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Fe_3O_4 nanoparticle-bonded β-cyclodextrin as an efficient and magnetically retrievable catalyst for the preparation of β-azido alcohols and β-hydroxy thiocyanate

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Abstract A novel Fe_3O_4 nanoparticle-bonded β-cyclodextrin (β-CD@MNP) has been synthesized and characterized by scanning electron microscopy, vibrating sample magnetometry, and thermogravimetric analysis. It is found that the nanoparticles can be used as an efficient and magnetically retrievable nanocatalyst for the preparation of β-azido alcohols and β-hydroxy thiocyanates under ultrasound irradiation.

Keywords Magnetic nanoparticles · β-CD@MNP · Azido alcohols · Hydroxy thiocyanate

Introduction

Recently, much attention has been given to develop the application of magnetically recoverable nanocatalyst systems for sustainable organic synthesis [1–4]. Surface functionalization of magnetic nanoparticles (MNPs) is a well-designed way to bridge the gap between heterogeneous and homogeneous catalysis. Ferrite (Fe_3O_4) can be used as a versatile support for functionalization of metals, organocatalysts, *N*-heterocyclic carbenes, and chiral catalysts. Homogeneous organocatalysts can be successfully decorated with linkers/ligands on the surface of magnetite or, alternatively, the organocatalysts can be directly immobilized on the surface of magnetite [5].

The use of water as a solvent features many benefits such as improving reactivities and selectivities, simplifying the workup procedures, enabling the

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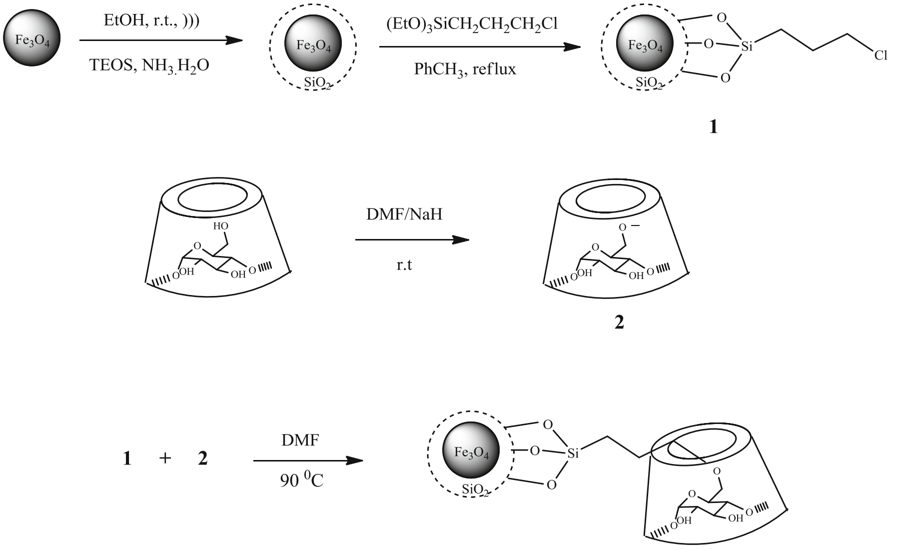
recycling of the catalyst, and allowing mild reaction conditions and protective-group free synthesis in addition to being benign itself [6–8]. In addition, development of organic chemistry in water can lead to uncommon reactivities and reverse selectivities compared to organic solvents [9].

Epoxides are among the most versatile intermediates in organic synthesis [10]. Also, a number of biologically significant molecules contain these strained three-membered rings within their structures [11]. A literature survey indicate that there is a considerable interest in ring-opening reactions of epoxides by nucleophilic addition for the stereoselective preparation of 1,2-disubstituted products in aqueous medium, which is due to the special physical properties and structure of water (e.g. pH control, H-bonding capabilities, and excellent activation of ionic nucleophiles) [12–16]. Herein we report on the synthesis and application of a magnetically separable nanoparticle-bonded β-cyclodextrin as a highly efficient heterogeneous catalyst for the ring-opening reaction of epoxides.

Results and discussion

It has been demonstrated that immobilization of β-cyclodextrin on magnetic nanoparticles as a hybrid organic–inorganic nanocomposite could be used as heterogeneous nanocatalyst in organic synthesis [17]. In this study, a Fe_3O_4 nanoparticle-bonded β-cyclodextrin catalyst was prepared based on the procedures outlined in Scheme 1.

The morphology and particle size range of the β-CD@MNP was determined by SEM images (Fig. 1). The magnetic nanoparticle micrographs show an almost



Scheme 1 Synthesis of β-CD@MNP

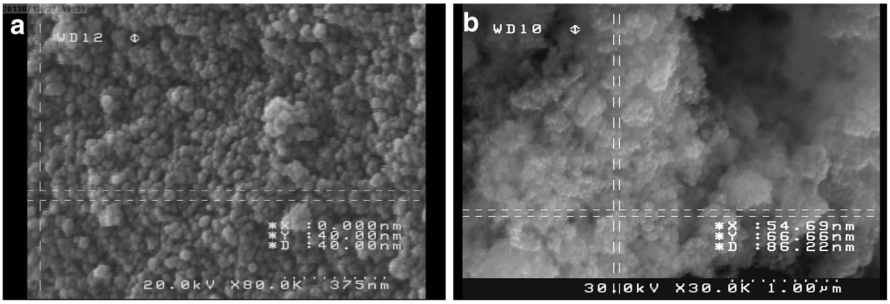


Fig. 1 SEM images of Fe_3O_4 (**a**) and Fe_3O_4-bonded β-cyclodextrin (**b**)

spherical shape of average particle dimensions approximately 67 × 86 nm, which indicates that the shell diameter is 46 nm.

We also used thermogravimetric (TG) analysis to study the composition and thermal stability of the β-CD@MNP (Fig. 2). As depicted from the thermogram, there are two steps of weight loss in the region from room temperature to 600 °C. While the small mass loss (~5 % w/w) below 150 °C is associated to the removal of the adsorbed water, the main mass loss (~30 % w/w) in the range of 250–325 and 325–450 °C may be attributed to the thermal decomposition of β-CD and linkers, respectively.

In order to investigate the magnetic properties of β-CD@MNP at room temperature, a vibrating sample magnetometer (VSM) was used. Comparison of the diagrams indicate that the saturation magnetization of the neat Fe_3O_4 and β-CD@MNP changed from 58.5 to 6.4 emu/g because of surface modification and

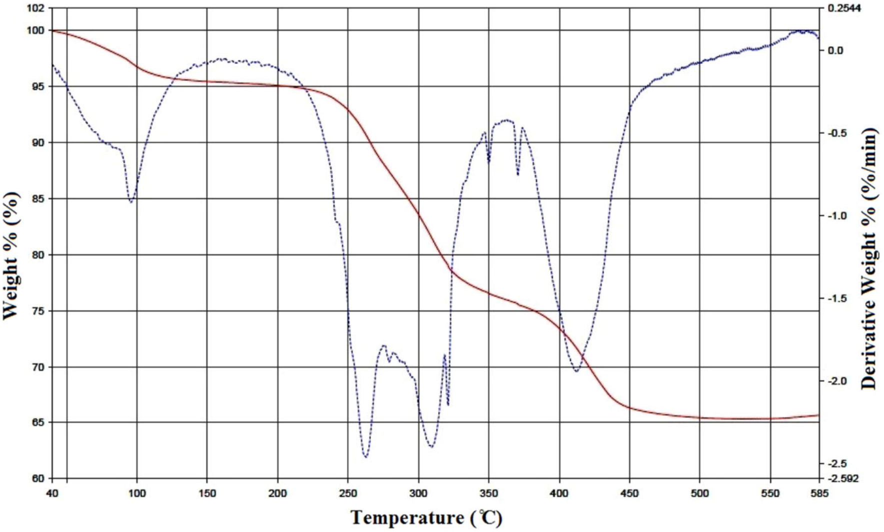


Fig. 2 TG–DTG analysis for Fe_3O_4 nanoparticle-bonded β-cyclodextrin

functionalization of the magnetite particles (Fe_3O_4) with a non-magnetic SiO_2 shell and bulky β-CD molecules and the linker moiety (Fig. 3).

Next, the catalytic ability of the β-CD@MNP magnetic nanoparticles with combination of ultrasound promoted ring opening of epoxides was investigated in aqueous media. The reaction between epoxycyclohexane and sodium thiocyanate in the present of β-CD@MNP was used as a model for the optimization of reaction conditions. The use of 1 mmol reactant, 1.2 mmol thiocyanate ions, and 0.05 g of the catalyst in water showed to be the most effective conditions to perform the reaction. When the reaction was carried out in the absence of the nanocatalyst or with Fe_3O_4 no product was observed, but after a prolonged reaction time, some diol was isolated (60 min, yield was 15 and 17 %, respectively). It should be noted that in the presence of β-CD, the reaction was completed in 5 min, but because of the simpler work-up procedure and recycling β-CD@MNPs catalyst system was preferred. Also, without sonication the reaction rate was decreased significantly.

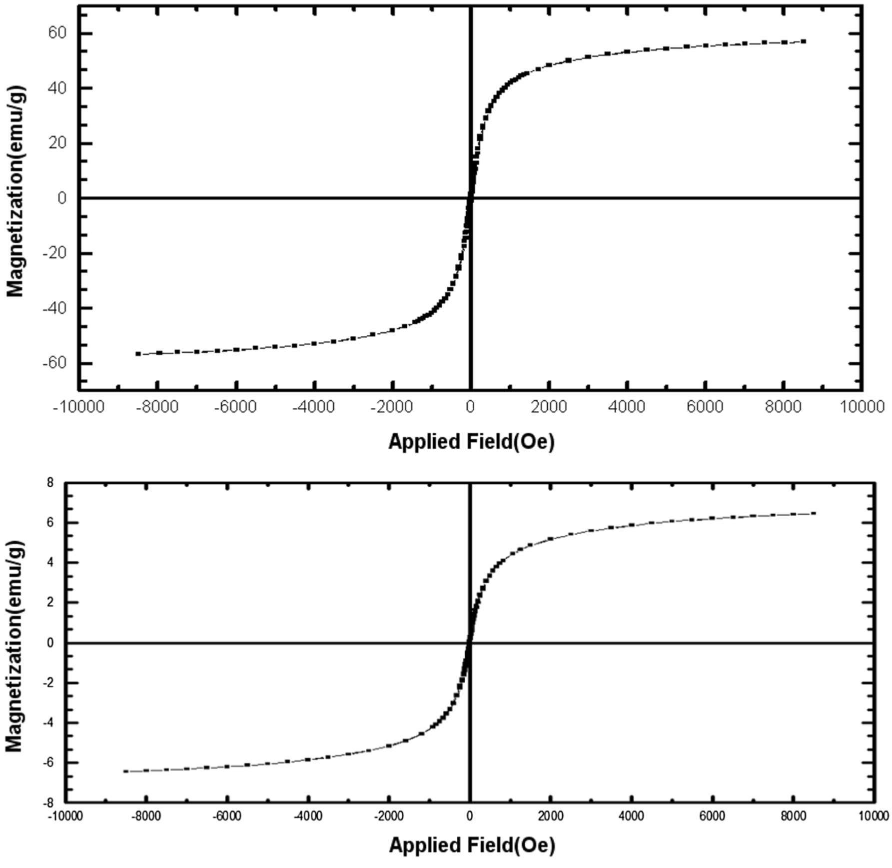


Fig. 3 The magnetic curve of Fe_3O_4 nanoparticles at room temperature (*upper curve*), β-CD@MNP (*lower curve*)

With these results in hand, various epoxides converted to their corresponding β-azido alcohols and β-hydroxy thiocyanate in good to excellent yields (Table 1).

In styrene oxide (Table 1, entry 1) epoxide ring opening occurred from both sides. This is probably because the positive charge on the oxygen appears to be localized on the more highly substituted benzylic carbon leading to the major product, whereas in the case of aliphatic epoxides, steric factors predominate over electronic factors, thereby facilitating attack at the less hindered carbon atom of the epoxide ring [19]. Otherwise, in the case of cyclohexene oxide (Table 1, entry 6), the reaction was completely antistereoselective, and the trans product was obtained.

The catalyst recycling and reuse by the magnetic cleansing technique is the major practical advantage of Fe_3O_4 supported organocatalysts from the point of view of green chemistry [20]. Fortunately, β-CD@MNP dispersion showed response to a magnetic field and the nanoparticles separated from the aqueous reaction media once an external magnet is approached (Fig. 4). It is noteworthy that in this method the reusing experiment of the nanoparticles did not show significant loss of their catalytic activity or magnetic nature (Table 2).

In cyclodextrin chemistry, inclusion complexation is accomplished by the intermolecular interaction between cyclodextrin and guest, which leads to the penetration of the guest molecule partly or completely into the cavity of the cyclodextrin [21]. Accordingly, it is surmised that β-CD@MNP could act as a microreactor and hydrogen bonding of epoxide to the outer OH of β-CD facilitate the ring-opening with the nucleophile.

Experimental

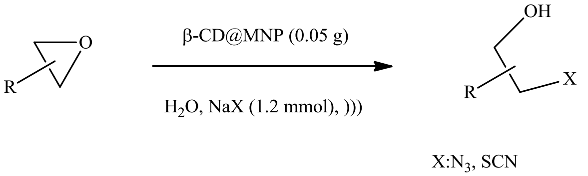
Materials and instruments

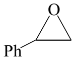
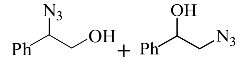
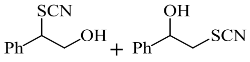
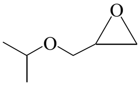
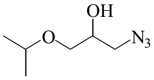
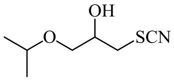
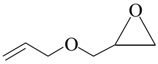
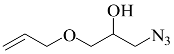
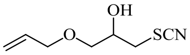
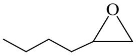
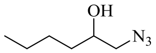
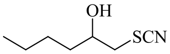
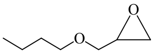
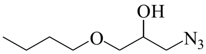
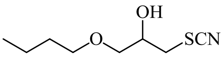
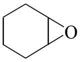
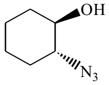
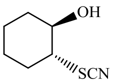
All the chemicals and reagents were used as received from the supplier, except toluene and dimethylformamide (DMF), which were dried prior to use. Thin-layer chromatography was performed on aluminum-backed silica gel 60 F_{254} plates (0.2 mm thickness, Merck). SEM images were obtained from a Philips XL30 instrument. Thermogravimetric analysis was performed under nitrogen with a heating rate of 10 °C/min using a Perkin-Elmer, Pyris 1 TGA.

Preparation of Fe_3O_4 nanoparticle-bonded β-cyclodextrin

Fe_3O_4 and silica-coated nanoparticles were synthesized based on the known common methods [22, 23]. For the synthesis of compound **1**, $Fe_3O_4@SiO_2$ (0.5 g) were dispersed in dry toluene (20 mL) by sonication for 15 min, and then (3-chloropropyl)triethoxysilane (1.5 mL, 6.25 mmol) was added. The whole mixture was stirred and refluxed for 48 h under nitrogen atmosphere. After cooling to room temperature, the solid materials were filtered off, washed with acetone and dried in a vacuum. For the synthesis of compound **2**, β-cyclodextrin (1.13 g, 1 mmol) was dissolved in anhydrous DMF (25 mL) to which NaH(0.2 g) was added. The mixture was stirred at room temperature until no gas was produced [24]. After removing

Table 1 Preparation of β-azido alcohols and β-hydroxy thiocyanate catalyzed by Fe_3O_4 nanoparticle-bonded β-cyclodextrin



Entry	Epoxide	Product[a]	Time (min)	Yield (%)[b]
1			5	84 (>10)[c]
			15	85 (5)[c]
2			5	92
			10	91
3			25	96
			10	87
4			10	91
			20	88
5			5	92
			10	91
6			10	85
			20	86

[a] Products were identified by comparison of their physical and spectral data with those of authentic samples [14, 18, 19]

[b] Isolated yields

[c] According to GC analysis

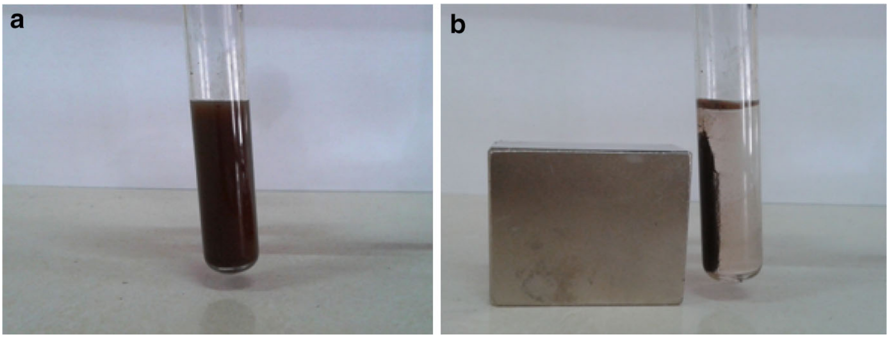


Fig. 4 Photographs of β-CD@MNP dispersed in reaction medium (**a**) and separated with a NbFeB magnet (**b**)

Table 2 Catalyst recycling and reuse for successive four run

Run	1	2	3	4
Time (min)	20	20	20	20
Yield (%)	86	84	80	80

Reaction conditions: epoxycyclohexane (1 mmol), NaSCN (1.2 mmol), H_2O (3 mL), ultrasound

excessive NaH by filtration, precursor **1** was added to the filtrate and stirred at 90 °C for 12 h. The obtained nanoparticles (β-CD@MNP) were separated with a magnet and washed thoroughly with water and dried at room temperature.

General procedure for the ring opening of epoxides

A mixture of epoxide (1.0 mmol), NaN_3 or NaSCN (1.2 mmol), β-CD@MNP catalyst (0.05 g) and water (5 mL) were transferred to a glass test tube. Under ultrasonic irradiation (220 W, 50 kH), the reaction was allowed to proceed at room temperature for the time shown in Table 1. After completion of the reaction as monitored by thin layer chromatography [using *n*-hexane/ethylacetate (5:1) as eluent], the catalyst was magnetically separated and washed with diethyl ether before reusing. The filtrate was extracted with ethylacetate (3 × 5) and then the combined organic phase was washed with water; dried over $CaCl_2$ and evaporated under vacuum to give the desire product in 84–96 % isolated yields.

Conclusion

It can be concluded that this novel magnetic nanocatalyst (β-CD@MNP) can be applied successfully in the ring-opening of epoxides with azide and thiocyanate as nucleophiles. The magnetic nanoparticles not only promote the reaction rate,but also simplify the work-up procedure. In addition, the nanocatalyst acts as a microreactor and gathers the reactants together and speed up the reaction rate. The advantages of β-CD@MNP are short reaction times, high yield of the products, facile reaction work-up, utilizing green solvent, and eco-friendly procedure.

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