. PEI@Si-MNP catalyzed three-component synthesis of compound 4

Entry	Product	Yield[a]	Time (min)	m.p.[b] (°C)	Entry	Product	Yield[a]	Time (min)	m.p. (°C)
1	 5a	94	60	>250	4	 5c	91	60	221-223
2	 5a	20	10 h[c]	>250	5	 5d	89	55	>250
3	 5b	96	50	>250	6	 5e	81	70	>250

3.3. Catalyst recycling

To evaluate the stability and level of reusability of the catalyst, we decanted the vessel by use of an external magnet and the left used catalyst was washed with ethanol several times to remove residual product, dried under vacuum and reused in a subsequent reaction. A new reaction was then conducted with fresh reactants under similar conditions. It was found that the developed catalyst could be used at least five times and the conversion stayed with no detectable loss, more than 90%. (See Fig. 5). Moreover, the FT-IR spectrum of the recovered catalyst showed no change after using it for five times. This indicates that no leaching of the PEI species occurred from support on using and reusing the catalyst.

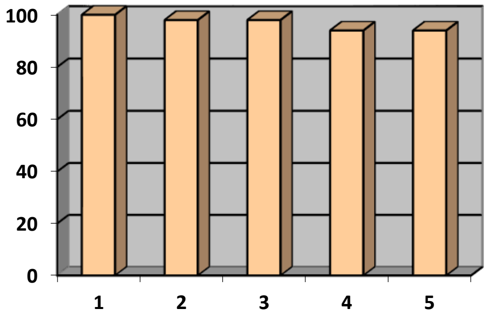


Fig. 5. Catalyst recycling experiments

Conclusions

In summary, we showed that PEI grafted on silica coated Fe_3O_4 nanoparticles fabricated by covalently anchoring, was a novel and effective heterogeneous catalyst for the one-pot synthesis of benzopyranes derivatives from commercially available starting materials. The present method requires remarkably small amounts of non-toxic and environmentally friendly PEI@Si-NMP as catalyst. In addition the aqueous conditions, excellent yields, operational simplicity, practicability, product purity, cost efficiency and environmentally benefits are the worthy advantages of this protocol. The introduced magnetically nano catalyst was highly stable and could be reused in 5 successive runs with no significant structural change and loss of activity. Based on these observations, it could be concluded that this green and cost-effective catalyst, with simple experimental and work-up procedure, which avoids the use of large volumes of hazardous organic solvents, makes it a useful alternative for the scale-up of these three component reactions.

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