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Boric Acid-Functionalized Fe₃O₄@SiO₂ as a Novel Superparamagnetically Recoverable Nano Catalyst for Mukaiyama-Aldol Reaction

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We have reported the fabrication of boric acid incorporated into surface of magnetite nanoparticles. The catalyst was characterized using spectroscopic, magnetic and thermal techniques (FT-IR, SEM, XRD, ICP, VSM and TGA). It catalyzed Mukaiyama aldol reaction of a ketene silyl acetal type nucleophile ((1-methoxy-2-methylprop-1-enyloxy) trimethylsilane), and various aldehydes (aromatic, aliphatic, α,β -unsaturated), in acetonitrile and the yields were in the range of 45-98%. Magnetic Fe₃O₄-boric acid was multi-functional. The Fe₃O₄ core of the catalyst made easy separation and recycling while its boric acid portion catalyzed Mukaiyama aldol reaction. Nano size nature of the catalyst increased its activity in a way that boric acid, which is a weak Lewis acid, functioned similar to a more strong one like BF₃. Boric acid functionality had the advantage of being moisture insensitive, economically reasonable and environmentally friendly. Furthermore Fe₃O₄@SiO₂@Boric acid was magnetically recovered *via* an external permanent magnet and was reused at least 6 times with a negligible change in its activity.

Keywords: Mukaiyama, Boric acid, Magnetic catalyst

INTRODUCTION

The Mukaiyama aldol reaction (reaction of an enoxy silane with a carbonyl compound) is one of the most important C-C bonds forming reactions that results in the formation of β -hydroxy carbonyl compounds, as a structural unit found in many natural molecules and pharmaceuticals [1]. In the last four decades, many catalysts have been used to promote this reaction through activating the electrophile (carbonyl compound) or the nucleophile, (enoxy silane). The list of catalysts includes Lewis bases like fluoride ion [2] and Bronsted or Lewis acids such as silica sulfuric acid [3], metal based compounds (salts [4-6], complexes [7-9], metal organic frameworks [10] and mesoporous molecular sieves [11]), hydrogen bonding catalysts [12], trityl salts [13], halogens [14], N-heterocyclic carbenes [15], silicon [16] and boron [17] compounds. Mukaiyama aldol reaction may proceed without any catalyst in highly polar solvents such as DMSO [18], ionic liquids [19], water [20] or DBU

[21]. Potential drawbacks of the reported catalysts include being expensive and environmentally hazardous as well as cumbersome and non-cost effective separation of the catalyst from the reaction mixture. Moreover, some of these reactions have been carried out under strictly anhydrous conditions which necessitate specialized equipment. In order to overcome some of these problems, boric acid which is a weak, inexpensive and water compatible Lewis acid, was employed. The latter was immobilized on the surface of silica coated magnetite nanoparticles. This facilitated easy separation from the reaction mixture using an external magnet. To the best of our knowledge, there is a few magnetic Lewis acid catalysts reported for the Mukaiyama-aldol reaction [22]. This paper reports the use of boric acid immobilized silica coated magnetite nanoparticles in a hope to be employed as a more inexpensive and mass economical catalyst for Mukaiyama aldol reaction.

EXPERIMENTAL

All reagents and solvents used were in analytical grade

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and used with no further purification. FT-IR spectra were collected with a Nicolet IR100 FT-IR over the 400-4000 cm^{-1} region using spectroscopic grade KBr. The X-ray diffraction pattern was obtained at room temperature with a Philips X-pert 1710 diffractometer with $\text{Co K}\alpha$ ($\alpha = 1.78897 \text{ \AA}$), 40 kV voltage, 40 mA current and in the range 10^0 - $90^0(2\theta)$ with a scan speed of $0.02^0/\text{s}$. SEM (Philips XL 30 and S-4160) was used to study the catalyst morphology. Magnetic saturation of the catalyst was obtained using a vibrating magnetometer/Alternating Gradient Force Magnetometer (VSM/AGFM, MDK Co., Iran). Thermal gravimetric analysis was performed using a thermal analyzer with a heating rate of $20 \text{ }^\circ\text{C min}^{-1}$ over a temperature range of 25-1100 $^\circ\text{C}$ under flowing nitrogen.

Synthesis of Boric Acid Functionalized Silica Coated Magnetite Nanoparticles ($\text{Fe}_3\text{O}_4 @\text{SiO}_2 @\text{Boric Acid}$)

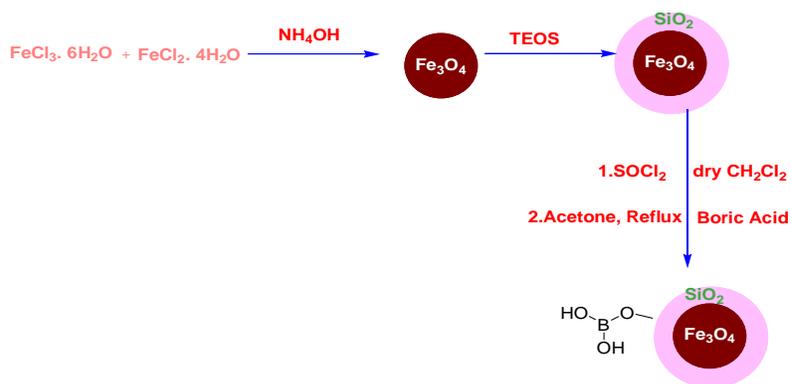
Preparation of silica coated magnetite nanoparticles. Fe_3O_4 nanoparticles were prepared according to the conventional coprecipitation method [23]. $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (2.7029 g, 10 mmol) and $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (0.9941 g, 5 mmol) were dissolved separately in deionized water (20 ml). Then, the solutions were mixed and ultrasonicated for 2 min while stirred vigorously (800 rpm) by a mechanical stirrer at room temperature. Then, pH of the reaction vessel was adjusted between 11 and 13 by dropwise addition of a concentrated (37% w/w) ammonia solution. The resultant mixture was stirred for another 1 h at room temperature and 6 h at 80 $^\circ\text{C}$. Then, the mixture was let cool to ambient temperature.

Ethanol (40 ml) was added and the resulting mixture was stirred at 40 $^\circ\text{C}$ for 1 h. Tetraethylorthosilicate (TEOS) (10 ml) was charged to the vessel and continuously stirred at 40 $^\circ\text{C}$ for another 24 h. The resulting brown precipitate was collected by an external magnet, and washed several times with deionized water to reach neutral condition and then washed 5 times with ethanol and diethyl ether and dried at room temperature for 2 days.

Boric acid immobilization on the surface of silica coated magnetite nanoparticles. To the as prepared silica coated magnetite nanoparticles (1.5 g) in dry CH_2Cl_2 (20 ml), thionyl chloride (1 ml) was added drop wise while keeping the mixture in an ice bath (0 $^\circ\text{C}$) for 2 min. Then, ice bath was removed and the mixture was mechanically stirred for 1 h at room temperature. Subsequently, a saturated solution of boric acid (prepared with the aid of an ultrasonic bath) in acetone (40 ml) as a dry and non-nucleophilic solvent was added. To assure the maximum loading of boric acid on the surface of nanoparticles, a small amount of solid boric acid (0.05 g) was added and the mixture was refluxed for 12 h. The resulting nanoparticles were collected using a permanent magnet, washed 5 times with deionized water, ethanol and diethyl ether and dried at 100 $^\circ\text{C}$ for 12 h.

General Procedure for the Mukaiyama Aldol Reaction in the Presence of $\text{Fe}_3\text{O}_4 @\text{SiO}_2 @\text{Boric Acid}$

To a mixture of aldehyde (1 mmol) and ketene silyl acetal ((1-methoxy-2-methylprop-1-enyloxy)trimethyl-



Scheme 1. Preparation of $\text{Fe}_3\text{O}_4 @\text{SiO}_2 @\text{Boric acid}$

silane) (1 mmol) in acetonitrile (2 ml), 50 mg (6.1 mol%) of catalyst was added. The mixture was stirred at 80 °C for 8 h under an argon atmosphere. Progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, catalyst was removed from the reaction mixture using an external magnet. Then, HCl (1 N, 5 ml) was added to the residual mixture and the resulting solution stirred for 12 h at room temperature. Then, reaction mixture was transferred to a 250 ml round-bottom flask and reaction vessel was washed with ethyl acetate (3 × 10). Then, all organic solvents were removed under reduced pressure. CH₂Cl₂ (30 ml) was added to the flask and the mixture was transferred to a separatory funnel. After neutralizing with a saturated aqueous solution of NaHCO₃, the product was extracted with CH₂Cl₂ (3 × 10 ml) and organic phase was dried over MgSO₄. Then, solvent was removed under

reduced pressure and the crude product purified using column chromatography (Ethyl acetate/hexane).

RESULTS AND DISCUSSION

Catalyst Characterization

The FT-IR spectra of silica coated magnetite nanoparticles and boric acid coated on magnetite nanoparticles are shown in Fig. 1. The broad band at 3400 cm⁻¹ or 3200 cm⁻¹ was/is attributed to surface hydroxyl groups of the aforementioned nanoparticles. A strong band seen in 562 cm⁻¹ was/is ascribed to Fe-O stretching vibrations. The strong bands at 802 cm⁻¹, 1094 cm⁻¹ and 465 cm⁻¹ were/are assigned to symmetric, asymmetric stretching and bending vibrations of Si-O-Si group, respectively [24]. Characteristic Bands ascribed to the vibrations of B-O

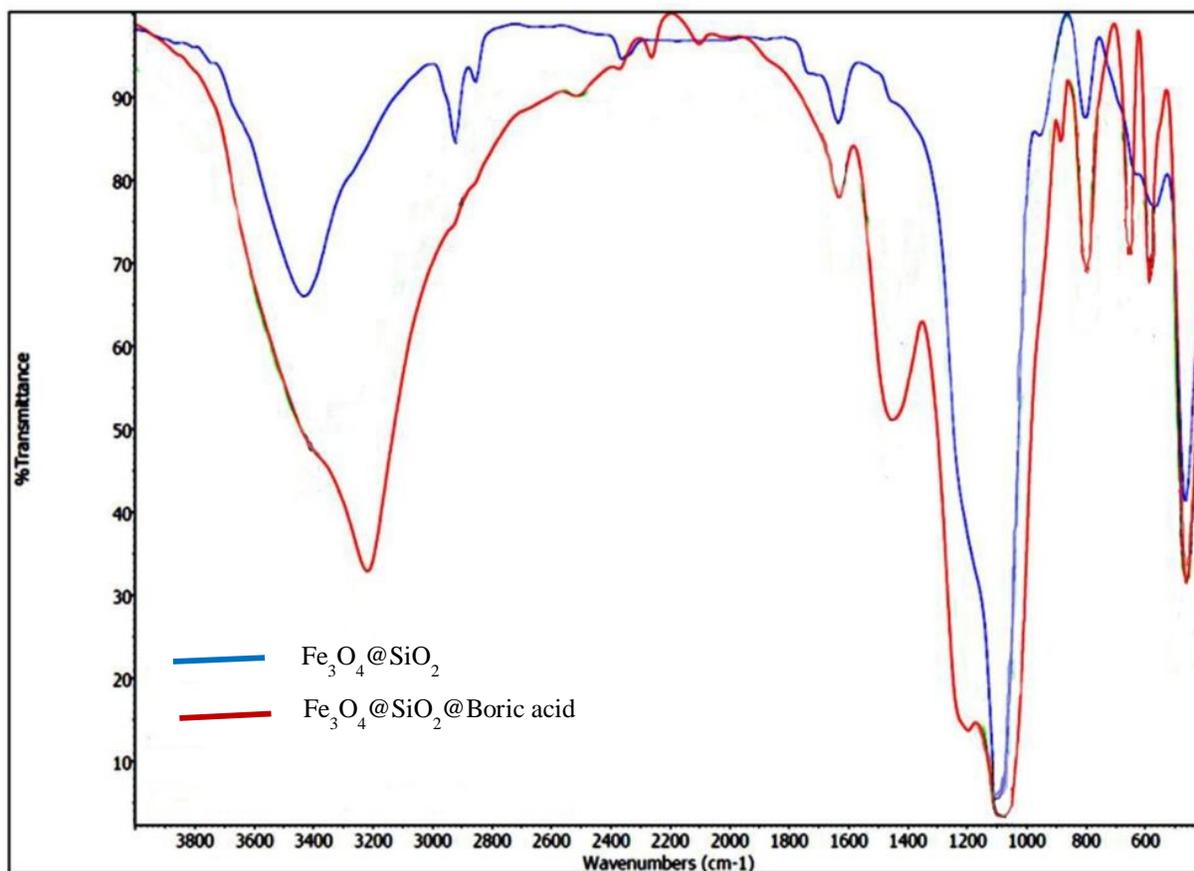


Fig. 1. FT-IR spectra of Fe₃O₄@SiO₂ and Fe₃O₄@SiO₂@Boric acid.

bonds of boric acid [25] appeared at 1440 cm^{-1} and 1450 cm^{-1} which are characteristic bands of, proved successful immobilization of boric acid on the surface of nanoparticles.

The XRD pattern of the catalyst (Fig. 2) showed diffraction peaks of Fe_3O_4 ($2\theta = 35.2^\circ, 41.6^\circ, 50.7^\circ, 63.3^\circ, 67.6^\circ, 74.6^\circ$) corresponding to the reflection planes of (220), (311), (400), (422), (511), (440), respectively (JCPDS 75-0033) (Fig. 2). The average particle size was calculated using Scherrer's formula [26]:

$$\tau = K\lambda/\beta\cos\theta$$

Where τ is the mean size of crystalline phase, K is a dimensionless shape factor, which is close to unity. λ is the X-ray wavelength, β is the FWHM of diffraction peak and θ is the diffraction angle. The resulting mean particle size from this equation is 50.4 nm.

Size and morphology of the nanoparticles were determined by scanning electron microscopy (SEM) (Fig.). The average particle size was determined to be about 47 nm. Boric acid weight percentage of the catalyst was estimated using thermal gravimetric analysis by heating the sample at the rate of $10\text{ }^\circ\text{C min}^{-1}$ up to $800\text{ }^\circ\text{C}$. The weight

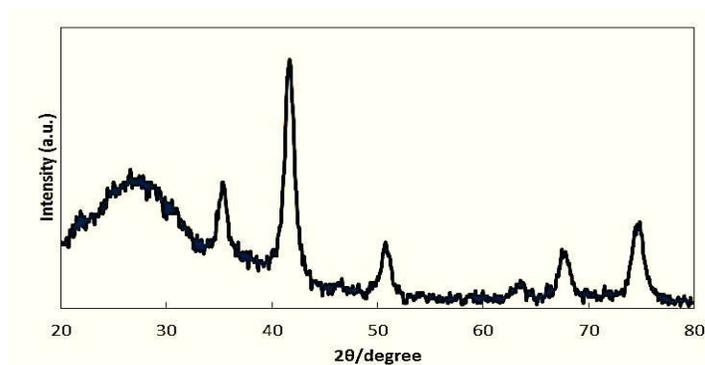


Fig. 2. XRD pattern of $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{Boric acid}$.

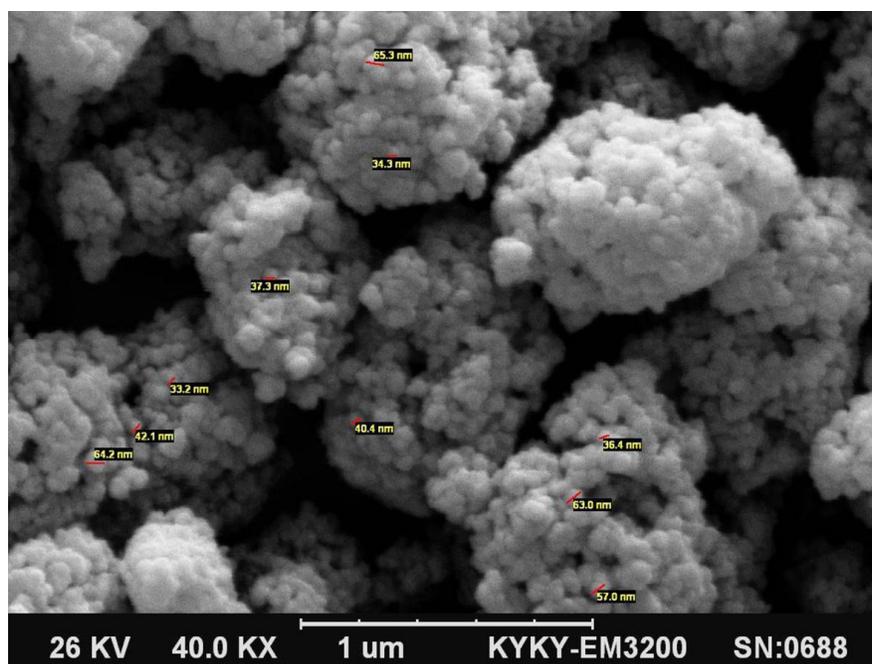


Fig. 3. SEM of $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{Boric acid}$.

losses below 350 °C can be assigned to the release of physisorbed on the surface. The 8% (W/W) weight loss in the range of 350-600 °C is attributed to the removal of boric acid which is equivalent to 1.2 mmol boric acid per gram of the catalyst (Fig. 4). The Boron content of the catalyst was also determined 1.218 mmol g⁻¹ using inductively coupled plasma analysis (ICP).

Superparamagnetism of the nanoparticles was proved using vibrating sample magnetometry with an applied magnetic field with the field range of -10000 to +10000 Oersted at room temperature. As shown in Fig. 5, the hysteresis loop is completely reversible, indicating that the nano particles are super paramagnetic. Saturation magnetization of nanoparticles was 18 emu g⁻¹ which has been significantly decreased compared to that of the pure

Fe₃O₄ (46.7 emu g⁻¹) [27] which can be assigned to silica coating and functionalization with boric acid. Zero remaining magnetization and reversibility of magnetization indicate no aggregation of nanoparticles in the magnetic field.

CATALYTIC ACTIVITY

After characterization, catalytic activity of the catalyst was examined in the Mukaiyama aldol reaction (Scheme 2).

Mukaiyama aldol reaction of a ketene silyl acetal A ((1-methoxy-2-methylprop-1-enyloxy)trimethylsilane) and benzaldehyde was selected as a model reaction to optimize the reaction conditions (Table 1).

As seen in the optimization table, reaction does not

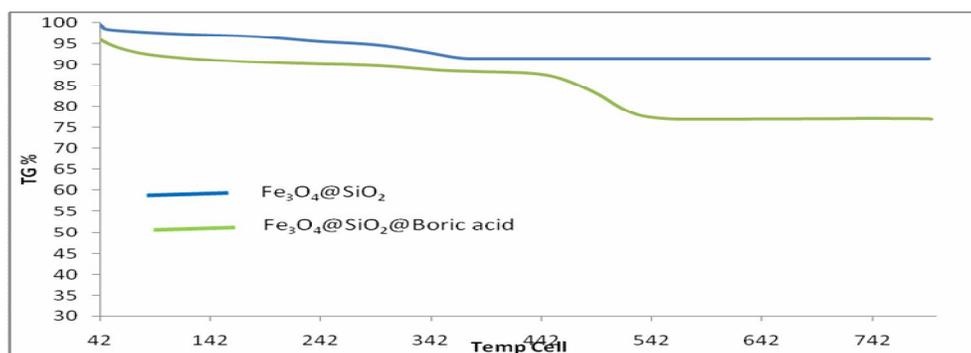


Fig. 4. Thermal gravimetric analysis of Fe₃O₄@SiO₂ and Fe₃O₄@SiO₂@Boric acid.

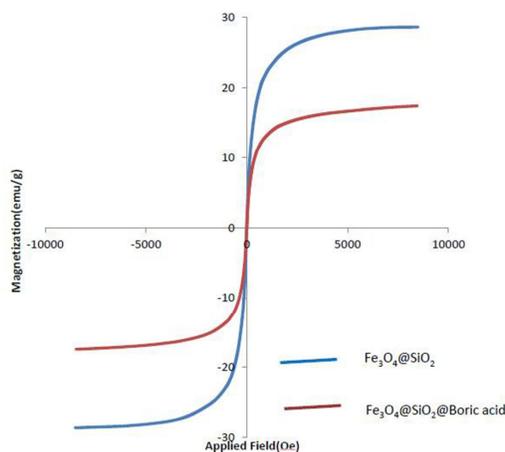
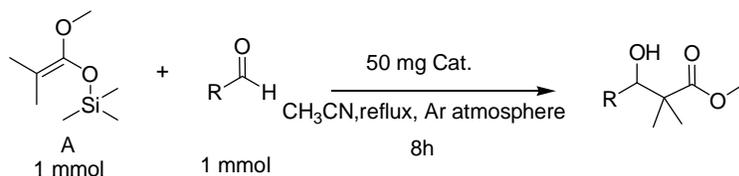


Fig. 5. Hysteresis loop of Fe₃O₄@SiO₂ and Fe₃O₄@SiO₂@Boric acid.



Scheme 2. Mukaiyama-aldol reaction using ((1-methoxy-2-methylprop-1-enyloxy)trimethylsilane

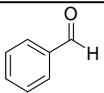
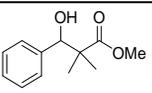
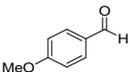
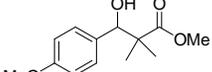
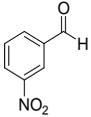
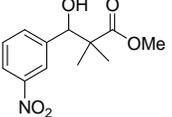
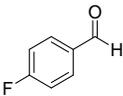
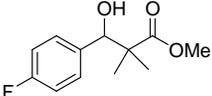
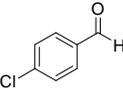
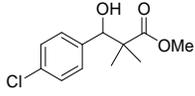
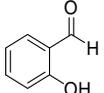
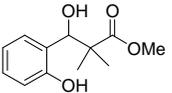
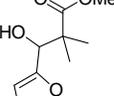
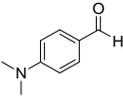
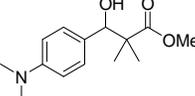
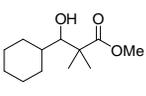
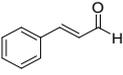
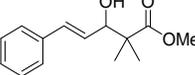
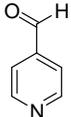
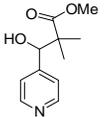
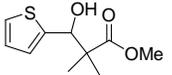
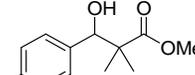
Table 1. Optimization of Reaction Conditions of Mukaiyama Aldol Reaction

Entry	Catalyst (mg)	Solvent	Temp. (°C)	Time (h)	Yield (%) ^a
1	-	-	r.t.	24	No reaction
2	-	-	80	24	No reaction
3	25	-	r.t.	24	<10
4	25	-	80	24	30
5	25	CH ₂ Cl ₂	40	24	20
6	25	CH ₃ CN	80	8	50
7	50	CH ₃ CN	80	8	97
8	-	CH ₃ CN	80	8	No reaction
9	50	DMF	80	24	<10
10	50	Toluene	80	80	50
11	100	CH ₃ CN	80	8	98
12	50 ^b	CH ₃ CN	80	8	<10
13	50	H ₂ O	80	24	<10

Reaction conditions: benzaldehyde (1 mmol), ketene silyl acetal (1 mmol), solvent (2 ml) in the presence of Fe₃O₄@SiO₂@Boric acid as catalyst and under argon atmosphere

^aIsolated yield. ^bFe₃O₄@SiO₂ as catalyst.

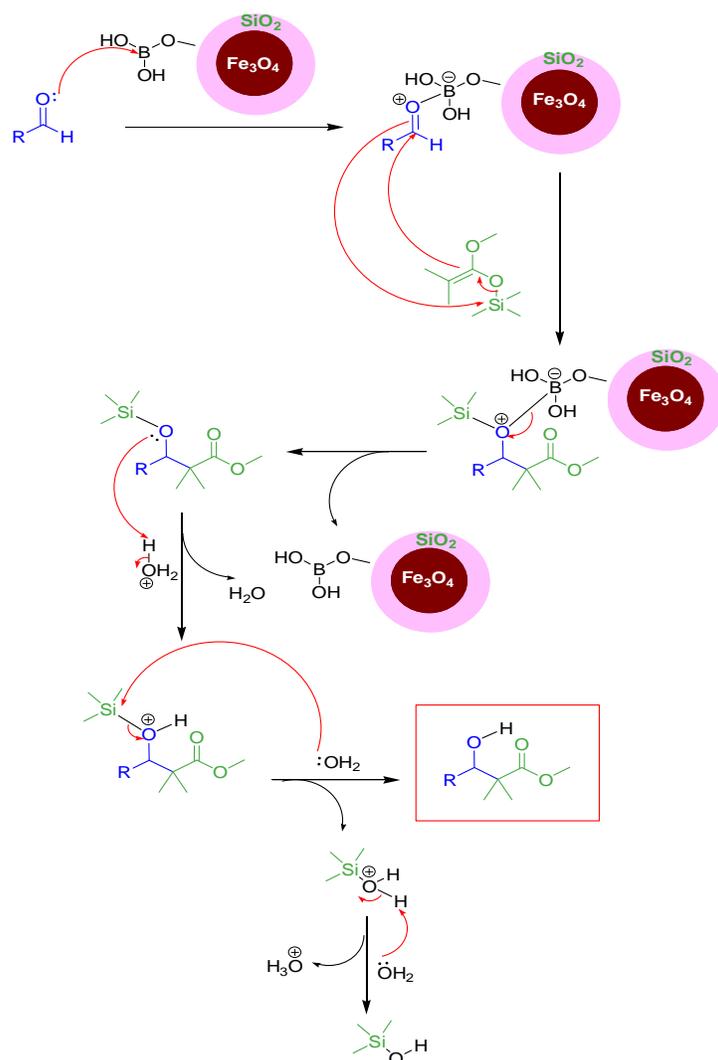
Table 2. Mukaiyama Aldol Reaction of Various Aldehydes in Presence of Fe₃O₄@SiO₂@Boric Acid

Entry	Substrate	Product	Yield (%) ^a
1			97
2			80
3			98
4			85
5			82
6			72
7			75
8			90
9			45
10			65
11			78
12			90
13			88

Reaction condition: aldehyde (1 mmol), ketene silyl acetal A (1 mmol), Fe₃O₄@SiO₂@Boric acid (50 mg), 80 °C, acetonitrile, reaction time 8 h, Ar atmosphere. ^aIsolated yield.

proceed in the absence of a catalyst at room or even elevated temperatures under solvent free conditions (Entries 1, 2). Using 25 mg of boric acid immobilized silica coated magnetite nanoparticles as catalyst resulted in a low yield of the product under solvent free condition. When the reaction was carried out at room temperature, only a small amount of product was detected (Entry 3). Elevating the temperature to 80 °C under the same conditions increased the yield to 30% (Entry 4). The use of dichloromethane as the solvent did not result in significantly enhanced yield (Entry 5). When acetonitrile was used as solvent, product had been formed in an improved yield (Entry 6). Increasing the

amount of catalyst to 50 mg resulted in a good yield (Entry 7). Acetonitrile improved the yield compared to that of the DMF and toluene. To optimize the catalyst loading in the reaction, more than 50 mg of catalyst was used and no significant improvement in yield was observed (Entry 11). To investigate essential presence of boric acid in this reaction, we examined reaction under the same conditions in the absence of boric acid. Reaction was carried out under the same conditions of solvent and temperature in the presence of silica coated magnetite nanoparticles and only a small amount of product was obtained (Entry 12). To test if the reaction could be performed in aqueous conditions,



Scheme 3. Proposed Mechanism for Fe₃O₄@SiO₂@Boric acid catalyzed Mukaiyama aldol reaction

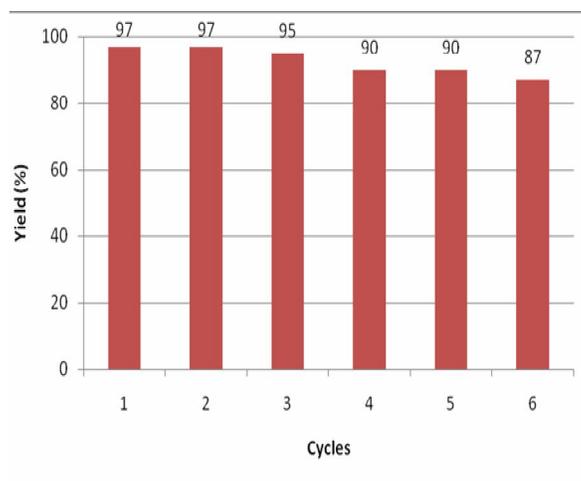


Fig. 6. Reusability of Fe₃O₄@SiO₂@boric acid (50 mg) in Mukaiyama aldol reaction of benzaldehyde (1 mmol) and Ketene silyl acetal A (1 mmol), 80 °C, acetonitrile, 8 h.

water was chosen as a solvent which resulted in negligible yield (Entry 13). The optimum conditions were obtained using 50 mg of the catalyst (6.1 mol% of boric acid), acetonitrile as the solvent in 80 °C for 8 h (Entry 9).

The optimized reaction condition was applied to the various aldehydes (aromatic, aliphatic, α,β -unsaturated), using the aforementioned ketene silyl acetal A as the nucleophile. Results are shown in Table 2.

A plausible mechanism for the reaction has been proposed in Scheme 3. At first, boric acid coordinates to carbonyl group of aldehyde and makes it more active to be attacked by silyl ketene acetal as nucleophile. Then, a silyl group is transferred to the just formed alkoxide group and after the acidic working up it is removed and the β -hydroxyl group is formed.

Catalyst Reusability

Reusability of the catalyst was tested using the reaction of benzaldehyde with ketene silyl acetal A as a model reaction. After completion of the reaction, catalyst was removed with the aid of a permanent magnet, washed with dichloromethane and methanol and dried for the reuse in the subsequent run. The recycled catalyst could be used 6 times with no considerable lost in catalytic activity (Fig.). Heterogeneity of the catalyst was checked by hot filtration test. After 2 h from the beginning of the reaction, catalyst

was removed, and the reaction was continued for another 24 h. The results demonstrated that no product formation was observed in the absence of the catalyst. The leakage of boric acid from the catalyst surface was checked by ICP analysis of the solution mixture after each run. The overall leakage of boric acid from the catalyst surface was 0.06%.

CONCLUSIONS

In conclusion, a new boric acid functionalized nanomagnetic catalyst was prepared by a simple and economical method. This catalyst exhibits good catalytic activity in Mukaiyama aldol reaction. Fe₃O₄@SiO₂@Boric acid can be used at least six times, without significant loss of catalytic activity. The most important advantages of this catalyst are its low cost, easy separation, and recoverability which is made possible by using a permanent magnet.

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