SO₃H-functionalized magnetic Fe₃O₄ nanoparticles as an efficient and reusable catalyst for one-pot synthesis of α -amino phosphonates

HOSEIN HAMADI* and MEYSAM NOROUZI

Chemistry Department, Faculty of Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran
E-mail: H.Hammadi@scu.ac.ir

MS received 22 January 2018; revised 24 June 2018; accepted 23 July 2018; published online 6 September 2018

Abstract. Nanomagnetic Fe₃O₄@SiO₂-SO₃H (SO₃H-MNPs) was prepared *via* grafting sulfonic acid on the silica-coated Fe₃O₄ magnetite nanoparticles (MNPs). The catalytic activity of the prepared SO₃H-MNPs was probed through the one-pot synthesis of N-hydroxy- α -amino phosphonates and α -amino phosphonates via three-component couplings of phenylhydroxylamine or amines with aldehydes and trialkyl phosphites at room temperature. The synthesized SO₃H-MNPs were characterized by XRD, FT-IR, and SEM. The recoverability of the catalyst was achieved by a simple magnetic decantation and reused at least five times without significant degradation in catalytic activity.

Keywords. Magnetic nanoparticle; N-hydroxy- α -amino phosphonate; catalysis; one-pot synthesis; multicomponent reaction.

1. Introduction

The amino phosphonates compounds and their derivatives are known as biologically active compounds with broad range applications in different fields. These compounds are structural analogues of natural amino acids and their biological effects as anti-cancer agents,¹ enzyme inhibitors,² antibiotics,³ anti-thrombotic agents,⁴ peptidases, proteases,⁵ HIV protease,⁶ fungicides,⁷ herbicides, insecticides and plant growth regulators,⁸ indicate the importance of scientific research to develop their synthetic procedures.^{9–11}

Although a number of synthetic methods have been developed for the synthesis of α -amino phosphonates, there are only a few methodologies for the synthesis of N-hydroxy- α -amino phosphonates. The basic method for the preparation of α -amino phosphonates, involves the condensation of a primary or secondary amine, a carbonyl compound (aldehyde or ketone) and dialkyl or trialkyl phosphite,^{12–17} which have been promoted by Lewis or Brønsted acids such as Yb(OTf)₃,¹⁸ ytterbium perfluorooctanoate [Yb(PFO)₃],¹⁹ Cu(OTf)₂,²⁰ InCl₃,²¹

SmI₂,²² ZnCl₂,²³ SnCl₄,²⁴ TaCl₅-SiO₂,²⁵ SiO₂-ZnBr₂,²⁶ alumina supported reagents,²⁷ MgClO₄,²⁸ LiClO₄,²⁹ Sn(OTf)₂,³⁰ CF₃CO₂H,³¹ Scandium tris(dodecyl sulphate) Sc(DS)₃,³² BF₃-Et₂O,³³ aq. HCOOH,³⁴ (CO OH)₂,³⁵ Cd(ClO₄)₂·xH₂O,³⁶ PEG-SO₃H,³⁷ KH₂PO₄,³⁸ Magnetic nanoparticle,³⁹ Aluminium pillared interlayered clay (Al-PILC),⁴⁰ Pentafluorophenylammonium triflate (PFPAT),⁴¹ and Cellulose-SO₃H.⁴²

On the other hand, N-hydroxy-amino phosphonic acids which are fascinating biologically active compounds, are phosphorus analogue of N-hydroxy- α -amino acid, which have an important role in many metabolic and biological processes.⁴³ N-hydroxy- α -amino phosphonates were also announced as suitable synthons for pseudo peptides and illustrate herbicidal and growth-regulating activity.⁴⁴ They are also used for the preparation of α -amino phosphonates and phosphorylated nitrones.⁴⁵

The efficient oriented synthesis of N-hydroxy- α -amino phosphonates has been reported using different reagents and catalysts. However, these methods have various drawbacks like their difficulties in the preparation of catalysts such as LPDE (lithium perchlorate-diethyl ether) and reagents such as dimethyl (trimethylsilyl) phosphate.^{45,46} Palladium hydrogenation of

*For correspondence

Scheme 1. Synthesis of α -amino phosphonate derivatives catalyzed by $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$.

N-hydroxy- α -imino phosphonates using Brønsted acid as activator also reported to produce the N-hydroxy- α -amino phosphonates.⁴³ As an alternative, the use of ionic liquid [bmim][BF₄] as a catalyst has been reported to catalyze the combination of hydroxylamine derivatives with carbonyl groups.⁴⁷

Among various catalyst separations in organic reaction, a simple magnetic isolation process eliminates the requirement of catalyst filtration and centrifugation. Magnetic nanoparticles (MNPs) have gained considerable attention as a solid support for immobilization of homogeneous catalysts.^{48,49} Nanoparticles can be well dispersed in the reaction medium providing a large surface for ready access of catalytic sites. After completing the reactions, the MNPs supported catalysts can be isolated efficiently from the solution through a simple magnetic separation.^{50,51} Furthermore; there are no reports on the use of the nanomagnetic catalysts as promoters for three-component coupling reaction of aldehydes, hydroxylamines and trialkyl phosphites to produce N-hydroxy- α -amino phosphonates.

As part of an ongoing development of efficient protocols for the preparation of phosphonate compounds and in continuation of our recently reported work on MCR,³⁹ herein, we report SO_3H -functionalized silica-coated magnetic nanoparticles [$\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$] as an efficient and recoverable catalyst for the synthesis of N-hydroxy- α -amino phosphonates and α -amino phosphonates at room temperature (25 °C), through three-component reaction of aromatic aldehydes, trialkyl phosphite and phenylhydroxylamine or amines (Scheme 1). The reaction occurred via *in situ* formations of nitron, a highly reactive intermediate, or

imine. All the products are well known and compared with the reported literature.

2. Experimental

2.1 General

Iron (II) chloride tetrahydrate (99%), iron (III) chloride hexahydrate (98%), aromatic aldehydes and other chemicals were purchased from Fluka and Merck companies and used without further purification. Products were characterized by comparison of their physical data, IR and ¹H NMR and ¹³C NMR spectra with known samples. NMR spectra were recorded on a Bruker Advance DPX 400 MHz instrument spectrometer using TMS as an internal standard. The infrared spectra were recorded on a Perkin Elmer spectrum two FT-IR spectrometers. The purity determination of the products and reaction monitoring was accomplished by TLC on TLC-Cards Silica gel-G/UV 254 nm. X-ray diffraction (XRD) patterns of samples were taken on a Philips X-ray diffractometer (Model PW 1840) in the range 2 θ range 50–70. SEM images were also recorded using Philips XL30 scanning electron microscope.

2.2 Preparation of the $\text{Fe}_3\text{O}_4@\text{SiO}_2$

Fe_3O_4 MNPs and Silica-coated Fe_3O_4 nanoparticles (Si-MNPs) were prepared according to the procedure reported by Kiasat and Ghasemzadeh.^{52–54} Briefly, a solution of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (55.98 mmol, 15.13 g) and $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (31.9 mmol, 6.34 g) in 640 mL of deionized water was stirred at 80 °C and then 80 mL of concentrated ammonia (25%) was added until the pH reached 11–12. The mixture was stirred vigorously at 80 °C until precipitation. Afterwards, the

Figure 1. FT-IR spectra of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$.

Figure 2. X-ray diffraction for $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$.

prepared magnetic NPs were separated magnetically, washed with deionized water and then dried at 70 °C for 8 h.

In order to prepare the Silica-coating Fe_3O_4 nanoparticles, 2 g of the prepared Fe_3O_4 NPs were sonicated in a mixture of ethanol (450 mL), deionized water (120 mL) and concentrated ammonia aqueous solution (10 mL, 25 wt%), followed by the addition of TEOS (2 mL). After stirring at room temperature for 15 h, the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ was separated using an external magnet and washed several times with deionized water and dried under vacuum at 60 °C overnight.

2.3 Preparation of the $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$

According to the literature⁵⁶ the as-synthesized $\text{Fe}_3\text{O}_4@\text{SiO}_2$ (2.5 g) was added to dry CH_2Cl_2 (75 mL) in a 500 mL suction flask bearing constant pressure dropping funnel

Figure 3. SEM image of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$.

Table 1. Optimization of the reaction conditions^a.

Entry	Catalyst (g)	Solvent	Temp. (°C)	Time (h)	Yield (%)
1	No catalyst	Neat	25	4	Trace
2	No catalyst	Neat	100	4	Trace
3	0.05	CH ₂ Cl ₂	25	3	66
4	0.05	CH ₃ CN	25	4	45
5	0.05	EtOH	25	4	20
6	0.05	CHCl ₃	25	3	62
7	0.07	CH ₂ Cl ₂	25	3	78
8	0.1	CH₂Cl₂	25	2	88
9	0.1	CH ₂ Cl ₂	40	2	89
10	0.15	CH ₂ Cl ₂	25	2	88

^aBenzaldehyde (1.0 mmol), phenylhydroxylamine (1.2 mmol), triethyl phosphite (1.2 mmol), Fe₃O₄@SiO₂-SO₃H.

Scheme 2. Synthesis of N-hydroxy- α -amino phosphonates **4**.

linked to the gas outlet. The mixture was homogenized by ultrasonic for 10 min. Then chlorosulfonic acid (1.75 g, ca. 1 mL, 15 mmol) in dry CH₂Cl₂ (20 mL) was added dropwise over a period of 30 min at room temperature. After completion of the addition, the mixture was shaken for 90 min, while the residual HCl was eliminated by suction. Then, the Fe₃O₄@SiO₂-SO₃H was separated by an external magnet from the mixture and washed several times with dried CH₂Cl₂. Finally, Fe₃O₄@SiO₂-SO₃H was dried under vacuum at 60 °C. The identities of the catalyst were confirmed according to the reference by XRD, SEM and FT-IR.

2.4 General procedure

0.1 g the catalyst (Fe₃O₄@SiO₂-SO₃H) was added to the solution of Aldehyde (2 mmol), phenylhydroxylamine (2 mmol, 22 mg), and diethyl phosphite (2 mmol, 28 mg) in 2 mL CH₂Cl₂ and stirred at room temperature (25 °C) for the appropriate time (Table 2). The progress of the reaction was monitored by TLC. In the end, CH₃Cl was added to dilute the

Figure 4. Recyclability of the catalyst.

reaction mixture and the organic layer was simply decanted by means of an external magnet. The isolated solution was purified on a silica-gel plate to obtain the pure product. The

Scheme 3. The proposed mechanism for the synthesis of N-hydroxy- α -amino phosphonates.

identities of the products were confirmed by FT-IR and ^1H NMR spectral data related to reference.^{47–49,51,55,56}

2.5 Representative spectroscopic data

4a: Viscous liquid; ^1H NMR (400 MHz, CDCl_3): δ 1 (t, $J = 6.8$ Hz, CH_3), 1.26 (t, $J = 6.8$ Hz, CH_3), 3.51–3.56 (m, 1H), 3.79–3.85 (m, 1H), 4.11–4.18 (m, 2H), 4.98 (brs, OH), 5.24–5.31 (d, 1H, $J_{P-H} = 22$ Hz), 6.51–6.59 (d, $J = 8.1$ Hz, 2H), 6.61–6.63 (t, $J = 7.6$ Hz, 1H), 7.01–7.06 (m, 3H), 7.17–7.21 (m, 1H), 7.48–7.50 (m, 2H) ppm. IR (KBr, ν_{max} cm^{-1}): 3375, 2970, 1602, 1499, 1227, 1022, 967, 748, 670.

6g: Yellow solid, M.p.: 123–125 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3): 1.18–1.22 (t, $J = 7.1$ Hz, CH_3), 1.26–1.34 (t, $J = 7.1$ Hz, CH_3), 3.88–3.90 (m, 1H), 4.03–4.09 (m, 1H), 4.13–4.19 (m, 2H), 4.85–4.91 (d, $J_{P-H} = 24.8$ Hz, 1H), 6.55–6.57 (d, $J = 8$ Hz, 2H), 6.74–6.78 (t, $J = 6.8$ Hz, 1H), 7.12–7.15 (t, $J = 7.6$ Hz, 2H), 7.67–7.70 (m, 2H), 8.20–8.23 (d, $J = 8.8$ Hz, 2H) ppm.

6i: Viscous liquid; ^1H NMR (400.13 MHz, CDCl_3): 1.05–1.10 (t, $J = 7.2$ Hz, CH_3), 1.32–1.36 (t, $J = 7.2$ Hz, CH_3), 3.61–3.64 (m, 1H), 3.89–3.93 (m, 1H), 4.21–4.28 (m, 2H), 4.08–4.19 (m, 2H), 5.35–5.41 (d, $J_{P-H} = 24.4$ Hz, 1H), 6.62–6.64 (d, $J = 8.4$ Hz, 2H), 6.70–6.73 (t, $J = 7.2$, 1H), 7.11–7.15 (t, $J = 8.4$ Hz, 3H), 7.27–7.30 (t, $J = 7.6$, 1H), 7.57–7.62 (t, $J = 8.4$, 2H) ppm.

6j: Yellow solid, M.p.: 62–65 $^\circ\text{C}$; ^1H NMR (400.13 MHz, CDCl_3): δ 1.02–1.05 (t, $J = 7.2$ Hz, CH_3), 1.19–1.23 (t, $J = 7.2$ Hz, CH_3), 3.54–3.65 (m, 1H), 3.84–3.87 (m, 1H), 4.01–4.07 (m, 2H), 4.66–4.72 (d, $J_{P-H} = 24.4$ Hz, 1H),

6.51–6.53 (d, $J = 7.6$ Hz, 2H), 6.6–6.64 (t, $J = 7.6$ Hz, 1H), 7.01–7.05 (m, 2H), 7.18–7.21 (m, 1H), 7.24–7.27 (m, 2H), 7.39–7.40 (m, 1H) ppm. IR (KBr, ν_{max} cm^{-1}): 3298, 2988, 1607, 1494, 1241, 1047, 986, 799, 747.

6n: Viscous colorless liquid; ^1H NMR (400.13 MHz, CDCl_3): 1.10–1.14 (t, $J = 7.2$ Hz, CH_3), 1.23–1.26 (t, $J = 7.2$ Hz, CH_3 Hz), 3.73–3.77 (m, 1H), 3.96–3.99 (m, 1H), 4.06–4.14 (m, 2H), 5.48–4.56 (dd, 1H), 5.8 (brs, NH), 6.45–6.47 (d, $J = 8.4$ Hz, 1H), 6.56–6.60 (t, $J = 1.2$ Hz, 1H), 7.25–7.36 (m, 4H), 7.52–7.54 (t, $J = 1.2$ Hz, 2H), 8.05–8.07 (t, 1H) ppm.

3. Results and Discussion

The catalyst was synthesized according to the report⁵² and characterized by X-ray powder diffraction (XRD), Scanning electron microscope (SEM) and Fourier transform infrared (FT-IR). The Fe_3O_4 magnetic nanoparticles as the catalyst core were prepared by a simple method using the co-precipitation of FeCl_2 and FeCl_3 in ammonia solution. The synthesis of sulphuric acid immobilized on Si-MNPs was achieved by using the reported method.⁵²

The FT-IR spectrum of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$ shows the peaks at 1090, 806 and 462 cm^{-1} assigned to the Si-O-Si. The presence of sulphonyl group is confirmed by 1217 and 1124 cm^{-1} bands that were covered by a stronger absorption of the Si-O bond at 1092 cm^{-1} . In addition, the characteristic peaks of Fe-O at 580 cm^{-1} and Si-OH at 956 cm^{-1} were also observed (Figure 1).

Table 2. Synthesis of α -amino phosphonates (**6**) in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SO}_3\text{H}$ via Scheme 1^a.

Entry	Aldehyde	Amine	P(OR) ₃		Time (min)	Yield (%) ^b
a	$\text{C}_6\text{H}_5\text{CHO}$	$\text{C}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OEt})_3$		45	92
b	$\text{C}_6\text{H}_5\text{CHO}$	$\text{C}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OMe})_3$		50	96
c	$\text{C}_6\text{H}_5\text{CHO}$	$4\text{-CNC}_6\text{H}_4\text{NH}_2$	$\text{P}(\text{OEt})_3$		60	92
d	$4\text{-MeC}_6\text{H}_4\text{CHO}$	$4\text{-CNC}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OEt})_3$		40	90
e	$4\text{-PhC}_6\text{H}_4\text{CHO}$	$\text{C}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OMe})_3$		55	92
f	$4\text{-PhC}_6\text{H}_4\text{CHO}$	$\text{C}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OEt})_3$		55	85
g	$4\text{-NO}_2\text{C}_6\text{H}_4\text{CHO}$	$3\text{-BrC}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OEt})_3$		60	88
h	$4\text{-HOC}_6\text{H}_4\text{CHO}$	$\text{C}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OEt})_3$		60	82
i	$2\text{-ClC}_6\text{H}_4\text{CHO}$	$\text{C}_6\text{H}_5\text{NH}_2$	$\text{P}(\text{OEt})_3$		70	88

Table 2. continued

Entry	Aldehyde	Amine	P(OR) ₃		Time (min)	Yield (%) ^b
j	2-BrC ₆ H ₄ CHO	C ₆ H ₅ NH ₂	P(OEt) ₃		70	85
k	4-NO ₂ C ₆ H ₄ CHO	4-CNC ₆ H ₅ NH ₂	P(OEt) ₃		65	82
l	4-NO ₂ C ₆ H ₄ CHO	C ₆ H ₅ NH ₂	P(OEt) ₃		55	84
m		C ₆ H ₅ NH ₂	P(OEt) ₃		70	84
n	C ₆ H ₅ CHO		P(OEt) ₃		90	65

^aAll reactions were carried out at room temperature, 1 mmol aldehyde, 1 mmol amine, 1 mmol trialkyl phosphite and 0.15 g catalyst.

^bIsolated yields.

The X-ray diffraction patterns of Fe₃O₄@SiO₂-SO₃H are shown in Figure 2. XRD diagram of the bare MNPs displayed patterns consistent with the patterns of spinel ferrites described in the previous report.⁵² The average MNPs core diameter Fe₃O₄@SiO₂-SO₃H was calculated to be 8.2 and 9.6 nm, respectively from the XRD results by Scherrer's equation. The average size of the crystallites can be calculated using the Scherrer equation ($D = K\lambda/\beta \cos \theta$), wherein this equation D is the mean crystalline size, K is a grain shape dependent constant (0.9), λ is the incident beam wavelength (0.154), θ is the Bragg reflection angle and β is the full width at half maximum (FWHM) of the main diffraction peak.^{57–59}

The SEM image of Fe₃O₄@SiO₂-SO₃H is presented in Figure 3, shows a spherical shape with nano dimension ranging from 117 to 220 nm.

The loading capacity of the Fe₃O₄@SiO₂-SO₃H was determined by titration and found to be 2.58 mmol/g.

A test reaction using phenylhydroxylamine, benzaldehyde, and triethyl phosphite at room

temperature and 100 °C in the absence of Fe₃O₄@SiO₂-SO₃H was performed in order to establish the real effectiveness of the catalyst (Table 1, entry 1, 2). It was found that no conversion to product was obtained even after 4 hours of heating (Monitoring by TLC). To optimize the catalyst loading, a model reaction using phenylhydroxylamine, benzaldehyde, and triethyl phosphite was carried out under different amount of catalyst in different solvents (Table 1). It was observed that 0.1 g loading of the catalyst in CH₂Cl₂ provides the maximum yield in minimum time (Table 1, entry 8). Higher percentage loading of the catalyst neither increased the yield nor lowered the reaction time.

By using the optimized reaction conditions, the efficiency of this protocol was studied for the synthesis of various N-hydroxy- α -amino phosphonates, and the results are summarized in Scheme 2. In most cases, the reaction proceeded with high efficiency and broad functional-group tolerance on aldehyde which displayed high reactivity under the optimized reaction

Table 3. Comparison of various catalysts in Synthesis of N-hydroxy- α -amino phosphonates and α -amino phosphonates.

Reaction	Catalyst	Solvent	Temp. (°C)	Time	Yield (%)	Ref.
Synthesis of N-hydroxy- α -aminophosphonates	[Bmim]BF ₄	—	r.t	2.5 h	92	[47]
	[Bmim]PF ₆	—	r.t	3.5 h	89	[47]
Synthesis of α -aminophosphonates	LPDE	—	r.t	15 min	90	[45,46]
	Fe ₃ O ₄ @SiO ₂ -SO ₃ H	CH ₂ Cl ₂	r.t	2 h	88	This work
	SbCl ₃ /Al ₂ O ₃	CH ₃ CN	r.t	3 h	91	[27]
	PEG-SO ₃ H	—	50	3.5h	98	[37]
	Nano Fe ₃ O ₄	—	50	48 min	94	[39]
	Cd(ClO ₄) ₂ ·xH ₂ O	—	r.t	40 min	92	[36]
	In/HCl	H ₂ O	r.t	1.5 h	88	[21]
	Fe ₃ O ₄ @SiO ₂ -SO ₃ H	CH ₂ Cl ₂	r.t	45 min	92	This work

conditions and generated the desired products in high yields. However, unfortunately, when some aliphatic aldehydes such as isobutyraldehyde and cyclohexane carboxaldehyde were used in this protocol under the above-optimized conditions, the desired products could not be obtained.

Since the catalyst was separated by simple magnetic decantation, it was washed with ether and reused in the subsequent reaction. Yields of the product decreased only slightly after four time's reuse of catalyst. For example, the reaction of benzaldehyde, phenylhydroxylamine and triethyl phosphite afforded the corresponding N-hydroxy- α -amino phosphonates in 88%, 86%, 85%, 85% and 84% yields over five cycles (Figure 4).

A possible mechanism for the synthesis of N-hydroxy- α -amino phosphonates catalyzed by Fe₃O₄@SiO₂-SO₃H has been proposed (Scheme 3). The reaction proceeds *via* the nitron intermediate, which was formed by the nucleophilic addition of phenylhydroxylamine to an aldehyde. Fe₃O₄@SiO₂-SO₃H as Brønsted acid plays a role in increasing the electrophilic character of the starting aldehyde. Subsequent nucleophilic addition of the triethyl phosphite provides the adduct intermediate that on subsequent reaction followed by elimination of MeOH afforded the product.

According to the mechanism of these reactions, the planar nitron and iminium intermediate are formed followed by nucleophilic attack of the trialkyl phosphite. It can be concluded that racemic mixture of the product is obtained.

Bearing in mind the important properties of α -amino phosphonates, we decided to explore this magnetically effective catalyst for the preparation of α -amino phosphonates using the optimized condition (Scheme 1). The results are summarized in Table 2.

We investigated various aromatic and heteroaromatic aldehyde containing electron withdrawing or electron donating functional groups as well as an amine with trialkyl phosphonate P(OR)₃ (R: Me, Et) at r.t. (25 °C) (Table 2). The given results in Table 2 show that this one pot, three component condensations completed within 45–95 min, with good isolated yields. The 2-aminopyridine gave less yield and required more time, probably due to the low reactivity of amino group. The reaction was compatible with various functional groups such as Cl, Br, CN, OMe, NO₂, and OH not interfering with the competitive complex formation with the catalyst.

The activity of Fe₃O₄@SiO₂-SO₃H by considering the yield for the model reaction is compared with various heterogeneous catalysts in Table 3. In addition to easily magnetic decantation of Fe₃O₄@SiO₂-SO₃H, it showed efficient catalytic activity in relatively short reaction time, with excellent yields.

4. Conclusion

In summary, this paper describes the three-component reaction of aromatic aldehydes, trialkyl phosphite and phenylhydroxylamine or amines to produce N-hydroxy- α -amino phosphonates and α -amino phosphonates using SO₃H-functionalized silica-coated magnetic nanoparticles [Fe₃O₄@SiO₂-SO₃H] as a novel promoter. The simple operation combined with easy recovery and reuse of this novel catalyst, make this a more convenient, economical and user-friendly process for the synthesis of N-hydroxy- α -amino phosphonates and α -amino phosphonates of biological and medicinal importance. Our results here did not detect leaching of acidic site species and the Fe₃O₄@SiO₂-SO₃H can be easily

removed by an external magnet and used 5 cycles in the reaction without significant loss in activity.

Supplementary Information (SI)

Supplementary Information is available at www.iac.ac.in/chemsci.

Acknowledgements

The authors thank Shahid Chamran University of Ahvaz for financial support (Grant No. 31400.02.3.95).

References

- Ramakrishna K, Thomas J M and Sivasankar C 2016 A Green Approach to the Synthesis of α -Amino Phosphonate in Water Medium: Carbene Insertion into the N-H Bond by Cu(I) Catalyst *J. Org. Chem.* **81** 9826
- Allen M C, Fuhrer W, Tuck B, Wade R and Wood J M 1989 Renin inhibitors. Synthesis of transition-state analog inhibitors containing phosphorus acid derivatives at the scissile bond *J. Med. Chem.* **32** 1652
- Atherton F R, Hassal C H and Lambert R W 1986 Synthesis and structure-activity relationships of antibacterial phosphonopeptides incorporating (1-aminoethyl)phosphonic acid and (aminomethyl)phosphonic acid *J. Med. Chem.* **29** 29
- Meyer J H and Barlett P A 1998 Macrocyclic Inhibitors of Penicillopepsin. 1. Design, Synthesis, and Evaluation of an Inhibitor Bridged between P1 and P3 *J. Am. Chem. Soc.* **120** 4600
- Miller D J, Hammond S M, Anderluzzi D and Bugg T D H 1998 Aminoalkylphosphinate inhibitors of D-Ala-D-Ala adding enzyme *J. Chem. Soc. Perkin Trans.* **1** 131
- Peyman A, Stahl W, Wagner K, Ruppert D and Ruppert K H X 1994 Non-peptide-based inhibitors of human immune deficiency virus-1 protease *Bioorg. Med. Chem. Lett.* **4** 2601
- Ali S A N, Ali S, Zakir S, Patel M and Farooqui M 2012 Synthesis of new α -aminophosphonate system bearing Indazole moiety and their biological activity *Eur. J. Med. Chem.* **50** 39
- Maier L and Diel P J 1991 Organic phosphorus compounds 97. Synthesis and properties of 1-amino-2-aryl- and 2-pyridylethylphosphonic acids and derivatives *Phosphorus, Sulfur Silicon Relat. Elem.* **62** 15
- Sobhani S and Khakzad F 2017 A novel hydrophobic copper complex supported on γ -Fe₂O₃ as a magnetically heterogeneous catalyst for one-pot three-component synthesis of α -aminophosphonates *Appl. Organometal. Chem.* **31** e3877
- Nakamura Y and Ukita T 2002 Construction of Heterocyclic Compounds by Use of α -Diazophosphonates: New One-Pot Syntheses of Indoles and Isocoumarins *Org. Lett.* **14** 2317
- Debrouwer W, Heugebaert T S A and Stevens C V 2014 Preparation of Tetrasubstituted 3-Phosphonopyrroles through Hydroamination: Scope and Limitations *J. Org. Chem.* **10** 4322
- Cheng X, Goddard R, Buth G and List B 2008 Direct Catalytic Asymmetric Three-Component Kabachnik-Fields Reaction *Angew. Chem. Int. Ed.* **47** 5079
- Zefirov N S and Matveeva E D 2008 Catalytic Kabachnik-Fields reaction: New horizons for old reaction *Arkivoc* part 1 1
- Cherkasov R A and Galkin V I 1998 The Kabachnik-Fields reaction: Synthetic potential and the problem of the mechanism *Russ. Chem. Rev.* **67** 857
- Kafarski P, Gorniak M G V and Andrasiak I 2015 Kabachnik-Fields reaction under green conditions – A critical overview *Curr. Green. Chem.* **2** 218
- Keglevich G and Balint E 2012 The Kabachnik-Fields Reaction: Mechanism and Synthetic Use *Molecules* **17** 12821
- Bera K, Nadkarni D and Namboothiri I N N 2013 Asymmetric synthesis of $\gamma\gamma$ -aminophosphonates: The Bio-isosteric analogs of $\gamma\gamma$ -aminobutyric acid *J. Chem. Sci.* **125** 443
- Qian C and Huang T 1998 One-Pot Synthesis of α -Amino Phosphonates from Aldehydes Using Lanthanide Triflate as a Catalyst *J. Org. Chem.* **63** 4125
- Tang J, Wang T, Zhang L, Wu S and Mao D 2011 A facile synthesis of α -aminophosphonates catalyzed by ytterbium perfluorooctanoate under solvent-free conditions *J. Fluorine Chem.* **132** 102
- Paraskar A S and Sudalai A 2006 A novel Cu(OTf)₂ mediated three component high yield synthesis of α -aminophosphonates *Arkivoc* **2006** 183
- Ranu B C, Hajra A and Jana U 1999 General Procedure for the Synthesis of α -Amino Phosphonates from Aldehydes and Ketones Using Indium(III) Chloride as a Catalyst *Org. Lett.* **1** 1141
- Xu F, Luo Y, Deng M and Shen Q 2003 One-Pot Synthesis of α -Amino Phosphonates Using Samarium Diiodide as a Catalyst Precursor *Eur. J. Org. Chem.* **2003** 4728
- Shamrao T D, Sandip R K, Sandeep S K, Thandankorai G S and Radha V J 2012 Choline chloride.2ZnCl₂ ionic liquid: An efficient and reusable catalyst for the solvent free Kabachnik-Fields reaction *Tetrahedron Lett.* **53** 2277
- Laschat S and Kunz H 1992 Carbohydrates as Chiral Templates: Stereoselective Synthesis of (R)- and (S)- α Aminophosphonic Acid Derivatives *Synthesis* **1992** 90
- Chandrasekhar S, Prakash S J, Jagadeshwar V and Nar-sihmulu C 2001 Three component coupling catalyzed by TaCl₅ – SiO₂: Synthesis of α -amino phosphonates *Tetrahedron Lett.* **42** 5561
- Sivala M R, Devineni S R, Golla M, Ametla V M, Pothuru G K and Chamarthi N R 2016 A heterogeneous catalyst, SiO₂-ZnBr₂: An efficient neat access for α -aminophosphonates and antimicrobial activity evaluation *J. Chem. Sci.* **128** 1303
- Kaboudin B and Nazari R 2001 Microwave-assisted synthesis of 1-aminoalkyl phosphonates under solvent-free conditions *Tetrahedron Lett.* **42** 8211
- Bhagat S and Chakraborti A K 2007 An Extremely Efficient Three-Component Reaction of Aldehydes/Ketones, Amines, and Phosphites (Kabachnik-Fields Reaction) for the Synthesis of α -Aminophosphonates Catalyzed by Magnesium Perchlorate *J. Org. Chem.* **72** 1263

29. Heydari A, Zarei M, Alijanianzadeh R and Tavakol H 2001 One-pot synthesis of N-trimethylsilyloxy- α -amino phosphonates from aldehydes using lithium perchlorate/diethyl ether as a catalyst *Tetrahedron Lett.* **42** 3629
30. Gallardo-Macias R and Nakayama K 2010 Tin(II) Compounds as Catalysts for the Kabachnik-Fields Reaction under Solvent-Free Conditions: Facile Synthesis of α -Aminophosphonates *Synthesis* **1** 57
31. Akiyama T, Sanada M and Fuchibe K 2003 Brønsted Acid-Mediated Synthesis of α -Amino Phosphonates under Solvent-Free Conditions *Synlett* **10** 1463
32. Manabe K and Kobayashi S 2000 Facile synthesis of α -aminophosphonates in water using a Lewis acid-surfactant-combined catalyst *Chem. Commun.* **0** 669
33. Ha H J and Nam G S 1992 Expedient Synthesis of α -Substituted α , β -Unsaturated γ -Amino Acids (Dipeptide Mimetics); Wittig Reaction of α -Amino Aldehydes with α -Substituted Alkoxy carbonyl Phosphoranes *Synth. Commun.* **22** 1143
34. Mohammadian E, Ghafuri H and Kakanejadifard A 2017 A new procedure for synthesis of α -aminophosphonates by aqueous formic acid as an effective and environment-friendly organocatalyst *J. Chem. Sci.* **129** 1883
35. Vahdat S M, Baharfar R, Tajbakhsh M, Heydari A, Baghbanian S M and Khaksar S 2008 Organocatalytic synthesis of α -hydroxy and α -aminophosphonates *Tetrahedron Lett.* **49** 6501
36. Dindulkar S D, Reddy M V and Jeong V T 2012 Cd (ClO₄)₂ · xH₂O as a novel catalyst for the synthesis of α -aminophosphonates under solvent-free conditions *Catal. Commun.* **17** 114
37. Reddy C B, Kumar K S, Kumar M A, Reddy M V N, Krishna B S, Naveen M, Arunasree M K, Reddy C S, Raju C N and Reddy C D E 2012 PEG-SO₃H catalyzed synthesis and cytotoxicity of α -aminophosphonates *Eur. J. Med. Chem.* **47** 553
38. Joshi R S, Mandhane P G, Dabhade S K and Gill C H 2010 Potassium dihydrogen phosphate: An inexpensive reagent for the solvent-free, One-pot synthesis of α -aminophosphonates *Green Chem. Lett. Rev.* **3** 191
39. Hamadi H, Kooti M, Afshari M, Ghiasifar Z and Adibpour N 2013 Magnetic nanoparticle supported polyoxometalate: An efficient and reusable catalyst for solvent-free synthesis of α -aminophosphonates *J. Mol. Catal. A: Chem.* **373** 25
40. AhmadDar B, Chakraborty A, Sharma P R, Shrivastava V, Bhowmik A, Vyas D, Bhatti P, Sharma M and Singh B 2013 Grinding-induced rapid, Convenient and solvent free approach for the one pot synthesis of α -aminophosphonates using aluminium pillared interlayered clay catalyst *J. Ind. Eng. Chem.* **19** 732
41. Malamiri F and Khaksar S 2014 Pentafluorophenylammonium triflate (PFPA⁺Tf⁻): A new organocatalyst for the one-pot three-component synthesis of α -aminophosphonates *J. Chem. Sci.* **126** 807
42. Kumar K S, Krishna B S, Reddy C B, Reddy M V N and Reddy C S 2017 Solvent-free synthesis of α -aminophosphonates: Cellulose-SO₃H as an efficient catalyst *Arab. J. Chem.* **10** S368
43. Goulioukina N S, Shergold I A, Bondarenko G N, Ilyin M M, Davankov V A and Beletskaya I P 2012 Palladium-Catalyzed Asymmetric Hydrogenation of N-Hydroxy- α -imino Phosphonates Using Brønsted Acid as Activator: The First Catalytic Enantioselective Approach to Chiral N-Hydroxy- α -amino Phosphonates *Adv. Synth. Catal.* **345** 2727
44. Gouverneur V and Lalloz M H 1996 N-Hydroxy- α -amino phosphonate derivatives as potential haptens for eliciting catalytic antibodies *Tetrahedron Lett.* **37** 6331
45. Hubber R and Vasella A 1990 The kinetic anomeric effect. Additions of nucleophiles and of dipolarophiles to N-glycosylnitrones and to N-pseudoglycosylnitrones *Tetrahedron* **46** 33
46. De Risi C, Dondoni A, Perroneb D and Pollinia G P 2001 O-Silyl triflate-promoted addition of diethyl phosphite to chiral aldonitrones. A rapid access to complex α -amino phosphonates and their N-hydroxy derivatives *Tetrahedron Lett.* **42** 3033
47. Yadav J S, Reddy B V S and Sreedhar P 2003 Three-Component One-Pot Synthesis of α -Hydroxylamino Phosphonates Using Ionic Liquids *Adv. Synth. Catal.* **34** 564
48. Lim C W and Lee I S 2010 Magnetically recyclable nanocatalyst systems for the organic reactions *Nano Today* **5** 412
49. Shylesh S, Schunemann V and Thiel W R 2010 Magnetically Separable Nanocatalysts: Bridges between Homogeneous and Heterogeneous Catalysis *Angew. Chem. Int. Ed.* **49** 3428
50. Riente P, Mendoza C and Pericas M A 2011 Functionalization of Fe₃O₄ magnetic nanoparticles for organocatalytic Michael reactions *J. Mater. Chem.* **21** 7350
51. Abu-Rezig R, Alper H, Wang D and Post M L 2006 Metal Supported on Dendronized Magnetic Nanoparticles: Highly Selective Hydroformylation Catalysts *J. Am. Chem. Soc.* **128** 5279
52. Kiasat A R and Davarpanah J 2013 Fe₃O₄@silica sulfuric acid nanoparticles: An efficient reusable nanomagnetic catalyst as potent solid acid for one-pot solvent-free synthesis of indazolo[2,1-b]phthalazine-triones and pyrazolo[1,2-b]phthalazine-diones *J. Mol. Catal. A: Chem.* **373** 46
53. Kiasat A R and Davarpanah 2015 Fe₃O₄@Silica sulfuric acid core-shell composite as a novel nanomagnetic solid acid: Synthesis, Characterization and application as an efficient and reusable catalyst for one-pot synthesis of 3,4-dihydropyrimidinones/thiones under solvent-free conditions *Res. Chem. Intermed.* **41** 2991
54. Ghasemzadeh M A and Azimi-Nasrabad M 2016 Nano-Fe₃O₄-encapsulated silica particles bearing sulfonic acid groups as a magnetically separable catalyst for the green and efficient synthesis of 14-aryl-14H-dibenzo[a,i]xanthene-8,13-dione derivatives *Res. Chem. Intermed.* **42** 1057
55. Bhattacharya A K and Rana K C 2008 Amberlite-IR 120 catalyzed three-component synthesis of α -amino phosphonates in one-pot *Tetrahedron Lett.* **49** 2598
56. Wu J, Sun W, Xia H G and Sun X 2006 A facile and highly efficient route to α -amino phosphonates via three-component reactions catalyzed by Mg(ClO₄)₂ or molecular iodine *Org. Biomol. Chem.* **4** 1663

57. Yan Y, Li S, Ou Y, Ji Y, Yu Z, Liu L, Yan C, Zhang Y and Zhao Y 2014 Effects of pressure and deposition time on the characteristics of In_2Se_3 films grown by magnetron sputtering *Electron. Mater. Lett.* **10** 1093
58. Azad S, Sadeghi E, Parvizi R and Mazaheri A 2017 Fast response relative humidity clad-modified multimode optical fiber sensor with hydrothermally dimension controlled ZnO nanorods *Mater. Sci. Semicond. Process.* **66** 200
59. Ingham B and Toney MF 2014 X-ray diffraction for characterizing metallic films In *Metallic Films for Electronic, Optical and Magnetic Applications* Katayun Barmak and Kevin Coffey (Eds.) 1st edn. (Cambridge: Woodhead Publishing) p. 3