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Synthesis and characterization of a novel nano-Fe_3O_4-copoly[(styrene/acrylic acid)/grafted ethylene oxide and its application as a magnetic and recyclable phase-transfer catalyst in the preparation of β-azido alcohols and β-nitro alcohols

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Abstract A facile method was developed for the synthesis of β-azido alcohols and β-nitro alcohols in the presence of a novel nano-Fe_3O_4-copoly[(styrene/acrylic acid)/grafted ethylene oxide (nano-Fe_3O_4-PS-Co-[PAA-g-PEG]) as a phase-transfer catalyst in water. The catalyst was characterized with IR, SEM, and TGA. This procedure offers several advantages, including excellent regioselectivity, high yields, short reaction times, a recyclable catalyst, easy separation of the catalyst through an external magnet, and easy workup.

Keywords Ring opening reaction · Epoxide · β-Azido alcohols · β-Nitro alcohols · Magnetic nanocatalyst · Phase-transfer catalyst (PTC)

Introduction

Due to the difficulties in separating homogeneous catalysts from products and reaction solvents, recycling of these catalysts is complicated and costly, especially when noble and/or toxic metal complexes are used. As such, heterogeneous catalysts have been proposed as a solution. However, during the recovery and recycling of the catalyst from these immobilized systems, similar problems are encountered. Therefore, an efficient technique for facile catalyst separation was needed, and for this reason, magnetic separation was introduced.

Magnetic nanoparticles have now been extensively employed as alternative catalyst supports given their high surface area, resulting in high catalyst loading

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capacity, high dispersion, outstanding stability, and convenient catalyst recycling. Magnetic separation renders the recovery of catalysts from liquid-phase reactions much easier than cross-flow filtration and centrifugation. As the catalysts are usually immobilized on the surface of the magnetic nanoparticles, easy access of reactants to the active sites can also be achieved [1–5].

Phase-transfer catalysis (PTC) is a very useful approach that typically involves simple experimental operations, mild reaction conditions, inexpensive and environmentally benign reagents and solvents, and large-scale reactions [6]. A practical limitation to the phase-transfer method, however, is that many of the catalysts used promote the formation of stable emulsions [7]. Immobilization of the phase-transfer catalyst on an insoluble polymeric matrix can provide a simple solution to this problem.

Poly(ethylene glycol) (PEG) and its derivatives are interesting catalysts and solvents. PEGs are inexpensive and thermally stable, have almost negligible vapor pressure, and are environmentally benign media for chemical reactions [8].

β-Azido alcohols are compounds of interest in organic synthesis as either precursors of vicinal amino alcohols or in the chemistry of carbohydrates, nucleosides, lactams, and oxazolines [9]. Generally, azidohydrins are prepared through the ring opening of epoxides using different azides in suitable solvents. Although the classical protocol uses sodium azide and ammonium chloride, the azidolysis reaction requires a long reaction time (12–48 h), and the azidohydrin is often accompanied by isomerization, epimerization, and rearrangement of products [10].

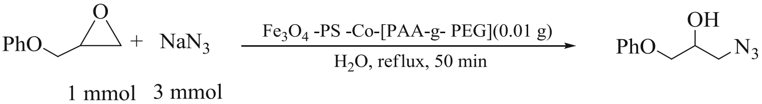
Although a few reagents and catalysts have recently been reported for the conversion of epoxides to β-azido alcohols, [11–18] disadvantages such as long reaction times, low product yields, difficulty in preparation and/or storage of reagents or catalysts, tedious workup, and in most cases, low regioselectivity, clearly necessitate the introduction of new methods for such functional group transformations.

Given the importance of ring-opening reactions of epoxides [19], and in continuation of our efforts in the synthesis of novel catalysts and their application in organic synthesis [20–23], Fe_3O_4-PS-Co-[PAA-g-PEG] was introduced as a novel heterogeneous phase-transfer catalyst for the one-pot preparation of β-azido alcohols under reflux conditions (Scheme 1).

Experimental

General

All commercially available chemicals were purchased from Fluka and Merck companies and used without further purification. Products were characterized by



Scheme 1 One-pot preparation of β-azido alcohols using Fe_3O_4-PS-Co-[PAA-g-PEG] as catalyst

their physical constant and comparison with authentic samples. Reaction monitoring was accomplished by thin-layer chromatography (TLC) on silica gel polygram SIL G/UV254 plates. The IR spectra were recorded on a Bomem MB-Series 1998 FTIR spectrophotometer using KBr pellets for the samples and the catalyst in the range of 4000–400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on a Bruker Avance DPX 400 MHz spectrometer using tetramethylsilane (TMS) as the internal standard. The SEM analyses were carried out using a LEO 1455 VP scanning electron microscope operating at 1–30 kV.

General procedure for the preparation of nano-Fe_3O_4

Nano-Fe_3O_4 was prepared using an improved chemical co-precipitation method [24]. A 500-mL round-bottom flask was charged with $FeCl_2{\cdot}4H_2O$ (3.1736 g, 16 mmol) and $FeCl_3{\cdot}6H_2O$ (7.57 g, 28 mmol) and dissolved in 320 mL of deionized water. The solution was stirred under nitrogen at 80 °C for 1 h, and 40 mL $NH_3{\cdot}H_2O$ (25 %) was rapidly injected into the reaction mixture, which was again stirred under a nitrogen atmosphere for 1 h, and then cooled to room temperature. The precipitated particles were washed five times with hot water and separated by magnetic decantation. Finally, the nano-Fe_3O_4 was dried under a vacuum at 70 °C.

General procedure for the preparation of cross-linked copoly(styrene/acrylic acid)/grafted ethylene oxide

A three-neck round-bottom flask was charged with styrene (104.4 mmol), acrylic acid (75.8 mmol), divinyl benzene (2.1 mmol), and 10 mL H_2O. The flask was equipped with a reflux condenser and a nitrogen atmosphere while it was stirred using a mechanical stirrer. After purging N_2 for 30 min, the mixture was refluxed for 12 h in an oil bath at 70 °C. The white copolymer [cross-linked copoly(styrene/acrylic acid)] was washed with water, methanol and acetone, and was dried at 70 °C for 4 h.

In the next step, the obtained cross-linked copoly(styrene/acrylic acid) (1.6 g) and polyethylene glycol 300 (40 mL) were charged in a round-bottom flask, and 3–4 drops of sulphuric acid (98 %) were added. The mixture was refluxed for 15 h. After cooling to room temperature, the grafted copolymer [cross-linked copoly(styrene/acrylic acid)/grafted ethylene oxide] was filtered using a Büchner funnel and washed several times with plenty of water and acetone. The cross-linked Co (styrene/acrylic acid)-g-PEG, after drying at 70 °C, was 1.97 g, which is equal to 0.19 g PEG per 1 g of the copolymer.

General procedure for the preparation of nano-Fe_3O_4@copoly[(styrene/acrylic acid)/grafted ethylene oxide

In a 50-mL round-bottom flask, Fe_3O_4 (0.1 g) was dispersed in 20 mL acetone and sonicated for 45 min. In another flask cross-linked Co (styrene/acrylic acid)-g-PEG (0.7 g) and 20 mL acetone was similarly sonicated. The two flasks were merged in a

100-mL flask and sonicated for 45 min, and this mixture was refluxed for 2 h. After evaporation of the acetone, the catalyst [nano-Fe_3O_4@copoly[(styrene/acrylic acid)/grafted ethylene oxide] was dried at 70 °C for 2 h. The resulting nanocomposite was stirred in sulfuric acid 1 M to remove any bare nano-Fe_3O_4 and was washed several times with water and methanol and dried in vacuum for an additional 2 h.

General procedure for the preparation of β-azido alcohols in the presence of nano-Fe_3O_4-PS-Co-[PAA-g-PEG]

A 25-mL RBF was charged with epoxide (1 mmol), sodium azide (2 mmol, 0.13 g), nano-Fe_3O_4-PS-Co-[PAA-g-PEG] (0.02 g), and 5 mL deionized water and refluxed in an oil bath for specific lengths of time (5–120 min). Completion of the reaction was indicated by TLC [TLC ethyl acetate/n-hexane (2:5)]. After completion of the reaction (as indicated in Table 2), the catalyst was separated utilizing an external magnet. The product was extracted with diethyl ether (3 × 10 mL), and the organic phase was concentrated and dried using $CaCl_2$. After evaporation of the solvent under reduced pressure using a rotary evaporator, the β-azido alcohols were obtained with 78–99 % yield.

General procedure for the preparation of β-nitro alcohols in the presence of nano-Fe_3O_4-PS-Co-[PAA-g-PEG]

A 25-mL RBF was charged with epoxides (1 mmol), sodium nitrite (10 mmol, 0.69 g), nano-Fe_3O_4-PS-Co-[PAA-g-PEG] (0.02 g) and 5 mL deionized water and refluxed in an oil bath for specific lengths of time (15–45 min). Completion of the reaction was indicated by TLC [TLC ethyl acetate/n-hexane (2:5)]. After completion of the reaction (as indicated in Table 3), the catalyst was separated using an external magnet. The product was extracted with diethyl ether (3 × 10 mL), and the organic phase was concentrated and dried using $CaCl_2$. After evaporation of the solvent under reduced pressure using a rotary evaporator, the β-nitro alcohols were obtained with 70–90 % yield.

Selected spectrum

1-Azido-3-allyloxypropan-2-ol (Entry 3, Table 2) IR (neat): ν_{max} N_3(2103 cm^{-1}); ^1H NMR (400 MHz, $CDCl_3$): δ: 3.45–3.54 (m, 2H), 3.8 (m, 1H), 3.96–4 (m, 2H), 4.18 (s br, 1H), 3.7 (m, 2H), 5.2 (dd, 1H), 5.3 (dd, 1H), 5.8 (dd, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 53.37, 69.87, 71.32, 72.07, 117.36, 134.36 ppm.

Results and discussion

Due to the importance of PTCs in organic reactions and the need to recycle the catalyst, we designed a recyclable PTC capable of enhancing nucleophilic ring-opening reactions. Among PTCs, polyethylene glycol (PEG) is an efficient solvent and also a nonionic surfactant that has terminal hydroxyl groups capable of immobilizing on solid supports. Thus, as shown in the SEM images, Fe_3O_4 nanoparticles 50 nm in size were prepared (Fig. 1).

The Fourier transform infrared spectroscopy (FTIR) spectrum of nano-Fe_3O_4 shows its characteristic Fe–O peak at 570 cm^{-1}. A broad peak at 3400 cm^{-1} is evident, which is due to OH groups on the surface of the nanoparticles (Fig. 2).

In the next step, the random copolymer of styrene/acrylic acid was prepared via suspension free-radical polymerization of styrene (57.3 %) and acrylic acid (41.5 %) in the presence of 1.2 % divinylbenzene (DVB) as cross-linking agent. Deionized water was used as the polymerization medium and dibenzoyl peroxide as radical initiator (Scheme 2).

The next step involved the grafting of PEG 300 to the prepared copolymer. Two methods were investigated. In the first method, copoly(styrene/acrylic acid) was refluxed in the presence of $SOCl_2$ so that carboxylic acid groups were transformed into acid chloride. After refluxing for 2 h, the excess thionyl chloride was distilled off and PEG 300 was added (Scheme 3, reaction A).

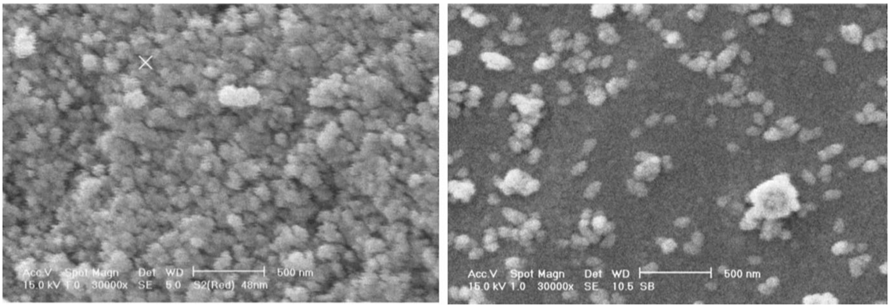


Fig. 1 SEM images of nano-Fe_3O_4

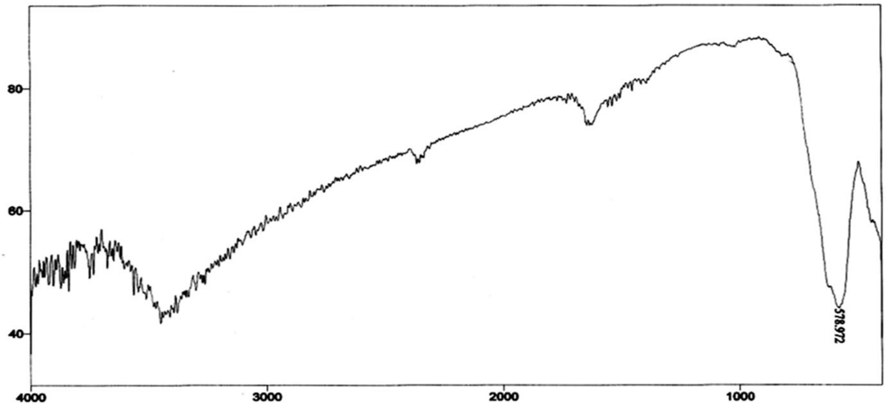
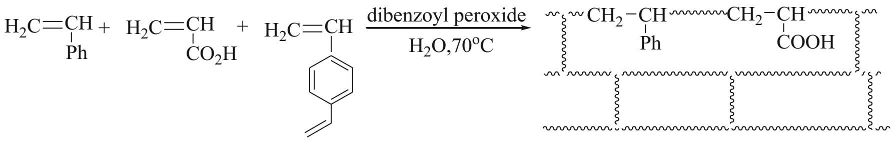
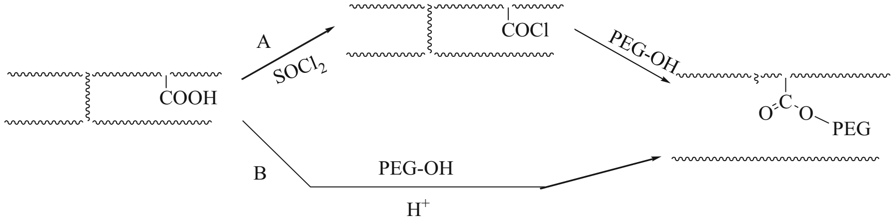


Fig. 2 FTIR spectrum of nano-Fe_3O_4



Scheme 2 Preparation of copoly(styrene/acrylic acid) via suspension free-radical polymerization



Scheme 3 Grafting PEG 300 onto copoly(styrene/acrylic acid) via A and B methods

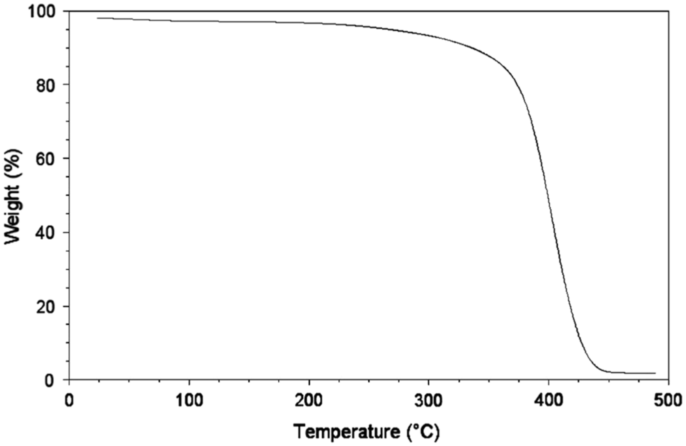


Fig. 3 TGA diagram of copoly(styrene/acrylic acid)/grafted PEG

In the second method, direct esterification was used for immobilization of PEG 300 onto the copolymer in the presence of sulphuric acid as catalyst (Scheme 3, reaction B).

A comparison of the two methods revealed that method A caused the copolymer to be brownish and jelly-like, and some decomposition was seen; therefore, we selected method B. Based on gravimetric analysis, 0.37 g of PEG was grafted onto 1.6 g of copolymer.

To evaluate the thermal stability of the grafted copolymer, thermogravimetric analysis (TGA) was conducted. As shown in the TGA diagram, the grafted copolymer is stable up to 400 °C (Fig. 3).

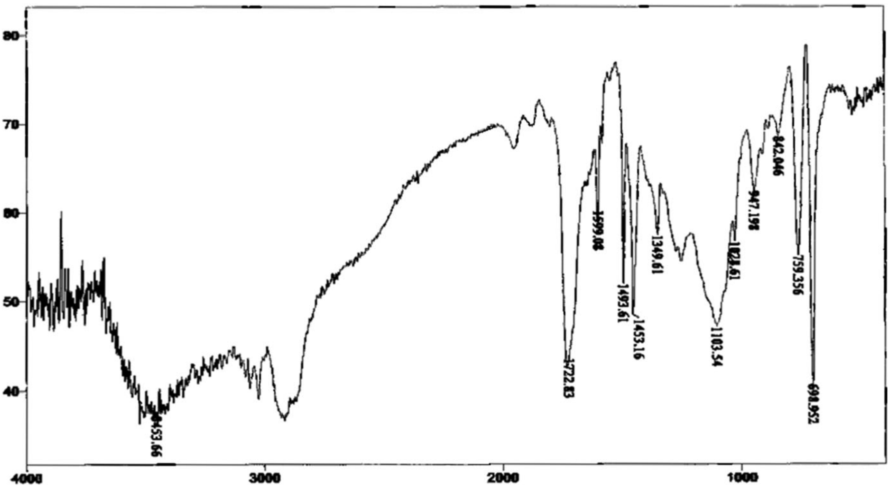


Fig. 4 FTIR spectrum of copoly[(styrene/acrylic acid)/grafted PEG]

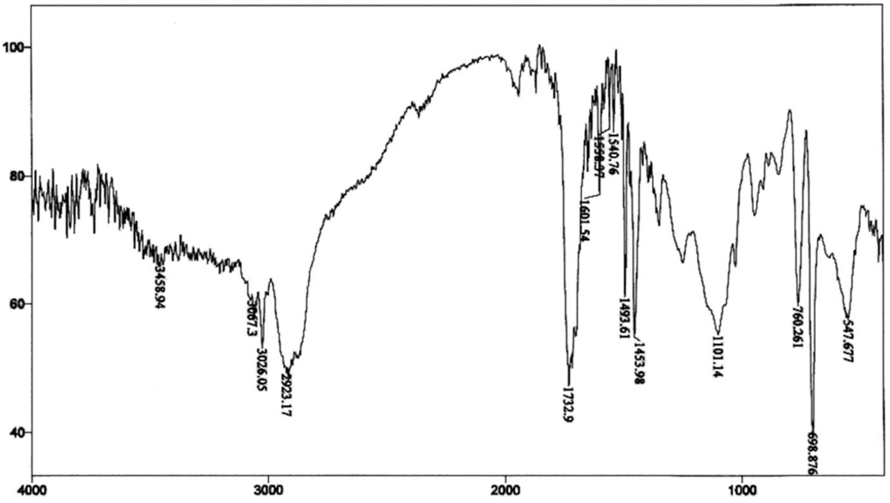


Fig. 5 FTIR spectrum of nano-Fe_3O_4-PS-Co-[PAA-g-PEG]

FTIR spectrum of the copoly(styrene/acrylic acid)/grafted PEG showed stretching peaks at 1722 cm^{-1} due to ester groups and a broad peak at 3453 cm^{-1} due to OH groups of grafted PEG (Fig. 4).

Finally, the nano-Fe_3O_4 was coated with the PEG-grafted copolymer in acetone via sonication, refluxing, and evaporation.

FTIR spectrum of nano-Fe_3O_4-PS-Co-[PAA-g-PEG] showed a characteristic peak of nano-Fe_3O_4 and also the grafted copolymer peaks (Fig. 5).

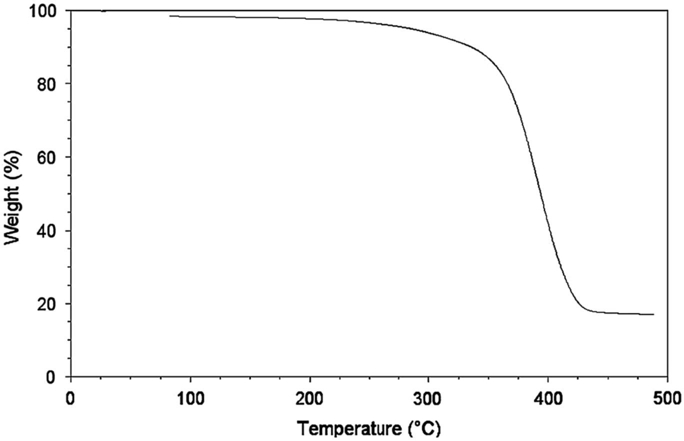


Fig. 6 TGA diagram of nano-Fe_3O_4-PS-Co-[PAA-g-PEG]

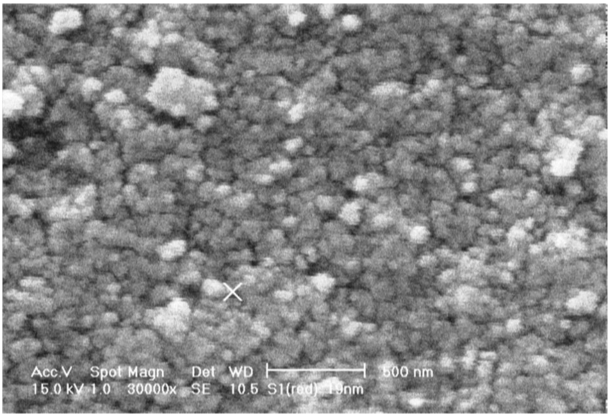


Fig. 7 SEM images of nano-Fe_3O_4-PS-Co-[PAA-g-PEG]

The TGA diagram of the catalyst is shown in Fig. 6. The catalyst is stable up to 390 °C.

SEM images of the magnetic catalyst were also recorded (Fig. 7).

The X-ray diffraction pattern of nano-Fe_3O_4 and the nanocomposite was recorded (Fig. 8). We can see that the sites and intensity of the diffraction peaks are consistent with the standard pattern for JCPDS Card No. (79 - 0417) Magnetite–synthetic [29].

After characterizing nano-Fe_3O_4-PS-Co-[PAA-g-PEG] (Fig. 9) using FTIR, SEM and TGA, we evaluated its catalytic activity as a phase-transfer catalyst in the ring opening of epoxides.

First, a model reaction of 2,3-epoxypropyl phenyl ether and sodium azide in the presence of the nanocomposite in 5 mL of deionized water was conducted under

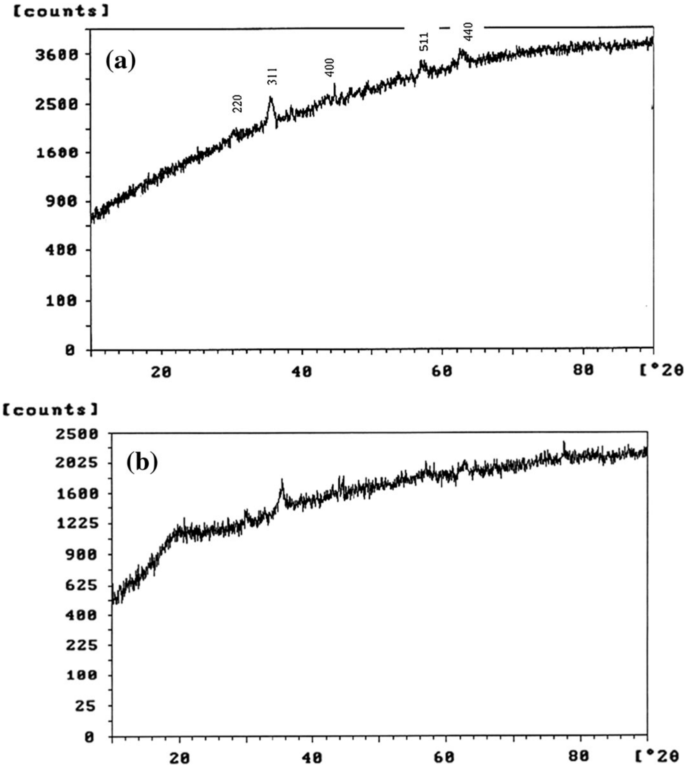


Fig. 8 X-ray diffraction pattern of the nano-Fe3O4 (**a**) and nanocomposite (**b**)

reflux conditions. According to TLC, only one spot was seen after 50 min. Optimization of the amount of reactants and the catalyst showed that 2 mmol of sodium azide and 0.02 g of the catalyst completed the reaction in the minimum length of time (Table 1).

Subsequently, under optimal conditions, 1 mmol epoxide: 2 mmol azide: 0.02 g nanocomposite and 5 mL deionized water under reflux conditions, the generality and synthetic scope of this coupling protocol were demonstrated by synthesizing a series of β-azido alcohols (Table 2) in 5–120 min and 78–99 % yield.

Regioselectivity in the ring opening reaction of epoxides is relevant to the reaction mechanism, specifically to electronic and steric effects. The azide anion attacks the less crowded carbon of all epoxides but styrene oxide. With styrene oxide, despite having a phenyl group as an electron-withdrawing group, the electronic effect precedes the steric effect such that 2-azido-2-phenyl ethanol is the major product, with 83 % yield (Table 2).

After the success of nano-Fe_3O_4-PS-Co-[PAA-g-PEG] in the preparation of β-azido alcohols, we decided to explore its catalytic activity in the preparation of β-nitro alcohols. Subsequently, the ring opening of epoxides (1 mmol) was conducted with sodium nitrite (10 mmol) using nano-Fe_3O_4-PS-Co-[PAA-g-PEG] (0.03 g) as

Fig. 9 Structure of nano-Fe_3O_4-PS-Co-[PAA-g-PEG]

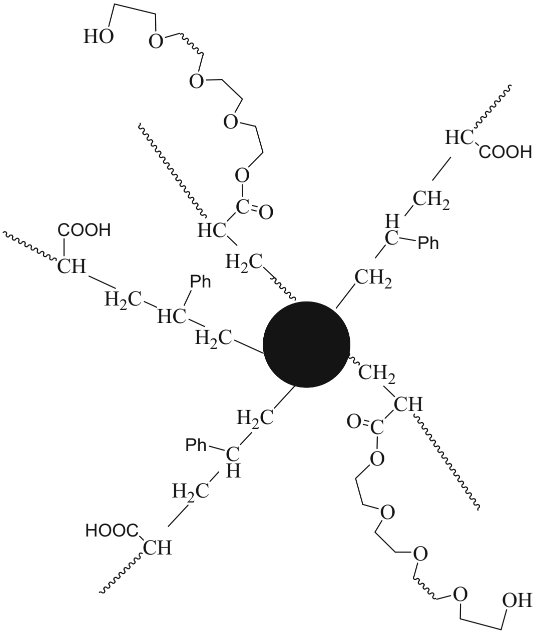


Table 1 Optimization of reaction conditions for the preparation of β-azido alcohol from 2,3-epoxypropyl phenyl ether, in the presence of the nanocatalyst in aqueous medium

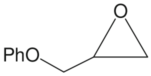
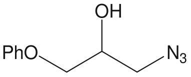
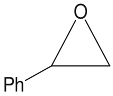
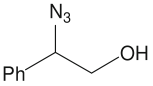
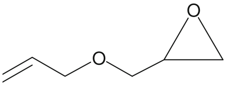
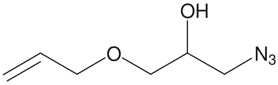
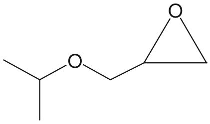
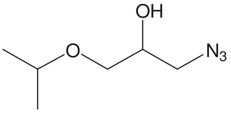
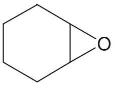
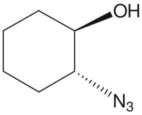
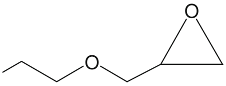
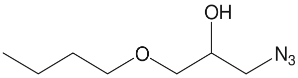
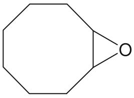
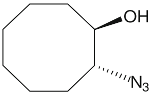
Entry	NaN_3 (mmol)	Nanocomposite (g)	Temp (°C)	Time (min)
1	1.5	0.01	Reflux	65
2	2	0.01	Reflux	55
3	3	0.01	Reflux	50
4	3	0.02	Reflux	35
5	2	0.02	Reflux	35
6	2	0.03	Reflux	35
7	2	0.02	r.t.	240

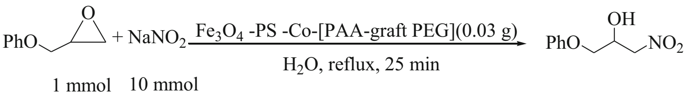
the magnetic PTC under the above optimized reaction condition. All epoxides reacted almost equally well to afford corresponding β-nitro alcohols in high to excellent yields (Scheme 4; Table 3).

We can postulate that the nanocomposite facilitates the nucleophilic attack of the azide anion by chelating the cation by PEG (Fig. 10).

Given the importance of green chemistry and the recycling of solvents and catalysts, the recyclability of the nanocomposite was assessed in the reaction of 2,3-epoxypropyl phenyl ether. The result is shown in Fig. 11. The activity of the nanocomposite was slightly decreased after reuse five times.

Table 2 Preparation of β-azido alcohols from corresponding epoxides and sodium azide in the presence of the nanocomposite in aqueous medium under reflux conditions

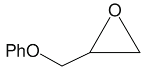
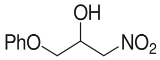
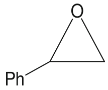
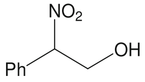
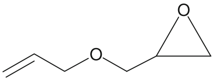
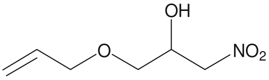
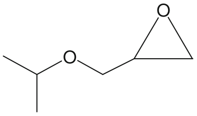
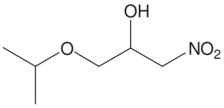
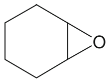
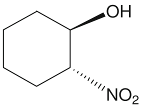
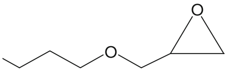
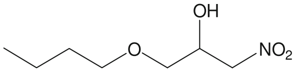
Entry	Reactant	Product	Time (min)	Yield (%)
1			35	99
2			10	83
3			5	85
4			25	80
5			15	85
6			15	96
7			120	78



Scheme 4 Ring opening of epoxides with nitrite using nano-Fe_3O_4-PS-Co-[PAA-g-PEG]

To demonstrate the superiority of nano-Fe_3O_4-PS-Co-[PAA-g-PEG] over the reported catalysts, the reaction of 2,3-epoxypropyl phenyl ether was considered as a representative example (Table 4). While in all of these cases, comparative yields of the desired product were obtained following the nano-Fe_3O_4-PS-Co-[PAA-g-PEG]-

Table 3 Preparation of β-azido alcohols from corresponding epoxides and sodium nitrite in the presence of the nanocomposite in aqueous medium under reflux conditions

Entry	Reactant	Product	Time (min)	Yield (%)
1			25	90
2			20	83
3			40	82
4			45	79
5			35	70
6			15	81

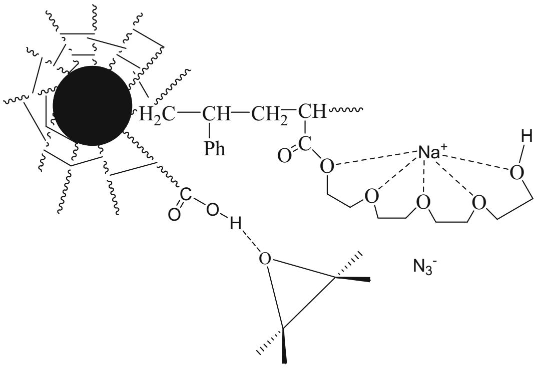


Fig. 10 Chelating sodium by PEG which is immobilized on the nanocomposite

catalyzed procedure (except entry 1), all of the reported procedures required long reaction times (except entries 5 and 6) or high catalyst loading (entries 5 and 6). These results clearly demonstrate that nano-Fe_3O_4-PS-Co-[PAA-g-PEG] is an equally or more efficient catalyst for this reaction.

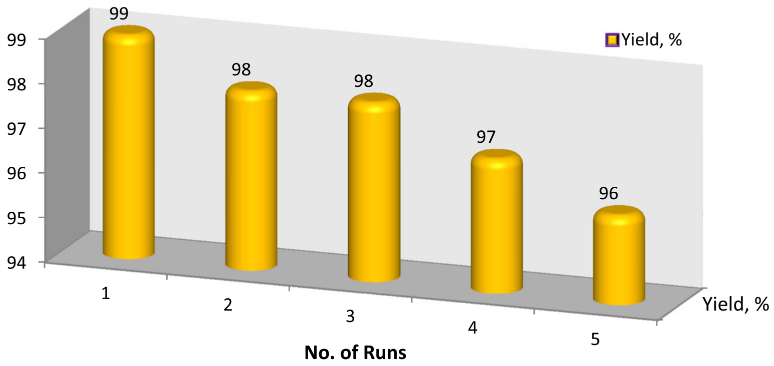


Fig. 11 Reusability of the nanocomposite in the reaction of 2,3-epoxypropyl phenyl ether and sodium azide

Table 4 Comparison of azidolysis of 2,3-epoxypropyl phenyl ether with other methods reported in the literature

Entry	NaN_3 (mmol)	Catalyst	Time (h)	Yield (%)	Ref.
1	1.33	β-cyclodextrin/1.13 g	5	45	[25]
2	1.1	$CeCl_3·7H_2O$/0.187 g	3	99	[11]
3	5	PTC[a]/0.1 g	12	94	[12]
4	1.5	AMP[b]/(10 mol%)	3–5	96	[26]
5	1.2	PEG-g-Dowex resin/0.1 g	0.75	96	[19]
6	3	MPTC[c]/0.2 g	0.5	85	[27]
7	2	–	1	90	[28]
8	2	Fe_3O_4-PS-Co-[PAA-graft PEG]/0.02 g	0.5	99	This work

[a] Cross-linked poly acrylamide

[b] Ammonium-12-molybdophosphate $(NH_4)_3[PMo_{12}O_{40}]$

[c] Multi phase-transfer catalyst

Conclusions

In conclusion, A novel nano-Fe_3O_4@copoly[(styrene/acrylic acid)/grafted ethylene oxide was synthesized and its application as a magnetic and recyclable phase-transfer catalyst in the preparation of β-azido alcohols and β-nitro alcohols was investigated. The experimental results showed that the regioselective ring opening of epoxides in the presence of azide and nitro anions in aqueous medium led to the corresponding products in 5–120 min and 78–99 % yield. In addition to the recyclability of the catalyst via an external magnet, the short reaction times, high product yield, regioselectivity, facile workup, and eco-friendly and green nature of the procedure are notable advantages of this method.

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