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Silica-coated magnetic $NiFe_2O_4$ nanoparticles-supported $H_3PW_{12}O_{40}$; synthesis, preparation, and application as an efficient, magnetic, green catalyst for one-pot synthesis of tetrahydrobenzo[*b*]pyran and pyrano[2,3-*c*]pyrazole derivatives

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Abstract A powerful, magnetic, supported, acid catalyst, $NiFe_2O_4$@SiO_2–$H_3PW_{12}O_{40}$, was prepared by chemical support of Keggin ($H_3PW_{12}O_{40}$) heteropolyacid (HPA) on silica-coated $NiFe_2O_4$ magnetic nanoparticles. XRD, TEM, SEM, VSM, and FTIR confirmed that the keggin HPA is well dispersed on the surface of silica-coated $NiFe_2O_4$ magnetic nanoparticles. The magnetically recoverable catalyst could be easily recycled at least six times without significant loss of catalytic activity. After full characterization, its catalytic activity was investigated in the synthesis of tetrahydrobenzo[*b*]pyran and pyrano[2,3-*c*]pyrazole derivatives.

Graphical Abstract (1) Novel silica-coated magnetic $NiFe_2O_4$ nanoparticles-supported $H_3PW_{12}O_{40}$ was fabricated and characterized. (2) Recyclability of the catalyst. (3) Avoiding use of corrosive acid catalysts. (4) Green chemistry.

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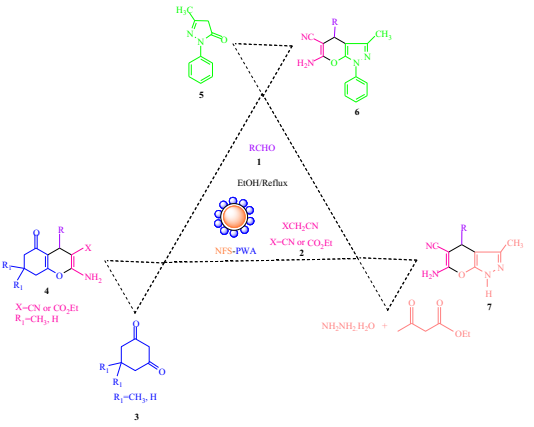


Keywords Nanomagnetic catalyst · Heteropolyacid · Keggin · Tetrahydrobenzo [*b*]pyran · Pyrano[2,3-*c*]pyrazole

Introduction

Among a variety of solid acids, HPA have unique physicochemical properties. Their acidity is substantially higher than that of traditional mineral acids. Furthermore, HPA are capable of protonating and activating substrates, and are sometimes more effective than conventional inorganic acids and traditional acid catalysts. Because the high solubility of these materials often makes their separation from the reaction mixture difficult, immobilization of HPA on supports with high surface area facilitates their use as catalysts in a variety of heterogeneous reactions [1–3].

Heterogeneous application of HPA to the surface of silica-coated magnetic nanoparticles (MNP) has been an interesting approach in recent years. This strategy has enabled research groups to overcome problems with the separation and recycling of homogeneous catalysts [4–10]. Thus, in this study, an efficient magnetic supported acid catalyst $NiFe_2O_4@SiO_2–H_3PW_{12}O_{40}$ (NFS–PWA) was prepared by chemical support of Keggin HPA on silica-coated $NiFe_2O_4$ magnetic nanoparticles.

Pyrans, a group of heterocyclic compounds, are extremely important in the pharmaceutical and agrochemical industries and in synthetic chemistry. They have a wide range of biological and pharmacological properties, for example anti-allergy, anti-inflammatory, anti-tumor, spasmolytic, diuretic, anti-cancer, anti-coagulant, and anti-anaphylactic activity [11, 12]. Also, 4*H*-benzo[*b*]pyrans can be used as cognitive enhancers, for treatment of neurodegenerative diseases, including Alzheimer's disease, amyotrophic lateral sclerosis, AIDS-associated dementia, and Down's syndrome, and for treatment of schizophrenia and Huntington's diseases [13].

In the literature several methods are reported for synthesis of tetrahydrobenzo[*b*]pyran and pyrano[2,3-*c*]pyrazole derivatives. The most convenient

methods are bicomponent condensation of 1,3-dicarbonyl compounds (1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclohexanedione) with α-cyanocinnamonitrile [14–18], or one-pot, three-component reaction of aldehydes, malonitrile, and 1,3-dicarbonyl compounds (1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclohexanedione) or 3-methyl-1-phenyl-2-pyrazoline-5-one, in the presence of a variety of catalysts [19]. Highly efficient synthesis of 4*H*-pyrano[2,3-*c*]pyrazole by four-component cyclocondensation of hydrazine hydrate or phenylhydrazine, ethyl acetoacetate, aldehydes, and malonitrile in the presence of L-proline and [Bimim]BF_4 at 50 °C has also been reported [20]. Catalysts used for one-pot, three-component reactions include piperidine [21], hexadecyltrimethyl ammonium bromide (HTMAB) [22], sodium bromide [23], ionic liquids [24–29], tetramethylammonium hydroxide [30], diammonium hydrogen phosphate [31], organocatalysts [32], sodium selenite [33], tetrabutylammonium bromide (TBAB) [34, 35], polyaniline–silica gel [36], alum [$KAl(SO_4)_2{\cdot}12H_2O$] [37], rare earth perfluorooctanoates, e.g. $Re(PFO)_3$ [38], Caro's acid [39], amines or amino acids [40], potassium phosphate [41], PPA–SiO_2 [42], microwave irradiation [43], $BF_3{\cdot}OEt_2$ [44], magnetic core–shell titanium dioxide nanoparticles (Fe_3O_4@SiO_2@TiO_2) [45], $NH_4H_2PO_4$–Al_2O_3 [46], DABCO–EtOH [47], TPPA [48], *t*-BuOK–*t*-BuOH [49], L-proline under ultrasound irradiation [50], and silica coated magnetite-polyoxometalate nanoparticles (Fe_3O_4@SiO_2@NH-NH_2–$H_3PW_{12}O_{40}$) [51]. Many of these methods suffer from one or more limitations, for example low yields, use of expensive reagents, long reaction times, tedious work-up procedures, and co-occurrence of several side reactions.

Experimental

Apparatus and analysis

All reagents were purchased from Merck and Sigma–Aldrich and used without further purification. IR spectra were recorded on a Shimadzu 435-U-04 spectrophotometer (KBr pellets). ^{1}H NMR spectra were obtained by use of a Bruker 300 MHz spectrometer in DMSO-d_6 or $CDCl_3$ as solvent and with TMS as internal reference. Melting points were determined in open capillary tubes in a Stuart BI Branstead Electrothermal apparatus (cat no: IA9200) and are uncorrected. The particle size and morphology of the synthesized catalyst were characterized by transmission electron microscopy (TEM; Philips CM-200 and Titan Krios) and by scanning electron microscopy (SEM; Philips XL 30 and S-4160) after gold coating. The size dispersion of the samples was obtained by use of a laser particle size analyzer (Cordouan Vasco3). X-ray diffraction (XRD) measurements were performed with a Bruker Axs (Germany) D8 Advance diffractometer.

Preparation of $NiFe_2O_4$@SiO_2–$H_3PW_{12}O_{40}$ (NFS–PWA)

Silica-coated MNP (NFS) were synthesized as reported elsewhere [62, 63]. Then, for immobilization of PWA on the NFS, 0.75 g PWA was dissolved in 5 ml

methanol. This solution was added dropwise to a suspension of 1.0 NFS in methanol (50 ml) and the mixture was then heated at 70 °C for 48 h, under vacuum, with mechanical stirring, to give the supported magnetic nano catalyst. The catalyst was collected by use of a permanent magnet, dried under vacuum overnight, then calcined at 250 °C for 2 h.

General procedure for synthesis of tetrahydrobenzo[*b*]pyrans and pyrano[2,3-*c*]pyrazoles

A mixture of aldehyde (1, 1 mmol), malononitrile or ethyl cyanoacetate (2, 2 mmol), 1,3-dicarbonyl compound (1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclohexanedione) (3, 1 mmol) or 3-methyl-1-phenyl-2-pyrazoline-5-one (5, 1 mmol) and NFS–PWA (0.02 g) in EtOH (96 %, 3 ml) was stirred on an oil bath under reflux condition for the appropriate time (Table 1). The reaction was monitored by TLC (*n*-hexane–ethyl acetate, 4:1). After completion of the reaction, the nanomagnetic catalyst was separated from the reaction mixture by use of an external magnetic field. The resulting crude product was poured into crushed ice, and the solid product which separated was isolated by filtration and recrystallized from ethanol (2 ml) to afford tetrahydrobenzo[*b*]pyrans and pyrano[2,3-*c*]pyrazoles.

Spectra data for selected compounds

*2-Amino-3-cyano-4-(phenyl)-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**4a**)*

IR (KBr) ν_{max}: 3314, 3202, 2214, 1688, 1624, 1507, 1482, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 1.04 (s, 3H), 1.13 (s, 3H), 2.11–2.21 (m, 2H), 2.42 (s, 2H),

Table 1 Optimization of the reaction conditions for synthesis of 2-amino-3-cyano-4-(phenyl)-7,7-dimethyl-5-oxo-4*H*-5,6,7,8- tetrahydrobenzo[*b*]pyran (**4a**)

Entry	Catalyst (g)	Conditions	Time (min)	Yield[a] (%)
1	NFS–PWA (0.03)	EtOH, reflux	5	94
2	NFS–PWA (0.03)	CH_3OH, reflux	5	87
3	NFS–PWA (0.03)	H_2O, reflux	15	79
4	NFS–PWA (0.03)	Solvent-free, 100 °C	10	83
5	PWA (0.03)	EtOH, reflux	5	74
6	SiO_2 (0.03)	EtOH, reflux	60	48
7	–	EtOH, reflux	60	32
8	NFS (0.03)	EtOH, reflux	60	54
9	NFS–PWA (0.02)	EtOH, reflux	10	72
10	NFS–PWA (0.04)	EtOH, reflux	5	92
11	NFS–PWA (0.03)	EtOH, 25 °C	60	Impure

[a] Isolated yields

4.67 (s, 1H), 6.52 (brs, 2H, D_2O exchangeable), 7.14–7.42 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 26.32, 27.65, 31.24, 35.09, 39.08, 49.98, 59.74, 113.09, 118.42, 125.86, 126.63, 127.54, 142.68, 158.54, 162.32, 194.24 ppm.

*2-Amino-3-cyano-4-(4-methylphenyl)-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**4c**)*

IR (KBr) ν_{max}: 3392, 3205, 2190, 1670, 1630, 1598, 1486, 1410 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 0.97 (s, 3H), 1.05 (s, 3H), 2.14 (d, 1H), 2.21 (d, 1H), 2.47–2.76 (m, 2H), 4.45 (s, 1H), 6.92 (brs, 2H, D_2O exchangeable), 7.04 (d, 2H), 7.09 (d, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 26.98, 28.34, 30.65, 33.98, 36.67, 39.08, 51.61, 61.54, 112.93, 118.82, 125.44, 126.61, 126.96, 142.64, 153.67, 162.32, 194.72 ppm.

*2-Amino-3-cyano-4-(3-methoxyphenyl)-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**4e**)*

IR (KBr) ν_{max}: 3370, 3180, 2185, 1660, 1624, 1509, 1492, 1380 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 0.92 (s, 3H), 1.01 (s, 3H), 2.05 (d, 2H), 2.66 (d, 2H), 3.45 (s, 3H), 4.17 (s, 1H), 7.06 (brs, 2H, D_2O exchangeable), 7.13–7.26 (m, 3H), 7.34 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 27.30, 28.78, 32.33, 35.52, 35.58, 38.43, 50.44, 58.41, 112.74, 120.19, 128.91, 129.63, 131.80, 144.16, 158.98, 163.61, 197.00 ppm.

*2-Amino-3-cyano-4-(4-nitrophenyl)-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**4h**)*

IR (KBr) ν_{max}: 3401, 3307, 2200, 1690, 1598, 1498, 1468, 1375 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 1.04 (s, 3H), 1.18 (s, 3H), 2.26–2.51 (m, 2H), 2.59 (s, 2H), 5.26 (s, 1H), 6.12 (brs, 2H, D_2O exchangeable), 7.56 (d, 2H), 8.09 (d, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 26.98, 27.44, 31.08, 35.87, 40.18, 51.88, 62.54, 113.67, 119.02, 127.74, 127.97, 129.02, 144.32, 161.61, 165.78, 197.24 ppm.

*2-Amino-3-cyano-4-(3-nitro phenyl)-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**5i**)*

IR (KBr) ν_{max}: 3346, 3297, 2189, 1680, 1588, 1498, 1478, 1389 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 1.02 (s, 3H), 1.06 (s, 3H), 2.16–2.24 (m, 2H), 2.39 (s, 2H), 4.84 (s, 1H), 6.09 (brs, 2H, NH_2, D_2O exchangeable), 7.19–7.32 (m, 3H), 7.44 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 26.32, 27.98, 31.53, 35.05, 39.73, 51.24, 59.74, 113.04, 118.19, 126.21, 126.89, 130.65, 141.76, 156.08, 161.91, 193.65 ppm.

*2-Amino-3-cyano-4-(2,4-dichlorophenyl)-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**4k**)*

IR (KBr) ν_{max}: 3388, 3289, 2187, 1698, 1624, 1595, 1489, 1379 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 1.01 (s, 3H), 1.12 (s, 3H), 2.13–2.22 (m, 2H), 2.47 (s, 2H), 4.45 (s, 1H), 5.85 (brs, 2H, D_2O exchangeable), 7.15–7.38 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 26.06, 26.42, 33.67, 35.12, 40.79, 51.45, 60.23, 113.12, 118.47, 122.12, 129.13, 130.18, 142.12, 155.45, 160.78, 193.14 ppm.

*2-Amino-3-ethylacetato-4-(phenyl)-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**4n**)*

IR (KBr) ν_{max}: 3423, 3265, 3020, 2980, 1667, 1614, 1520, 1462, 1378 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 1.01 (s, 3H), 1.08 (s, 3H), 1.24 (t, 3H), 2.16–2.25 (m, 2H), 2.34 (s, 2H), 4.24 (q, 2H), 4.37 (s, 1H), 5.52 (brs, 2H, D_2O exchangeable), 7.12–7.42 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 19.12, 26.52, 27.65, 31.44, 35.56, 39.68, 50.15, 60.63, 71.47, 113.09, 126.42, 126.86, 127.03, 142.54, 156.68, 161.87, 172.42, 196.01 ppm.

*2-Amino-3-cyano-4-(4-chlorophenyl)-oxo-4H-5,6,7,8-tetrahydrobenzo[b]pyran (**4t**)*

IR (KBr) ν_{max}: 3320, 3192, 2193, 1680, 1619, 1576, 1462, 1376 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 2.09–2.21 (m, 2H), 2.41–2.54 (m, 2H), 2.80–2.88 (m, 1H), 2.93–3.00 (m, 1H), 5.58 (s, 1H), 6.09 (brs, 2H, D_2O exchangeable), 7.15 (d, 2H), 7.44 (d, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 20.50, 27.55, 33.15, 37.09, 50.45, 59.13, 113.24, 118.67, 126.45, 126.06, 130.14, 140.05, 159.05, 162.34, 192.46 ppm.

*6-Amino-3-methyl-5-cyano-4-(4-bromophenyl)1,4-dihydropyrano[2,3-c]pyrazole (**6c**)*

IR (KBr) ν_{max}: 3392, 3278, 2221, 1610, 1568, 1445, 1346 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 2.01 (s, 3H), 4.89 (s, 1H), 6.05 (brs, 2H, D_2O exchangeable), 6.96–7.47 (m, 9H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 25.01, 40.76, 51.05, 61.63, 113.96, 119.04, 125.46, 126.09, 126.42, 128.01, 129.76, 130.05, 131.57, 142.42, 151.52, 161.43 ppm.

*6-Amino-3-methyl-5-cyano-4-(4-methoxyphenyl)1,4-dihydropyrano[2,3-c]pyrazole (**6e**)*

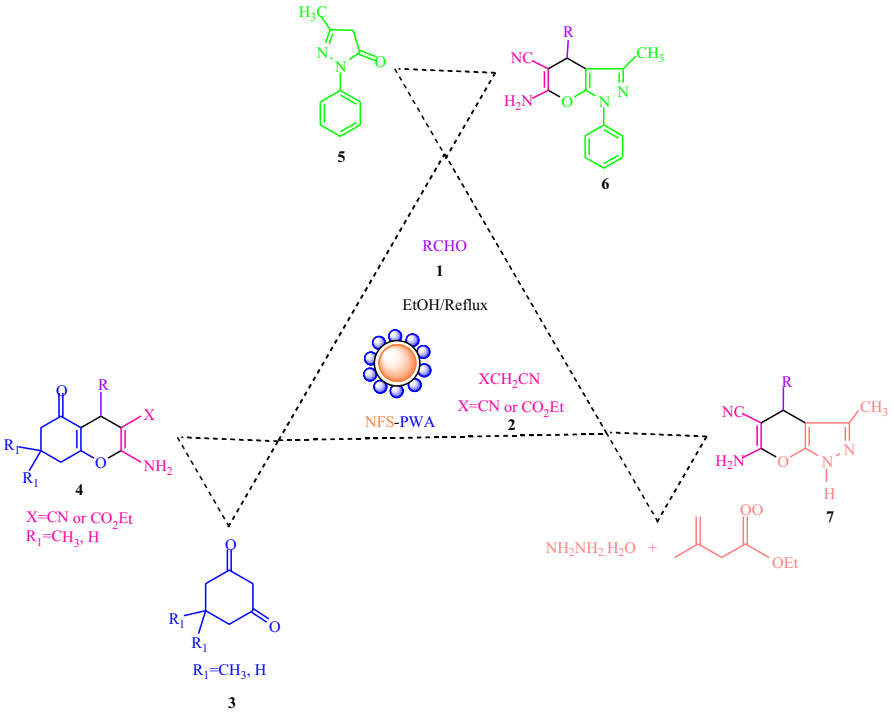
IR (KBr) ν_{max}: 3389, 3292, 2197, 1618, 1576, 1454, 1372 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 1.68 (s, 3H), 3.89 (s, 3H), 5.76 (s, 1H), 6.45 (brs, 2H, D_2O exchangeable), 7.09–7.98 (m, 9H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 25.32, 36.12, 40.04, 51.05, 59.61, 113.78, 119.14, 125.79, 126.54, 127.02, 128.38, 129.11, 130.18, 131.67, 140.67, 151.67, 158.52 ppm.

*6-Amino-3-methyl-5-cyano-4-(4-hydroxyphenyl)1,4-dihydropyrano[2,3-c]pyrazole (**6h**)*

IR (KBr) ν_{max}: 3654, 3379, 3289, 2198, 1610, 1576, 1471, 1382 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 1.89 (s, 3H), 5.17 (s, 1H), 6.15 (brs, 2H, D_2O exchangeable), 7.13–7.87 (m, 9H), 8.24 (brs, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 25.78, 41.96, 51.02, 60.08, 113.54, 118.43, 125.92, 126.09, 126.59, 128.44, 129.32, 130.32, 131.49, 140.42, 152.21, 160.22 ppm.

*6-Amino-3-methyl-4-(4-methoxyphenyl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (**7a**)*

IR (KBr) ν_{max}: 3483, 3254, 2191, 1641, 1608, 1492, 1390 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 1.79 (s, 3H), 3.45 (s, 3H), 4.56 (s, 1H), 6.88 (brs, 2H, D_2O exchangeable), 7.10 (d, 2H), 7.19 (d, 2H), 12.01 (s, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 10.22, 35.17, 36.01, 57.64, 97.82, 121.31, 126.04, 128.64, 136.19, 136.07, 141.64, 155.22, 161.35 ppm.



Scheme 1 One-pot synthesis of tetrahydrobenzo[*b*]pyrans and pyrano[2,3-*c*]pyrazoles

*6-Amino-3-methyl-4-(4-chlorophenyl)-1,4-dihydro- pyrano[2,3-c]pyrazole-5-carbonitrile (**7b**)*

IR (KBr) ν_{max}: 3481, 3252, 2187, 1643, 1593, 1492, 1410 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 1.78 (s, 3H), 4.86 (s, 1H), 6.78 (brs, 2H, D_2O exchangeable), 7.18 (d, 2H), 7.45 (d, 2H), 12.22 (s, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 10.02, 33.62, 55.17, 96.38, 120.71, 128.05, 129.36, 132.68, 133.30, 135.19, 140.64, 155.64, 161.08 ppm.

*6-Amino-3-methyl-4-(4-bromophenyl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (**7c**)*

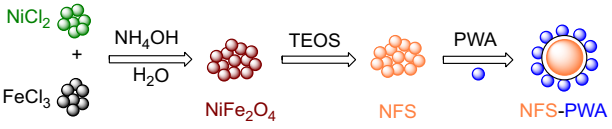
IR (KBr) ν_{max}: 3444, 3238, 2195, 1637, 1600, 1491, 1394 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 1.75 (s, 3H), 4.81 (s, 1H), 6.48 (brs, 2H, D_2O exchangeable), 7.09 (d, 2H), 7.32 (d, 2H), 12.12 (s, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 10.12, 33.62, 55.69, 96.23, 120.01, 128.45, 129.79, 132.54, 133.30, 135.21, 140.54, 155.89, 161.98 ppm.

Result and discussion

In continuation of our previous work on the development of new synthetic methods [52–63], in this research, an advance in the synthesis of biologically important materials, use of a separable magnetic nano catalyst, NFS–PWA, is reported. This new environmentally benign, heterogeneous, and highly re-usable catalyst had very good catalytic activity in the preparation of tetrahydrobenzo[*b*]pyrans and pyrano[2,3-*c*]pyrazoles (Scheme 1).

The catalyst was prepared by use of simple chemical methods. As shown in Scheme 2, first, $NiFe_2O_4$ nanoparticles were prepared by reaction of nickel and iron chloride under basic conditions. The $NiFe_2O_4$ nanoparticles were then coated with silica to form $NiFe_2O_4$@SiO_2 (NFS) and, finally, Keggin HPA (PWA) was supported on the surface of silica-coated magnetic nanoparticles to prepare the final catalyst NFS–PWA.

To determine the properties of this acidic, supported, nanomagnetic catalyst, it was characterized by use of a variety of techniques: FTIR (Fig. 1), SEM and TEM (Fig. 2), determination of particle size dispersion (Fig. 3), VSM (Fig. 4), and XRD (Fig. 5). The FTIR spectra of NFS, PWA, and NFS–PWA are compared in Fig. 1. The FTIR spectrum of NFS (Fig. 1a) contains highly intense absorption peaks at



Scheme 2 Preparation of $NiFe_2O_4$@SiO_2–$H_3PW_{12}O_{40}$ (NFS–PWA)

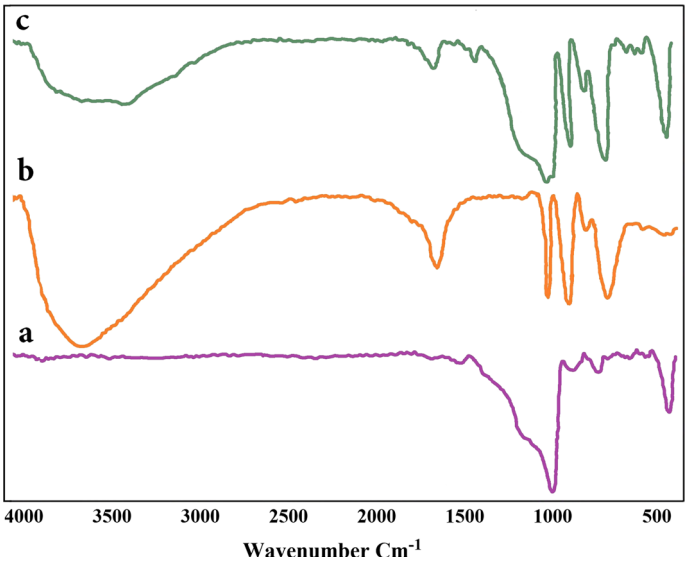


Fig. 1 FTIR spectra of **a** $NiFe_2O_4@SiO_2$ (NFS), **b** $H_3PW_{12}O_{40}$ (PWA), and **c** $NiFe_2O_4@SiO_2$–$H_3PW_{12}O_{40}$ (NFS–PWA)

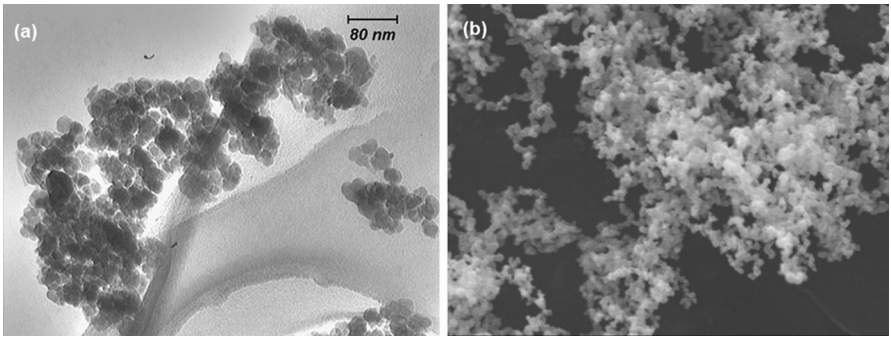


Fig. 2 **a** TEM and **b** SEM images of $NiFe_2O_4@SiO_2$ (NFS)

1200 and 1100 cm^{-1}; these peaks were assigned to the longitudinal and transverse stretching vibration modes, respectively, of the Si–O–Si asymmetric bond. Additional bands at 812 and 470 cm^{-1} were identified as characteristic peaks of the Si–O–Si bond. Other peaks at 950 cm^{-1} were assigned to SiO_3^{-2} vibrations, and are indicative of the presence of non bridging oxygen ions [64]. The spectrum of PWA (Fig. 1b) contains typical absorption bands at 1080 (P–O), 982 (W=O), 890 and 802 (W–O–W) cm^{-1} [65]. In the FTIR spectrum of NFS–PWA (Fig. 1c) peaks at approximately 984, 888, and 807 cm^{-1} confirm successful immobilization of the PWA on the surface of silica-coated nickel ferrite NPs.

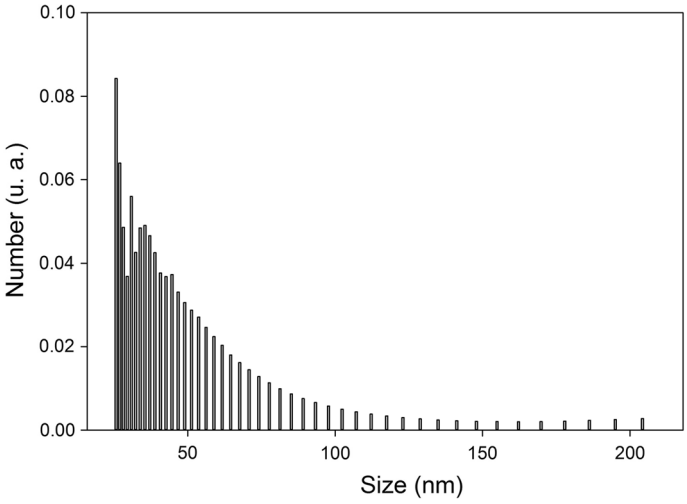


Fig. 3 Particle size dispersion of NFS

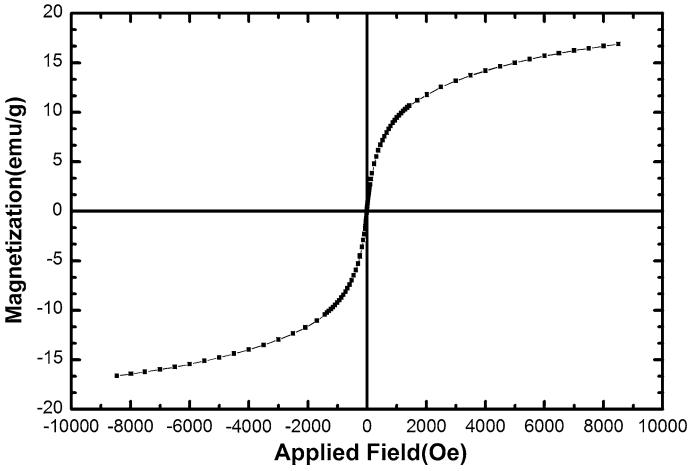


Fig. 4 VSM curve of $NiFe_2O_4$ at room temperature

The morphological features and distribution of the $NiFe_2O_4$@SiO_2 magnetic nanoparticles (NFS MNP) were investigated by use of TEM and SEM (Fig. 2a, b). The TEM and SEM photographs reveal that the NFS MNP are narrowly distributed, well dispersed, and also are almost spherical and regular in shape. Also, the particle size dispersion diagram (Fig. 3) obtained from the NFS NP shows that the size of these magnetic nanoparticles (MNP) is between 25 and 97 nm and the mean diameter is 53 nm.

It is of great importance that core/shell materials should have magnetic and superparamagnetic properties suitable for practical applications. Magnetic hysteresis

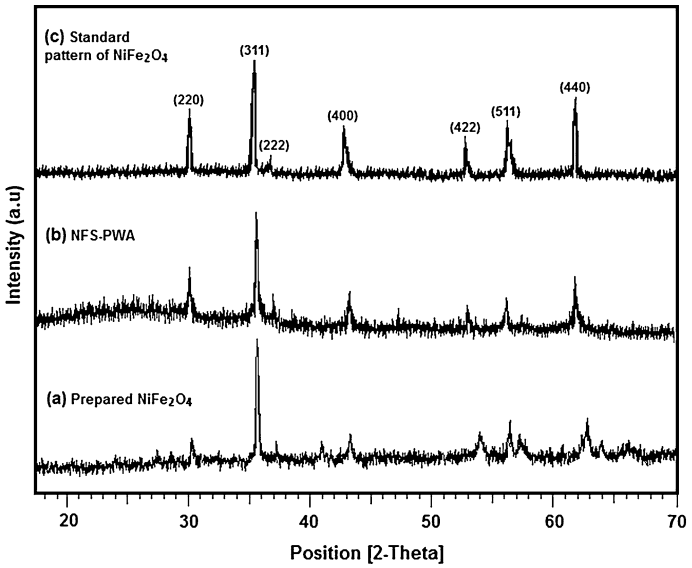


Fig. 5 XRD patterns of **a** prepared $NiFe_2O_4$ MNP, **b** $NiFe_2O_4$@SiO_2–$H_3PW_{12}O_{40}$ (NFS–PWA), and **c** standard pattern of bulk $NiFe_2O_4$ (JCPDS 10-325)

measurements of the $NiFe_2O_4$ were conducted in an applied magnetic field at r.t, with the field sweeping from −10,000 to +10,000 Oersted. As shown in Fig. 4, the $M(H)$ hysteresis loop of the sample was completely reversible, showing that the nanoparticles had superparamagnetic properties. The hysteresis loop reached saturation at the maximum applied magnetic field. The magnetic saturation value for $NiFe_2O_4$ was 16.71 $emug^{-1}$ at r.t. These MNP had high-permeability magnetization, and their magnetization was sufficient for magnetic separation with a conventional magnet.

The XRD diffraction patterns of $NiFe_2O_4$ and NFS–PWA and standard pattern of $NiFe_2O_4$ are shown in Fig. 5. The diffraction peaks in $NiFe_2O_4$ and NFS–PWA (Fig. 5a, b) indicate that these MNP have the spinel structure, with all the major peaks matching the standard pattern of bulk $NiFe_2O_4$ (Fig. 5c) (JCPDS 10-325) [65]. It should also 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.

Our initial attempt started with reaction of benzaldehyde (1 mmol), dimedone (1 mmol), and malononitrile (2 mmol) in the presence of NFS–PWA under reflux in ethanol (Table 1, entry 1). The effect of different solvents was then investigated; EtOH was the optimum solvent (Table 1, entries 2 and 3). The reaction was also conducted in the absence of solvent with 0.03 g catalyst at 100 °C; a yield of 83 % was achieved in 10 min (entry 4). It was found that use of PWA, SiO_2, and $NiFe_2O_4$@SiO_2 (NFS) without catalyst resulted in poor product yields, irrespective of the conditions (Table 1, entries 5–8). To determine the optimum amount of catalyst (Table 1, entries 9, 10) we performed the reaction with different amounts of

Table 2 One-pot synthesis of tetrahydrobenzo[*b*]pyran and pyrano[2,3-*c*]pyrazole derivatives by use of $NiFe_2O_4$@SiO_2–$H_3PW_{12}O_{40}$ (NFS–PWA)

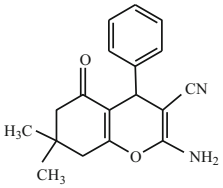
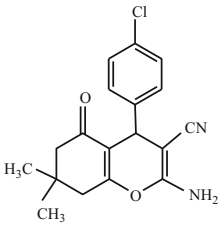
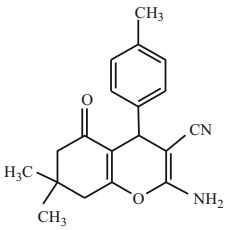
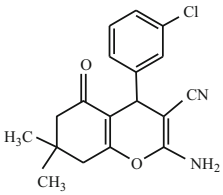
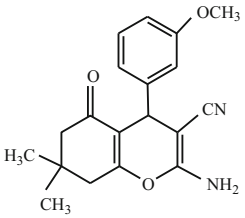
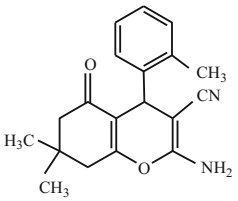
Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
4a		5	94	227–239	227–239 [22]
4b		5	95	209–211	206–207 [22]
4c		15	89	212–214	214–216 [22]
4d		5	91	232–235	233–234 [22]
4e		5	90	197–199	196–198 [58]
4f		15	82	211–212	212–214 [32]

Table 2 continued

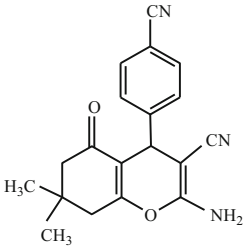
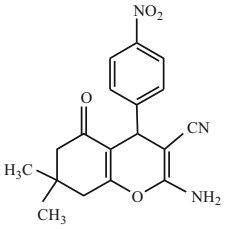
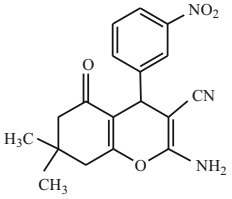
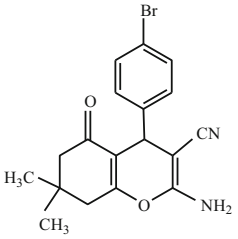
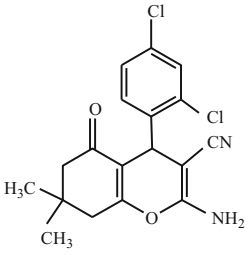
Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
4g		10	82	225–228	225–228 [32]
4h		10	85	180–182	177–179 [32]
4i		10	80	210–211	210–212 [32]
4j		5	87	195–197	196–198 [32]
4k		10	84	189–190	189–191 [37]

Table 2 continued

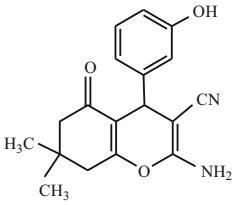
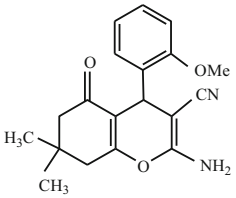
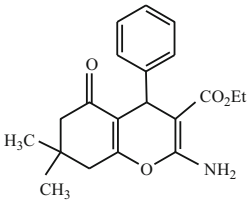
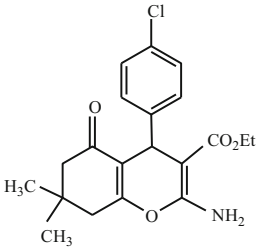
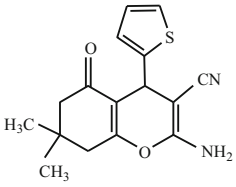
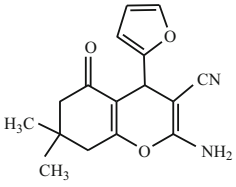
Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
4l		15	82	236–238	236–238 [37]
4m		10	80	211–212	212–214 [40]
4n		30	90	158–160	158–160 [31]
4o		45	86	151–153	153–155 [31]
4p		20	87	208–210	210–212 [41]
4q		25	84	216–217	217–219 [45]

Table 2 continued

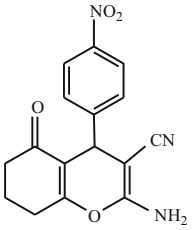
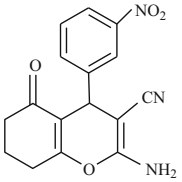
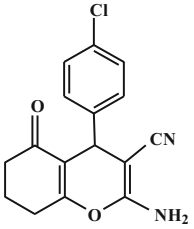
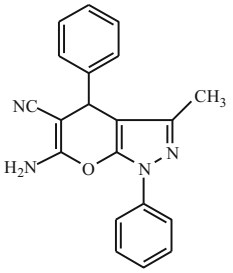
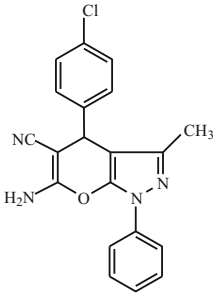
Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
4r		20	90	230–232	234–235 [43]
4s		25	85	237–239	239–241 [43]
4t		25	82	224–226	226–228 [43]
6a		5	84	165–166	168–170 [33]
6b		5	88	182–184	186–187 [20]

Table 2 continued

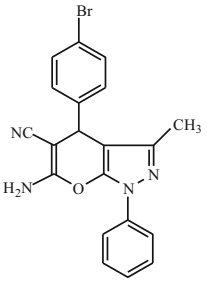
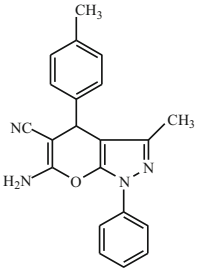
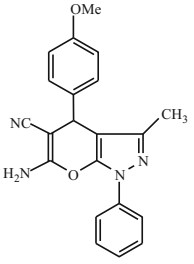
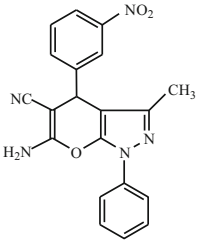
Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
6c		5	90	187–188	183–184 [20]
6d		10	81	174–176	174–175 [20]
6e		10	82	170–172	171–172 [20]
6f		15	94	190–192	188–190 [20]

Table 2 continued

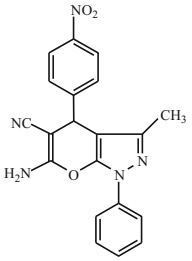
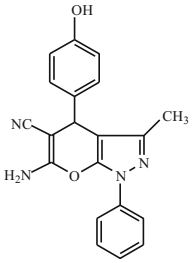
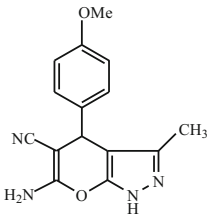
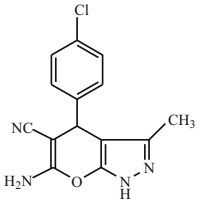
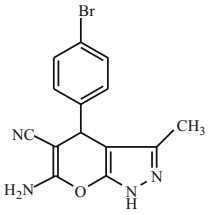
Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
6g		15	89	199–197	194–196 [20]
6h		20	76	208–210	206–207 [20]
7a		45	82	213–215	212–213 [20]
7b		45	88	234–236	234–235 [20]
7c		45	90	244–246	249–250 [20]

Table 2 continued

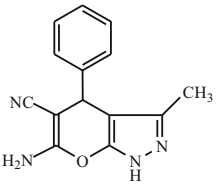
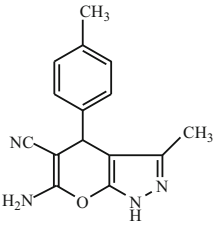
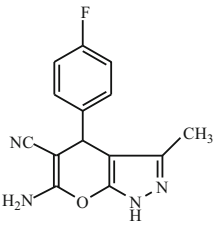
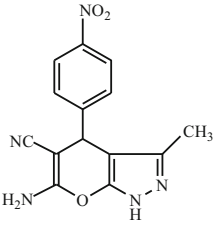
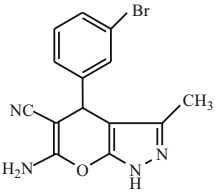
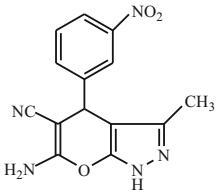
Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
7d		45	90	244–246	245–246 [20]
7e		60	86	196–198	197–198 [20]
7f		45	90	245–247	247–248 [20]
7g		50	90	251–253	251–252 [20]
7h		45	89	222–224	223–224 [20]

Table 2 continued

Entry	Tetrahydrobenzo[*b*]pyran or pyrano[2,3-*c*]pyrazole	Time (min)	Yield[a] (%)	M.p. (°C)	
				Found	Reported
7i		45	91	231–233	232–233 [20]

[a] Isolated yields

catalyst; we found that 0.03 g NFS–PWA effectively catalyzed the reaction and resulted in the highest yield (Table 1, entry 1). Moreover, this reaction occurred at room temperature (25 °C) and impure product was achieved (Table 1, entry 11). We believe that, at room temperature, the reaction was not complete, and stopped because the aldehyde and malonitrile reacted with each other, resulting in impurities plus the desired product.

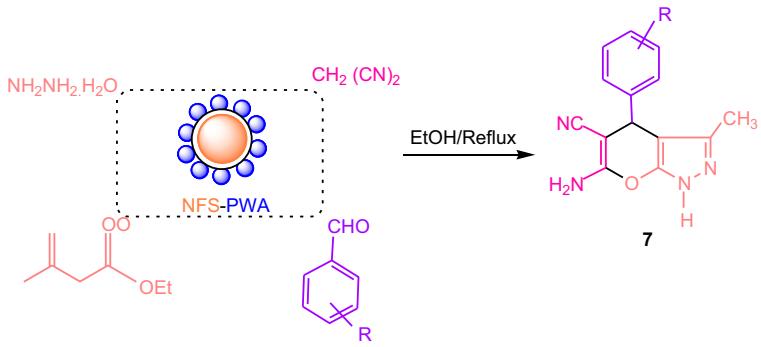
Under the optimized reaction conditions, the scope of one-pot synthesis of tetrahydrobenzo[*b*]pyran was investigated by use of different aldehydes and 1,3-dicarbonyl compounds (1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclohexanedione) as substrates (Table 2).

To broaden the scope of the method, replacement of malononitrile with ethyl cyanoacetate was examined. Successful condensation was achieved under similar reaction conditions, affording the corresponding tetrahydrobenzo[*b*]pyran derivatives in high yields (Table 2, entries **4n–o**).

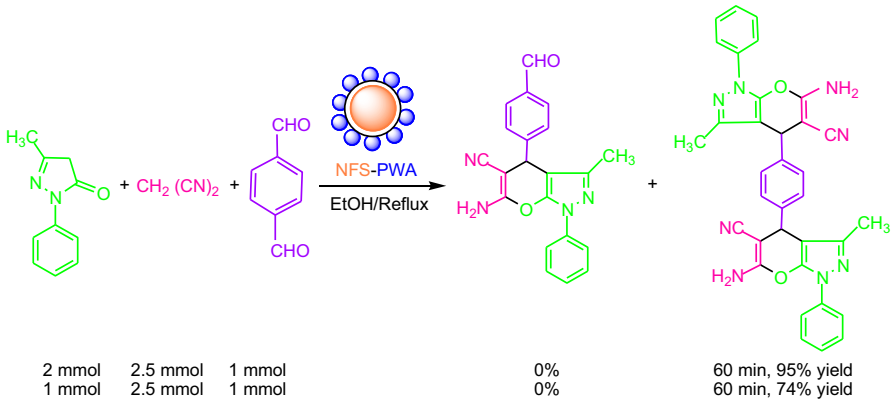
Encouraged by these results, we replaced the cyclic 1,3-dicarbonyl compounds (1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclohexanedione) with 3-methyl-1-phenyl-2-pyrazoline-5-one (Table 2, entry **5**) under the same conditions (Scheme 1). Reaction of 3-methyl-1-phenyl-2-pyrazoline-5-one (Table 2, entry **5**) with different aldehydes and malononitrile was performed for synthesis of 6-amino-5-cyano-4-aryl-1,4-dihydropyrano[2,3-*c*]pyrazoles derivatives in EtOH under reflux (Table 2).

Finally, we developed this synthetic method for efficient, one-pot synthesis of 6-amino-5-cyano-4-aryl-1,4-dihydropyrano[2,3-*c*]pyrazoles by polycondensation of aldehydes with hydrazine hydrate, malononitrile, and ethyl acetoacetate. To determine the optimum reaction conditions, reaction of benzaldehyde (1 mmol) with hydrazine hydrate (1.2 mmol), malononitrile (1.2 mmol), and ethyl acetoacetate (1.2 mmol) in the presence of NFS–PWA was selected as model reaction and the effects of such reaction conditions as amount of the catalyst and temperature were studied in detail. The best result was obtained with 0.02 g NFS–PWA in EtOH under reflux. Several structurally diverse aldehydes (Scheme 3; Table 2) were subjected to condensation with hydrazine hydrate, malononitrile, and ethyl acetoacetate with NFS–PWA (0.03 g) as catalyst.

The practical synthetic efficiency of this reaction was emphasized by reaction of terephthalaldehyde with 3-methyl-1-phenyl-2-pyrazoline-5-one and malononitrile to



Scheme 3 Preparation of 6-amino-5-cyano-4-aryl-1,4-dihydropyrano[2,3-*c*]pyrazoles by four-component condensation



Scheme 4 Reaction between terephthalaldehyde, 3-methyl-1-phenyl-2-pyrazoline-5-one, and malononitrile

give a bispyrano[2,3-*c*]pyrazole derivative (Scheme 4). Use of 2 equiv. 3-methyl-1-phenyl-2-pyrazoline-5-one, one equiv. terephthalaldehyde, and 2.5 equiv. malononitrile with NFS–PWA (0.02 g) afforded only 4,4′-(1,4-phenylene)-bis (6-amino-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile) in 95 % yield. When 3-methyl-1-phenyl-2-pyrazoline-5-one (1 mmol), terephthalaldehyde (1 mmol), malononitrile (2.5 mmol), and NFS–PWA (0.02 g) were used under the same conditions we expected one of the formyl groups on the aromatic ring of terephthalaldehyde would react with 3-methyl-1-phenyl-2-pyrazoline-5-one and malononitrile. However, both formyl groups condensed with methyl-1-phenyl-2-pyrazoline-5-one and malononitrile [66].

The catalyst could be easily separated without noticeable reduction in activity. For this purpose, the same model reaction was again studied under the optimized conditions. After completion of the reaction, the nanomagnetic catalyst was separated from the reaction mixture by use of an external magnetic field, dried at 100 °C for 2 h, and re-used in the same reaction. The catalyst was recovered in excellent yields and used six times without significant loss of activity (Fig. 6). The FTIR spectra of NFS–PWA catalyst before use (fresh) and after re-use six times

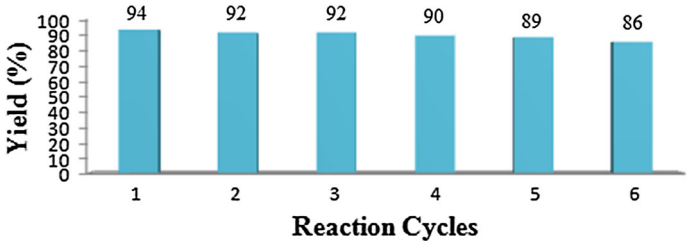
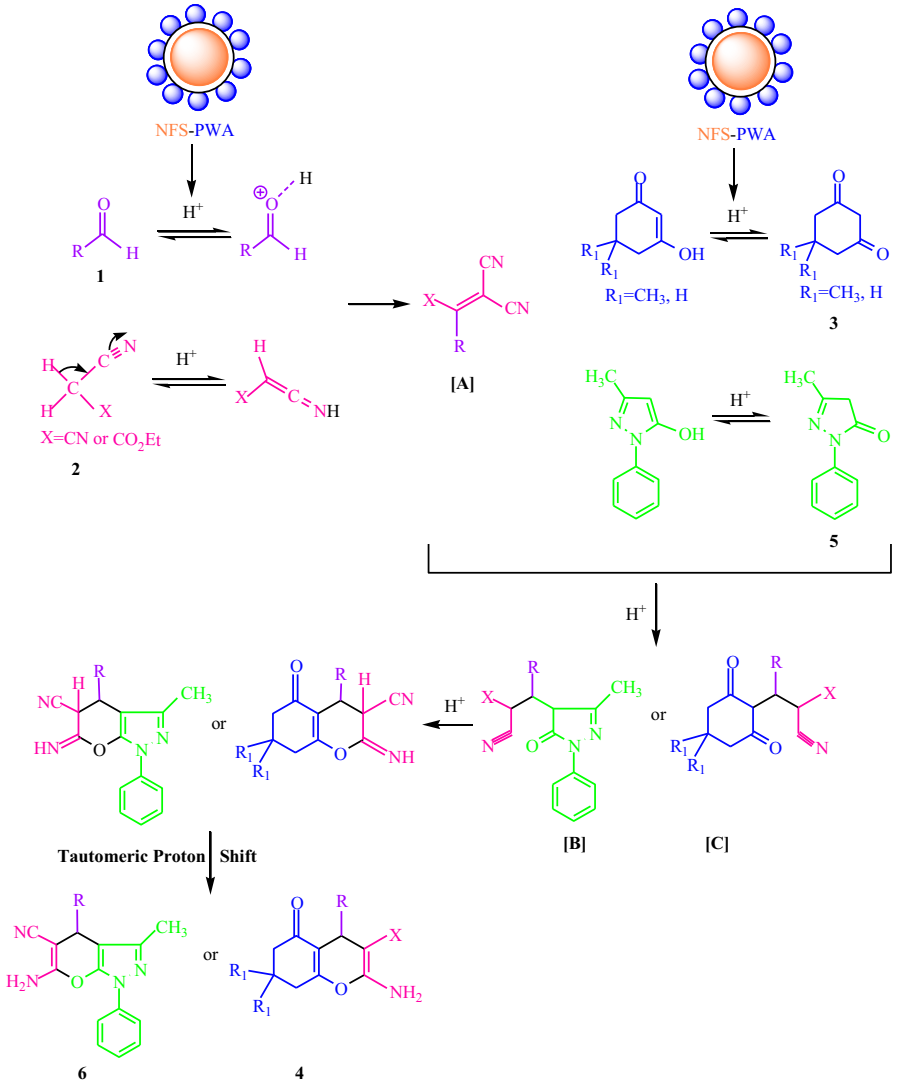


Fig. 6 Re-use of the $NiFe_2O_4$@SiO_2–$H_3PW_{12}O_{40}$ (NFS–PWA) for synthesis of **4a**



Scheme 5 Proposed mechanism

(recovered) were studied. The spectra showed that the structure of the recovered NFS–PWA catalyst remained almost the same after re-use six times. In addition, the weight of the recovered catalyst was the same as that of the fresh catalyst used for the first time in the reaction.

A plausible mechanism for the one-pot synthesis of tetrahydrobenzo[*b*]pyrans and pyrano[2,3-*c*]pyrazoles is given in Scheme 5. The first step involves Knoevenagel condensation of the alkyl nitrile (**2**) with the aldehyde (**1**) to furnish the cyano olefin [**A**]. Subsequently, enolates of **3** and **5** add to [**A**] by Michael addition to give the intermediates [**B**] and [**C**]. The nitrile group is then attacked by the enolate oxygen, and this is followed by tautomeric proton shift to give the target compounds **4** and **6**.

Conclusion

We have developed a simple and efficient catalytic method for synthesis of tetrahydrobenzo[*b*]pyrans and pyrano[2,3-*c*]pyrazoles by one-pot condensation of aldehydes, malononitrile, and 1,3-dicarbonyl compounds (1,3-cyclohexanedione or 5,5-dimethyl-1,3-cyclohexanedione) or 3-methyl-1-phenyl-2-pyrazoline-5-one, with NFS–PWA as a re-usable, safe, and green heterogeneous catalyst. The notable advantages of this method are operational simplicity, generality, availability of inexpensive reactants, short reaction times, and easy work-up.

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