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Fe$_3$O$_4$@silica sulfuric acid nanoparticles as a potent and recyclable solid acid catalyst for the synthesis of indole derivatives

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Abstract

Fe$_3$O$_4$ magnetic nanoparticles were synthesized by co-precipitation of Fe^{2+} and Fe^{3+} in aqueous NaOH. Then silica was coated on the obtained nanoparticles and the whole composite was functionalized with chlorosulfonic acid in CH$_2$Cl$_2$. The obtained nanocomposite (Fe$_3$O$_4$@SiO$_2$-SO$_3$H) was characterized by FT-IR, VSM and XRD techniques and was used as an efficient catalyst in condensation reaction of indoles and aldehydes, and excellent yields of the desired products were obtained. The catalyst was recycled and used for successive runs with no considerable loss of activity. The indole products in their conjugated form were capable of selective sensing of CN- anion in solution.

Keywords: Nanoparticle; heterogeneous; catalyst; bis(indolyl)methane.

Introduction

The development of new synthetic methods leading to indole derivatives with respect to the principles of green chemistry continues to receive much attention in organic synthesis [1]. Indole derivatives occur in many pharmacologically and biologically active compounds [2]. Bis(Indolyl)methanes possess a wide

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range of biological activity and their synthesis has received a considerable amount of interest [3,4]. These are generally prepared by the condensation of indoles with various aldehydes or ketones in the presence of either protic[5] or Lewis acids [6-8]. Magnetic core-shell nanocatalysts, on the other hand, have been emerged as a new class of composites which have priviledges such as ease of functionalization and ease of recovery by using an external magnet [9]. For example, acid functionalized magnetic core-shell nanoparticles have been used as a reusable solid acid catalyst in preparation of indazolo[2,1-b]phthalazine-triones [10]. Our recent studies on indoles and solid acid catalysts [11-13] prompted us to investigate the application of acid functionalized magnetic nanoparticles to improve condensation reaction of indoles and aldehydes with respect to the reaction time, catalyst loading, and above all, reuse of the catalyst which promises minimization of the waste.

Experimental

General

Fe_3O_4 MNPs were synthesized with higher efficiency by using a five-necked reactor. A stock solution of $FeCl_3.6H_2O$ (10.4 g), $FeCl_2.4H_2O$ (4.0 g) and HCl (1.7 mL, 12 mol L^{-1}) in 50 mL of deionized water which was degassed with nitrogen gas for 20 min before use, added dropwise (by using a dropping funnel connected to one neck) into 500 mL of degassed NaOH solution (1.5 mol L^{-1}) at 80 °C during 30 min. Central neck was connected to a home-made condenser allowing circulation of cold water to prevent vaporization of solution. A glassware stirrer rotating at 1000 rpm was passed through the condenser and central neck. Third neck was used to sparge nitrogen gas during the synthesis. The other necks were used for temperature monitoring and sampling. After completion, the obtained Fe_3O_4 nanoparticles were separated from the reaction medium by a magnetic field (1.4 *T* strength), and washed with 500 mL deionized water four times. Silica coating and functionalization with chlorosulfonic acid was performed according to Kiasat *et al.* [10]. For the synthesis of bis(indolyl)methanes, 20 mg of the catalyst was added to a solution of 2-methylindole (2 mmol) and corresponding aldehyde (1 mmol) in 5 mL of ethanol. After completion of the reaction as was monitored by TLC (*n*-hexane: ethylacetate, 10:4), the precipitated product was collected and recrystallized in acetonitrile. IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker DRX-400 (or DRX-100) Avance spectrometer. Analytical GC evaluations of product mixtures were carried out on a Varian CP-3800 chromatograph (using a split/splitless injector, CP Sil 8CB column, FID assembly). X-ray powder diffraction (XRD) measurements were performed using a Philips diffractometer with mono chromatized Cu k_α radiation. The morphology of synthesized samples was characterized with a scanning electron microscope (SEM) from Philips Company (XL30 ESEM).

Results and discussion

The obtained MNPs were characterized by using XRD. Figure 1a shows the XRD pattern of the synthesized MNPs, which matched well with library patterns (JCPDS No. 19-629), indicating that the sample has a cubic crystal system.

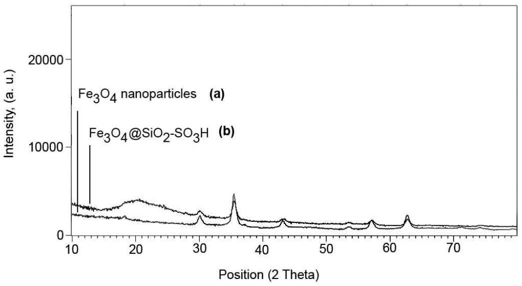


Figure 1. XRD patterns of Fe_3O_4 nanoparticles (a) and -SO_3H functionalized silica coated Fe_3O_4 nanoparticles (b)

Amorphous SiO_2 shell was coated on the obtained magnetite nanoparticles and functionalized with chlorosulfonic acid according to Kiasat *et al.* [10]. XRD Pattern of the final product is shown in Figure 1b. As it is obvious, the crystal structure of magnetite nanoparticles were preserved and a broad peak ranging from 2θ= 15-30 was appeared which is characteristic of amorphous silica. In the FTIR spectrum of the final product (Figure 2), basic characteristic vibrations of Fe-O at 578 cm^{-1} and Si-O-Si asymmetric stretching, symmetric stretching and bending vibrations at 1047, 795 and 451 cm^{-1} were observed. Characteristic band of the sulfonyl groups was observed at 1229 cm^{-1}. Broad absorption around 3400 cm^{-1} is also, attributable to the OH stretching of the acid functionality.

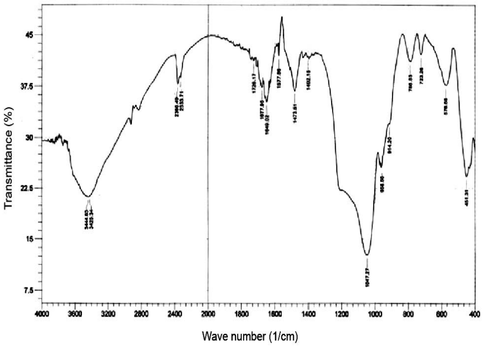


Figure 2. FTIR spectrum of the Fe_3O_4@SiO_2-SO_3H nanoparticles

TEM image of the Fe_3O_4@SiO_2-SO_3H nanoparticles shown aggregates of many ultrafine particles with the size ranged from 20 to 30 nm as shown in Figure 3.

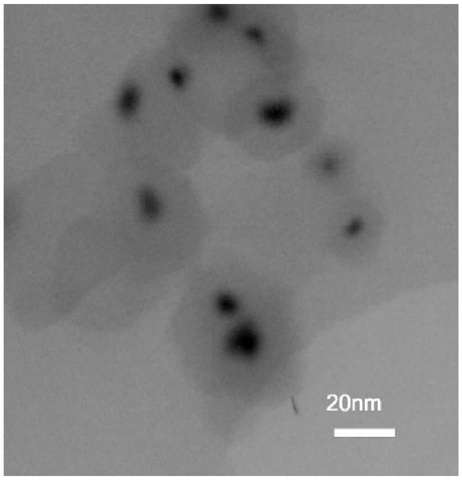
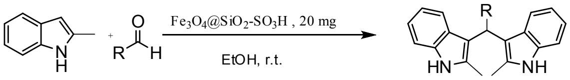


Figure 3. TEM image of the Fe_3O_4@SiO_2-SO_3H nanoparticles

Having the characterized catalyst in hand, its potential in the condensation reaction of indoles and aldehydes was evaluated, since these are key intermediates in the synthesis of hyperconjugate indole products with interesting properties as we shown previously [14]. At first, 2-methylindole and vanillin were selected as model substrates and reaction conditions were optimized with regard to the catalyst loading, solvent, temperature *etc.* Aside from the many experimental parameters tested, the optimum conditions were 20 mg of the catalyst per mmol of indole at room temperature in ethanol. This resulted in the excellent yield of 98% in 10 min. In order to extend the reaction to other aldehydes, various aromatic aldehydes with either electron withdrawing or electron releasing groups were tested and the results were as anticipated. Scheme 1 depicts the reaction conditions.



Scheme 1. Fe_3O_4@SiO_2-SO_3H catalyzed condensation reaction of 2-methylindole and aromatic aldehydes

Typical results of the Fe_3O_4@SiO_2-SO_3H catalyzed condensation reaction are shown in Table 1, and indicate the scope of the reaction. As anticipated, electron withdrawing groups on the aldehyde moiety resulted in higher yields and lower reaction times are in accord with the other reports. In order to evaluate reusability of the catalyst, the reaction of 2-methylindole and vannilin was carried out in the presence of the recycled catalyst in successive runs. From reaction run 1 to 5, the yields were 98%, 98%, 95%, 94% and 92%, respectively (Figure 4). Therefore after five runs, 6% decrease in the efficiency of the catalyst system was observed. This result shows that Fe_3O_4@SiO_2-OSO_3H can be utilized as a moderate and recyclable catalyst for the condensation reaction. In order to confirm heterogeneity of the catalyst, the amount of sulfonic acid loading was determined for the fresh and the recycled catalyst of the 5th run and the results were 1.8 and 1.78 mmol SO_3H/g, which confirmed that no considerable leaching was occurred during the course of reaction.

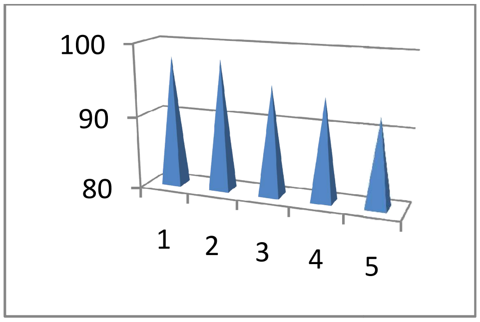


Figure 4. Catalyst efficiency in successive runs

Table 1. Fe_3O_4@SiO_2-SO_3H nanoparticles catalyzed condensation of 2-methylindole with various aldehydes

Entry [a]	Aldehyde	Product	Yiled[b] (%)	Time (Min)	M.p. °C (Lit.)
1	4-hydroxy-3-methoxybenzaldehyde	**1a**	98	10	233-235 (233-235) [8]
2	3,4-dimethoxybenzaldehyde	**2a**	94	15	204-206 (205-207) [7]
3	2-nitrobenzaldehyde	**3a**	98	10	190-192 (190-192) [8]
4	3-nitrobenzaldehyde	**4a**	97	10	281-283 (281-283) [6]
5	3-phenoxybenzaldehyde	**5a**	98	15	227-229 (226-228) [6]
6	4-chlorobenzaldehyde	**6a**	98	15	229-231 (229-231) [7]
7	2-chlorobenzaldehyde	**7a**	96	15	211-213 (211-213) [8]
8	4-nitrobenzaldehyde	**8a**	97	15	220-222 (219-221) [8]

[a]All reactions carried out according to general experimental procedure. [b]Isolated yield

An interesting observation was that product **8a** was unstable in the presence of oxidizing agents such sodium peroxide in acetonitrile solution and was easily dehydrogenated to its highly conjugated product, **8b**, by removal of the H atoms, one at *meso* position and the other at N atom of the indole ring system. Structure of 8b, was unambiguously identified from its FTIR and ^{1}Hnmr data.

Yield= 64%, Red solid, m.p. 120 °C, IR (KBr): υ (cm^{-1}); 3408, 2923, 1566, 1521, 1423, 1100, 853, 750. ^{1}H NMR (400 MHz, DMSO-*d*$_6$, 25 °C): δ = 2.08 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 6.65 (d, *J*= 8.0 Hz, 2H), 7.12 (t, *J*=7.6 Hz, 2H), 7.28 (t, *J*=7.6 Hz, 2H), 7.57 (d, *J*= 8.0 Hz, 2H), 7.80 (d, *J*= 8.4 Hz, 2H), 8.40 (d, *J*= 8.4 Hz, 2H) ppm.

The energy minimized structure of **8b** was calculated by Gaussian 03 software uisng B3LYP method and 3-21G basis set as a cost effective choice. The observed C_2 symmetry justifies the simplicity and position of the chemical shifts.

It is noteworthy that product **8b** found application in selective detection of cyanide anions in solution. Upon mixing of 1:1 solutions (5.0×10^{-4} M) of **8b** and any of the following anions: CN^-, Cl^-, Br^-, I^-, OAc^-, $H_2PO_4^-$, NO_3^-, NO_2, cyanide showed the most intense color change from red to yellow (Figure 5), which can be attributed to hydrogen bonding or deprotonation of **8b** by CN^-.

Figure 5. Color change of 5.0×10^{-4} M solution of 8b in presence of various anions From left to right: None, CN^-, Cl^-, Br^-, I^-, OAc^-, $H_2PO_4^-$, NO_3^-, NO_2

This promises **8b** as a selective chemosensor for detection of CN^- in solution.

Conclusion

In conclusion, we have extended the application of $Fe_3O_4@SiO_2-OSO_3H$ nanoparticles as a recyclable solid acid catalyst to a well-known organic reaction. Major advantages of the recent work include ease of recovery of the catalyst, high yields of the products, reusability, mild reaction conditions and rather short times.

Acknowledgments

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