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Introduction

Development of new methods for preparation of recyclable catalysts is of great economic and environmental importance in the chemical and pharmaceutical industries. Immobilization of homogeneous catalysts on various insoluble supports can lead to simplified catalyst recycling via filtration or centrifugation.1 At present, nanoparticles (NPs) are attractive candidates as solid supports for the immobilization of well defined homogeneous catalysts.² Because of the large surface area, which can carry a high amount of catalytically active species, these supported catalysts exhibit very high activity under mild conditions. Among these NPs, much attention has been directed toward the production of magnetic nanoparticles (MNPs),³⁻⁵ because these NPs can be well dispersed in the reaction mixtures without magnetic field providing large surface for readily access of substrate molecules. More importantly, after completing the reactions, the MNP catalysts can be isolated efficiently from the product solution through a simple magnetic separation

Synthesis, characterization and first application of keggin-type heteropoly acids supported on silica coated NiFe₂O₄ as novel magnetically catalysts for

the synthesis of tetrahydropyridines[†]

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In this study, two heteroploly acids with Keggin structures (phosphotungestic acid (PWA) and phosphomolybdic acid (PMA)) have been supported on silica coated nickel ferrite nanoparticles (NiFe₂O₄@SiO₂). The synthesized catalysts were characterized by several methods (FT-IR, SEM, TEM, VSM, XRD, BET and ICP-AES), and the catalytic activities of these new and magnetic catalysts in synthesis of tetrahydropyridine derivatives have been investigated. These new catalysts showed that they can carry out reactions at room temperature in a short time and under solvent-free conditions. Moreover, the obtained results indicated that PWA supported NiFe₂O₄@SiO₂ is a stronger acid than PMA to run these reactions. More importantly, the catalysts were easily isolated from the reaction mixture by a magnetic bar and reused at least five times without significant degradation in their activities.

process. Magnetic separation of super MNPs is simple, economic and promising for industrial applications.^{6,7}

Recently, Heydari and et al. reported synthesis of Fe₃O₄ MNPs for immobilizing HPAs catalyst, their synthesized catalyst showed that can act as a magnetic separable catalyst and after completing the reaction can be isolated by using an external magnet easily.8 Rafiee and et al. reported another MNPs with the formula Fe₂O₃ for supporting PWA HPA, they obtained good results in catalytic activity of these catalysts.9,10 In addition to Fe_3O_4 and Fe_2O_3 , there are iron oxides with ferrite structure and general formula (AFe₂O₄), where A can be Mn, Co, Ni, Cu and Zn.¹¹⁻¹³ Ni ferrites (NiFe₂O₄) are one of the most versatile magnetic materials, which have high saturation magnetization, high Curie temperature, chemical stability and relatively high permeability.14 Due to the sensitivity of the MNPs and strong surface affinity toward silica, these NPs can be directly coated with amorphous silica and give silica coated nickel ferrite (NiFe₂O₄@SiO₂ (designated as NFS)).

Heteropoly acids (HPAs) are an important class of catalysts having both redox and acid properties.^{15–17} Among them; HPAs with Keggin structures such as PWA (H₃PW₁₂O₄₀) and PMA (H₃PMo₁₂O₄₀) have received the most attention due to their unique structure and strong acidity.^{18,19} Several advantages to be highlighted of using supported HPAs compared to homogeneous examples include easier recovery and recycling after carrying out reactions, and simpler product separation.²⁰ However, separation and recovery of the immobilized HPAs are usually performed by filtration or centrifugation, which are not eco-friendly processes. The immobilization of PWA and PMA on

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[†] Dedicated to memory of Prof. Dr Mohammad Rahimizadeh.

silica-coated NiFe₂O₄ NPs (designated as NFS-PWA and NFS-PMA) can be employed to derive a novel heterogeneous catalyst system that possesses both a high separation efficiency and a relatively high surface area to maximize catalyst loading and activity.

Based on our earlier success in the preparation of MNPs as catalysts²¹⁻²³ and in continuation our achievements in synthesis of novel catalysts,²⁴⁻²⁸ in this report, we synthesized NFS-PWA and NFS-PMA as novel nanomagnetically-recoverable catalysts and assessed their catalytic activities in synthesis of tetrahydropyridine derivatives in room temperature and solvent-free conditions. To the best of our knowledge, there are no examples of the use of nano magnetic catalysts, especially NiFe₂O₄ and HPAs for the synthesis of tetrahydropyridine derivatives from condensation of aromatic aldehydes, substituted anilines and ethyl acetoacetate. Therefore, we wish to report a simple, green and an efficient synthetic method for synthesis of tetrahydropyridine derivatives using NFS-PWA and NFS-PMA as heterogeneous and reusable catalysts under room temperature and solvent-free conditions (Scheme 1).

Experimental

All reagents were purchased from Merck and Aldrich and used without further purification. Melting points were determined on an Electrothermal type 9100 melting point apparatus. The particle size and morphology of synthesized catalyst were characterized with a transmission electron microscope (TEM) (Philips CM-200 and Titan Krios) and scanning electron microscope (SEM) (Philips XL 30 and S-4160) with gold coating. The size dispersion of the samples was obtained using a laser particle size analyzer (CORDOUAN, Vasco3). X-ray diffraction (XRD) measurements were performed using a Bruker axs Company, D8 ADVANCE diffractometer (Germany). The BET

surface area of the material was measured by nitrogen adsorption isotherm method with (BET; NOVA 1200 Quanta Chromeinstrument). IR spectra were recorded on a Thermo Nicolet AVATAR-370 FT-IR spectrophotometer and ¹H NMR spectra were recorded on a Bruker DRX400 spectrometer.

Preparation of NFS-PWA and NFS-PMA

The silica coated MNPs (NFS, Fig. 1) were synthesized according to our previous reports^{21–23} and then for immobilization of different HPAs on the NFS, 0.75 g of PWA or 0.5 g of PMA was dissolved in 5 mL of methanol. This solution was added drop wise to a suspension of 1.0 NFS in methanol (50 mL) and then the mixture was heated at 70 °C for 48 h under vacuum while being mechanically stirred and give supported magnetic nano catalyst. The catalyst was collected by a permanent magnet and dried in a vacuum overnight and after first drying, the supported nano catalyst was calcined at 250 °C temperature for 2 h.⁸⁻¹⁰

Synthesis of tetrahydropyridine derivatives (4a-u)

A mixture of primary amines (2.0 mmol), ethyl acetoacetate (1.0 mmol) and catalyst (0.03 g) was stirred for 5–10 min. After that aromatic aldehydes (2.0 mmol) were added to the reaction mixture and stirred for 20–45 min at room temperature under solvent-free conditions. Upon completion, the chloroform was added to the reaction mixture to dissolve the product and then the catalyst could be placed on the side wall of the reaction vessel with the aid of an external magnet, and the reaction mixture was decanted to another vessel and the separated catalyst was washed and dried to be reused in the next run. To another vessel, the solvent was evaporated and the resulting crude product was recrystallized from ethanol and was collected and gave compounds (**4a–u**) in high yields.



Scheme 1 Synthesis of tetrahydropyridine derivatives in presence of NFS-PWA and NFS-PMA as nano acidic catalyst.



Fig. 1 Preparation of NFS-PWA and NFS-PMA.

The known products (**4a–p**), were reported previously in the literatures^{29–33} and the analytical and spectral data IR, ¹H, and ¹³C NMR spectroscopy, mass spectrometry, and elemental analysis for new products (**4q–u**) are described next.

Ethyl-(4-bromophenyl)-4-(4-bromophenylamino)-2,6-bis(4methoxyphenyl)-1,2,5,6 tetrahydropyridine-3-carboxylate (4q). White solid: IR (KBr): 3239, 3064, 2979, 2834,1647, 1603, 1462, 1370, 1248, 1068,cm⁻¹; ¹HNMR (400 MHz, CDCl₃) δ ppm: 1.47 (t, J = 8.0 Hz, 3H), 2.70 (dd, J = 15.4, 2.7 Hz, 1H), 2.83 (dd, J =15.4, 5.6Hz, 1H), 3.79 (s, 6H), 4.27–4.35 (m, 1H), 4.42–4.49 (m, 1H), 5.04 (s, 1H), 6.20 (d, J = 6.0, 2H), 6.29 (s, 1H),6.39 (d, J =6.80 Hz, 2H), 6.76–6.88 (m, 5H), 7.04–7.24 (m, 7H), 10.26 (br s, 1H); ¹³C NMR (400 MHz, CDCl₃) δ ppm: 15.93, 34.73, 55.83, 56.4, 56.48, 58.75, 61.06, 100.17, 109.47, 114.84, 115.29, 115.78, 120.3, 128.3, 128.52, 128.69, 132.7, 133.14, 135.11, 136.21, 138.2, 147.12, 156.45, 159.39, 160.06, 169.32; MS *m*/*z*: 692; Elemental analysis for: C₃₄H₃₂Br₂N₂O₄: C, 58.97; H, 4.66; N, 4.05. Found: C, 59.16; H, 4.43; N, 3.89%.

Ethyl-(3-iodophenyl)-4-(3-iodophenylamino)-2,6-bis(phenyl)-1,2,5,6tetrahydropyridine-3-carboxylate (4r). White solid: IR (KBr): 3252, 3051, 2986, 2872, 1652, 1592, 1448, 1373, 1253, 1070,cm⁻¹; ¹HNMR (400 MHz, CDCl₃) δ ppm: 1.53 (t, J = 7.2 Hz, 3H), 2.72 (dd, J = 14.4, 2.2 Hz, 1H), 2.84 (dd, J = 14.4, 5.4Hz, 1H), 4.30–4.33 (m, 1H), 4.40–4.48 (m, 1H),5.08–5.18 (m, 1H), 6.26–6.33 (m, 1H), 6.37 (s, 1H), 6.49 (m, 1H),6.63 (t, J = 7.0 Hz, 2H), 6.76 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 7.2 Hz, 2H), 6.94 (d, J = 6.0 Hz, 1H), 7.15–7.29 (m, 9H), 7.43 (d, J = 6.8 Hz, 1H), 10.29 (br s, 1H); ¹³C NMR (400 MHz, CDCl₃) δ ppm: 16.02, 34.55, 56.29, 59.29, 61.16, 95.14, 96.58, 99.88, 113.48, 122.74, 126.27, 126.53, 127.3, 127.3, 127.64, 127.8, 128.76, 129.6, 130.2, 131.46, 135.51, 136.07, 140.21, 142.91, 144.18, 149.28, 156.37, 169.24; MS *m*/*z*: 726; Elemental analysis for: C₃₂H₂₈I₂N₂O₂: C, 52.91; H, 3.89; N, 3.86. Found: C, 53.40; H, 3.63; N, 3.85%.

Ethyl-(3-bromophenyl)-4-(3-bromophenylamino)-2,6-bis(4chlorophenyl)-1,2,5,6 tetrahydropyridine-3-carboxylate (4s). White solid: IR (KBr): 3237, 3056, 2966, 2855,1647, 1604, 1451, 1372, 1252, 1071 cm⁻¹; ¹HNMR (400 MHz, CDCl₃) δ ppm: 1.50 (t, J = 7.5 Hz, 3H), 2.71 (dd, J = 14.6, 2.7 Hz, 1H), 2.79 (dd, J = 14.6, 5.4Hz, 1H), 4.32–4.37 (m, 1H), 4.44–4.50 (m, 1H), 5.09 (m, 1H), 6.30 (s, 1H), 6.37–6.43 (m, 4H), 6.61 (s, 1H), 6.78 (d, J = 7.6 Hz, 2H), 6.90–7.30 (m, 9H), 10.30 (br s, 1H); ¹³C NMR (400 MHz, CDCl₃) δ ppm: 15.97, 34.58, 55.89, 58.59, 61.36, 99.61, 112.8, 116.75, 120.98, 123.64, 124.51, 125.42, 128.68, 128.99, 128.18, 129.46, 129.95, 130.31, 131.25, 131.79, 133.64, 134.51, 140.1, 142.22, 142.53, 148.88, 156.05, 168.4; MS *m*/*z*: 700; Elemental analysis for: C₃₂H₂₆Br₂Cl₂N₂O₂: C, 54.81; H, 3.74; N, 3.99. Found: C, 54.65; H, 4.15; N, 4.05%.

Ethyl-(3-iodophenyl)-4-(3-iodophenylamino)-2,6-di(4-tolyl)-1,2,5,6 tetrahydropyridine-3-carboxylate (4t). White solid; IR (KBr): 3239, 3080, 2978, 2859,1647, 1603, 1454, 1371, 1255, 1068,cm⁻¹; ¹HNMR (400 MHz, CDCl₃) δ ppm: 1.52 (t, J = 7.6 Hz, 3H), 2.28 (s, 3H), 2.37 (s, 3H), 2.68 (dd, J = 15.5, 2.2 Hz), 2.81 (dd, J = 15.5, 5.6Hz), 4.34 (m, 1H), 4.47 (m, 1H), 5.05 (d, J = 2.5, 1H), 6.23–6.83 (m, 2H), 6.4 (s, 1H), 6.47–6.51 (m, 2H), 6.75–6.93 (m, 4H), 7.03–7.44 (m, 8H), 10.28 (br s, 1H). Elemental analysis for: C₃₄H₃₂I₂N₂O₂: C, 54.13; H, 4.28; N, 3.71. Found: C, 54.19; H, 4.35; N, 3.52%. Ethyl-(3-iodophenyl)-4-(3-iodophenylamino)-2,6-bis(4nitrophneyl)-1,2,5,6 tetrahydropyridine-3-carboxylate (4u). Light yellow solid; IR (KBr): 3246, 3058, 2979, 2872,1652, 1593, 1448, 1372, 1253, 1070,cm⁻¹; ¹HNMR (400 MHz, CDCl₃) δ ppm: 1.54 (t, J = 7.5 Hz, 3H), 2.8 (d, J = 15.2 Hz, 2H), 4.34–4.47 (m, 2H), 5.25 (m, 1H), 6.42–6.5 (m, 2H), 6.75–6.8 (m, 1H), 7.17 (m, 2H), 7.19 (m, 2H), 7.48–7.63 (m, 4H), 8.07–8.35 (m, 10H), 8.52 (d, J = 8.5, 2H), 10.28 (s, 1H, NH). Elemental analysis for: C₃₂H₂₆I₂N₄O₂: C, 47.08; H, 3.21; N, 6.86. Found: C, 47.45; H, 3.35; N, 6.52%.

Result and discussion

In order to determine the properties of these new acidic supported nanomagnetic catalysts, they were characterized by various techniques, such as FT-IR (Fig. 2), SEM and TEM (Fig. 3), particle size dispersion (Fig. 4), VSM (Fig. 5), XRD (Fig. 6), BET (Table 1), and ICP/AES. The FT-IR spectra of NFS, PWA, PMA, NFS-PWA and NFS-PMA are compared in Fig. 2. The FT-IR spectrum of NFS (Fig. 2a) exhibits high intense absorption bands at 1200 cm⁻¹ and 1100 cm⁻¹ and these bands are assigned to the longitudinal and transverse stretching vibration modes of the Si–O–Si asymmetric bond respectively. Additional bands at 812 cm⁻¹ and 470 cm⁻¹ are also identified as the characteristic bands of Si–O–Si bond respectively. The other band observed at 950 cm⁻¹ assigned to the SiO₃⁻² vibrations indicates the existence of non bridging oxygen ions.¹¹ The



Fig. 2 The FT-IR spectrum of (a) NFS (b) PWA (c) PMA (d) NFS-PWA and (e) NFS-PMA.



Fig. 3 (a) TEM and (b) SEM images of NFS.



Fig. 4 Particle size dispersion of NFS.



Fig. 5 Magnetization curve of NiFe₂O₄ at room temperature.

spectrum of PWA (Fig. 2b) shows typical bands for absorptions at 1080 (P–O), 982 (W=O), 890 and 802 (W–O–W) cm⁻¹, also the spectrum of PMA (Fig. 2c) shows determined bands for absorptions at 1064 (P–O), 962 (Mo=O), 882 and 767 (Mo–O–Mo) cm⁻¹.¹⁰ In the FT-IR spectrum of NFS-PWA (Fig. 2d) the appeared bands in the regions about 984, 888 and 807 cm⁻¹ confirm the successful immobilizing of the PWA on the surface of silica coated nickel ferrite NPs. In the last FT-IR spectrum corresponds to NFS-PMA (Fig. 2e), the characteristic bands at 963, 880 and 765 cm⁻¹ confirm that the PMA was supported well on the surface of NFS.

The morphological features and distribution of the NFS MNPs were investigated by TEM and SEM techniques (Fig. 3a and b). The TEM and SEM photographs demonstrate that the NFS MNPs are almost spherical with regular in shape. Also, the particle size dispersion diagram (Fig. 4) from the NFS NPs shows that these MNPs have a size between 25 to 97 nm and mean diameter is 53 nm.

It is of great importance that the core/shell material should possess sufficient magnetic and superparamagnetic properties for its practical applications. Magnetic hysteresis measurements for the NiFe₂O₄ were done in an applied magnetic field at r.t., with the field sweeping from $-10\ 000\ to\ +10\ 000\ Oersted$. As shown in Fig. 5, the *M* (H) hysteresis loop for the samples was completely reversible, showing that the nanoparticles exhibit superparamagnetic characteristics. The hysteresis loops of them reached saturation up to the maximum applied magnetic field. The magnetic saturation values of the NiFe₂O₄ are 16.71 emug⁻¹ at r.t. These MNPs showed high permeability in magnetization and their magnetization was sufficient for magnetic separation with a conventional magnet.

The XRD diffraction patterns of prepared NiFe₂O₄, NFS-PWA and standard pattern of NiFe₂O₄ are shown in Fig. 6. The diffraction peaks in NiFe₂O₄ and NFS-PWA (Fig. 6a and b) indicates that these MNPs have the spinel structure, with all the major peaks matching the standard pattern of bulk NiFe₂O₄ (Fig. 6c) (JCPDS 10-325).¹¹ In addition, it should be pointed out that no separate crystal phase characteristic of bulk PWA existed in the NFS-PWA, which confirms the high dispersion of PWA on the support NFS.

The surface area (BET) was determined by the nitrogen adsorption–desorption isotherms of previously degassed solids, at 120 °C. Measurements were carried out at liquid nitrogen boiling point, in a volumetric apparatus, using nitrogen as the probe. The NFS, NFS-PWA and NFS-PMA have surface area 58, 37 and 41 m² g⁻¹ respectively (Table 1). It is worth noting that reducing surface area is a consequence of successful immobilizing PWA and PMA onto the surface of silica coated Ni ferrite NPs and this result is in agreement with FT-IR result.

According to inductively coupled plasma/atomic electron microscopy (ICP/AEM), the content of PWA in the sample was confirmed. The weight percentage of PWA in the fresh catalyst was 32.1 wt%. For checking leaching stability of this supported catalyst, after completion the reaction, the catalyst was separated by using of an external magnet and washed with excess methanol and again; its PWA content was analyzed by ICP-AEM technique. The weight percentage of PWA in the recovered catalyst was 31.3 wt%. Based on these results, we can conclude that there is no substantial difference in weight percentage of PWA in the recovered and fresh catalyst. Furthermore, in order to further verify the stability of NFS-PWA during the reaction process, a control experiment was also carried out. Synthesis of tetrahydropyridines was first carried out at room temperature under solvent-free condition in the presence of NFS-PWA for 15 min and then the catalyst was removed from the reaction mixture. The reaction mixture (without NFS-PWA) was continued to be stirred under previous conditions for 15 min any more. As shown in Fig. 7, the yield of the reaction was stable



Fig. 6 XRD patterns of (a) prepared NiFe₂O₄ MNPs, (b) NFS-PWA and (c) standard pattern of bulk NiFe₂O₄ (JCPDS 10-325).

Table 1 BET surface area of NFS, NFS-PWA and NFS-PMA



Fig. 7 The results of the control experiments for the synthesis of tetrahydropyridines, (green diagram) without catalyst filtration and (blue diagram) catalyst filtration after 15 min.

after the removal of NFS-PWA. These results once again verified that NFS-PWA was stable under our reaction conditions. The reaction mixture was subjected to the elemental analysis by ICP-AEM technology and no W was detected, which also indicated that the supported PWA was not released into the reaction mixture from the NFS-PWA and PWA was strongly adsorbed on the surface of NFS NPs.

To investigate of the optimum amount of catalyst and solvent effect, the model reaction, including of benzaldehyde, aniline and ethyl acetoacetate was chosen. The efficiency of the

Table 2 Comparison of the amount of NFS-PWA and yields for synthesis of tetrahydropyridine derivative $(4 \mbox{p})$

Entry	Catalyst amount (g)	Time (min)	Yield (%)
1	None	120	None
2	0.01	45	54
3	0.02	30	79
4	0.03	30	96
5	0.05	30	96
6	0.10	30	97

Table 3Comparison of different solvents and solvent-free conditionsfor synthesis of tetrahydropyridine derivatives (4p) using NFS-PWA andNFS-PMA

Entry	Catalyst	Solvent	Time (min)	Temperature	Yield (%)
1	None	solvent-free	120	r.t.	No reaction
2	NFS-PWA	H_2O	60	r.t.	31
3	NFS-PWA	C ₂ H ₅ OH	60	r.t.	54
4	NFS-PWA	CH ₃ OH	60	r.t.	59
5	NFS-PWA	CH ₃ CN	60	r.t.	76
6	NFS-PWA	solvent-free	30	r.t.	96
7	NFS-PMA	solvent-free	30	r.t.	87
8	NFS-PMA	solvent-free	60	r.t.	92

Table 4	Synthesis of tetrahydropyridine	derivatives (4a–u) using of NFS-PW	A and NFS-PMA as a catalyst ^a
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Entry	R ₁	R ₂	Product ^b	Time (min)	Yield ^c (%)	Mp (°C)	Lit. Mp (°C) ref.
1	$4-CH_3C_6H_4$	$4-CH_3C_6H_4$	4a	22/25	94/90	172-174	169–171 (32)
2	$4-CH_3C_6H_4$	Ph	4b	35/41	82/80	230-231	230-231 (33)
3	$4-CH_3C_6H_4$	$4-BrC_6H_4$	4 c	45/40	83/80	237-238	237-239 (30)
4	$4-CH_3C_6H_4$	$4 - NO_2C_6H_4$	4d	36/40	90/86	213-215	216-217 (32)
5	$4-CH_3C_6H_4$	4-CH ₃ OC ₆ H ₄	4e	33/39	92/82	217-219	219-222 (32)
6	$4-NO_2C_6H_4$	Ph	4 f	32/40	89/88	249-251	247-250 (33)
7	4-CH ₃ OC ₆ H ₄	$4-ClC_6H_4$	4g	25/30	93/88	178-179	180-181 (30)
8	$4-ClC_6H_4$	$4-BrC_6H_4$	4h	32/35	94/90	200-201	200-202 (31)
9	$4-ClC_6H_4$	$4-CH_3C_6H_4$	4i	20/30	95/89	240-241	236-238 (31)
10	$4-ClC_6H_4$	Ph	4j	30/30	91/82	228-229	228-230 (31)
11	$4-ClC_6H_4$	$4-CH_3OC_6H_4$	4k	28/35	95/92	186-188	184-184 (29)
12	Ph	$4-BrC_6H_4$	41	43/45	96/94	194-196	197-198 (32)
13	Ph	4-ClC ₆ H ₄	4m	32/30	95/88	202-204	201-202 (33)
14	Ph	$4-CH_3C_6H_4$	4n	25/32	92/87	190-192	194–196 (32)
15	Ph	4-CH ₃ OC ₆ H ₄	40	45/45	89/80	172-174	172-173 (33)
16	Ph	Ph	4p	30/40	96/90	174-175	175-176 (33)
17	$4-CH_3OC_6H_4$	$4-BrC_6H_4$	4q	35/40	96/92	184-186	This work
18	Ph	3-IC ₆ H ₄	4r	43/45	90/85	170-172	This work
19	$4-ClC_6H_4$	$3-BrC_6H_4$	4s	39/42	91/84	183-185	This work
20	$4-CH_3C_6H_5$	$3-IC_6H_5$	4t	41/45	92/92	205-207	This work
21	$4-NO_2C_6H_5$	$3-IC_6H_5$	4u	38/45	90/88	140-142	This work

 a Benzaldehyde 1 (2.0 mmol), aniline 2 (2.0 mmol), ethyl acetoacetate 3 (1.0 mmol) and NFS-PWA and NFS-PMA (0.03 g) at room temperature under solvent-free conditions. b The known products were identified by comparing of their melting points and new products were characterized by (FT-IR and 1 H NMR). c Isolated yields.

reaction is affected mainly by the amount of catalyst (NFS-PWA) (Table 2). No product was obtained in the absence of the catalyst (entry 1) indicating that the catalyst is necessary for the reaction. Raising the amount of the catalyst increased the yield of

the product 4p (entries 2, 3). The optimum amount of NFS-PWA was 0.03 g (entry 4); increasing the amount of the catalyst beyond this value did not increase the yield noticeably (entries 5, 6).



Scheme 2 Proposed mechanism for reactions between substituted benzaldehydes 1, aniline derivatives 2 and ethyl acetoacetate 3 for generation of tetrahydropyridine derivatives 9.

The same model reaction in the presence of 0.03 g of the NFS-PWA was carried out in solvent-free conditions and also in different solvents to assess the effect of solvent on the reaction vield. As shown in Table 3, for the reason of anionic structure generation and hydrogen bonding formation in the polar solvents such as H₂O, MeOH, EtOH and MeCN, by the HPAs, the reaction could be carried out in moderate yields (entries 2-5), but the yields of the reaction under solvent-free conditions were greater and the reaction times were generally shorter than the conventional methods. The best result was obtained at room temperature for 30 min under solvent-free conditions (entry 6). Increasing the reaction time did not improve the yield. Subsequently, therefore, all reactions were carried out at room temperature in the presence of 0.03 g NFS-PWA under solventfree conditions (entry 7). Moreover, the model reaction in the presence of 0.03 g NFS-PMA was carried out, we observed that the yield of the reaction in the same time and presence of a second catalyst (NFS-PMA) was lower than first catalyst (NFS-PWA) (entry 7), however, increasing the time reaction moderately increased the yield of the reaction (entry 8). These results



Fig. 8 Reusability of NFS-PWA (blue columns) and NFS-PMA (brown columns) for model reaction.

show that, PWA is a stronger acid than PMA in catalyzed this reaction.

After optimization of the reaction conditions, the catalytic activities of these new catalysts were tested by different aromatic amines, number of aromatic aldehydes, and ethyl acetoacetate. The corresponding compounds (4a-t) were synthesized by the reaction of aldehydes, amines, and ethyl acetoacetate using 0.03 g NFS-PWA and NFS-PMA at room temperature and under solvent-free conditions. The results are shown in Table 4. As shown in Table 4, it was found that this method works well with a wide variety of substrates. The yields of the reactions in the presence of first catalyst (NFS-PWA) were good to excellent. However, in some cases, yield of the reactions in the presence of second catalyst (NFS-PMA) was not good (entry 2, 3). The reaction of methyl, methoxy, chloro, bromo, and iodo substituted aromatic amines reacted in higher yield compared with nitroaniline (entry 4). Similarly, the reaction of chloro, methyl, and methoxy benzaldehyde proceeds smoothly compared to nitrobenzaldehyde (entry 6), in which, the yields were low due to steric factors as well as the electronwithdrawing effect of the nitro group.

Based on the proposed mechanism in the literature,^{34,35} it is reasonable to assume that tetrahydropyridine derivatives **9** were formed from the initial condensation of aromatic aldehyde **1** and *b*-ketoester **2** with aniline **3** that their carbonyl groups were activated with HPAs supported nano catalysts (NFS-PWA and NFS-PMA) to give enamine **4** and imine **5** (Scheme 2). Next, enamine **4** reacts with imine **5** to produce intermediate **6** through an intermolecular Mannich-type reaction. The reaction between intermediate **6** and aldehyde gives intermediate **7** by the elimination of H₂O. Then, tautomerization of **7** generates intermediate **8**, which immediately undergoes an intramolecular Mannich-type reaction to give desired tetrahydropyridine derivatives **9**.

To determine the applicability of catalyst recovery, at the end of the reaction, with the aid of an external magnet, the catalyst



Fig. 9 FT-IR spectrum of (a) fresh and recovered (after five times) NFS-PWA and (b) fresh and recovered (after five times) NFS-PMA.

was held on the side wall of the reaction vessel, while the solution was decanted. The catalyst was washed with methanol and chloroform to remove the residual product, dried at 100 °C under vacuum and reused in a subsequent reaction in excellent yields. It showed the same activity as the fresh catalyst without any significant loss of its activity (Fig. 8).

The FT-IR spectra of NFS-PWA and NFS-PMA catalysts before use (fresh) and after reuse five times (recovered) were studied. As shown in Fig. 9, the FT-IR spectrum of the recovered NFS-PWA and NFS-PMA showed that the structure of catalysts remained almost the same after five-run reuse. In addition, the weight of the recovered catalyst is the same as the amount of the fresh catalyst that was used the first time in the reaction.

Conclusion

In summary, we prepared novel catalysts, including two types of Keggin structures supported on the silica nickel ferrite NPs. The prepared samples were characterized by FT-IR, SEM, TEM, XRD, VSM, and BET. The content of the W in catalysts was measured by inductively coupled plasma atomic emission spectroscopy (ICP-AEM). The synthesis of tetrahydropyridine derivatives was carried out using these nano acidic catalysts at room temperature in low time and under solvent-free conditions. Moreover, the catalyst could be readily separated by use of a magnetic force and reused at least five runs without any significant loss of its catalytic activity.

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