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ORIGINAL PAPER

Synthesis of 2-amino-4,6-diarylnicotinonitrile in the presence of $CoFe_2O_4$@SiO_2-SO_3H as a reusable solid acid nanocatalyst under microwave irradiation in solvent-freeconditions

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Abstract
The modification of silica-coated $CoFe_2O_4$ magnetic nanoparticles ($CoFe_2O_4$@SiO_2) with chlorosulfonic acid, which can be utilized as an organic-inorganic hybrid heterogeneous catalyst, introduces an astonishing and efficient system for the synthesis and simplicity of the recovery of the catalyst. The applied $CoFe_2O_4$ magnetic nanoparticles are 22.98–45.30 nm measured that can be utilized as a catalyst for the preparation of 2-amino-4,6-diarylnicotinonitrile under microwave irradiation in solvent-free conditions by four component reaction of aromatic acetophenone, aldehydes analogues, malononitrile and ammonium acetate. The so synthesized magnetic nanocatalyst was characterized by X-ray powder diffraction, SEM, TGA and FT-IR techniques. This simple protocol suggests advantages such as shorter reaction times, high yield, catalyst recovery, achieving the high purity of products by simple recrystallization and facile work-up. Other noticeable characteristics contain the catalyst can be recovered at least five times without any clear decrease in its catalytic activity.

Keywords Cobalt ferrite · Magnetic nanoparticles · Microwave irradiation · Solvent-free · 2-Amino-4,6-diarylnicotinonitrile

1 Introduction

Recently, magnetic nanocatalysts have attracted considerable attention in organic synthesis because of their high specific surface area, biocompatibility, reusability, economic and environmental benefits. Because magnetic nanoparticles are tending to aggregation and preventing air oxidation, the modification of iron oxide nanoparticles is essential [1–7].

The most significant goal of green chemistry is the removal of volatile organic solvents in organic synthesis. Solvent-free organic reactions also make methods easier, save energy and impede solvent wastes, hazards, and toxicity. So, microwave-assisted solvent-free reactions are clean and efficient [8].

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Multi-component reactions have earned great consideration from organic and medicinal chemists because these procedures do not need the isolation and purification of intermediates so decrease the cost, time and more importantly waste production [5, 9, 10].

Pyridine and its analogues are significant scaffolds found in numerous pharmaceutical active compounds of varied origin, from natural products to synthetic sources. They have a significant and unique position in medicinal chemistry [11–15]. Among them, 2-amino-3-cyanopyridines characterized by their highly important biological properties such as anti-tumor activity, cardiotonic, anti-inflammatory, anti-parkinsonism properties, IKK-b inhibiting, A2A adenosine receptor antagonizing and power inhibitor of HIV-1integrase [16–18]. In addition to, these analogues are significant and benefit intermediates in the synthesis of the diversity of heterocyclic compounds. To date, several effective methods have been presented for the preparation of pyridine derivatives, including multi-component reactions (MCRs). In spite of the existence of wide literature for the synthesis of 2-amino-3-cyanopyridines, some of the approaches require long times, toxic benzene as the solvent, harsh reaction conditions, tedious work-up and low yields. Therefore, efficient and novel one-pot catalytic procedures

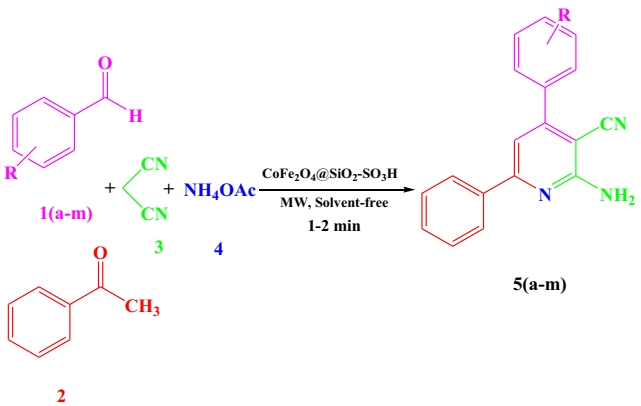
for the preparation of 2-amino-3-cyanopyridines under mild conditions are still strongly demanded [19–21].

As part of our efforts towards the development of synthetic methodologies, herein, SO_3H-functionalized silica-coated magnetite nanoparticles with a core–shell structure, $CoFe_2O_4$@Silica sulfuric acid, were successfully prepared as a reusable and highly efficient acid magnetic nanocatalyst by a simple method without need to N_2 atmosphere for the synthesis of 2-amino-3-cyanopyridines analogues under eco-friendly conditions, as shown in Scheme 1.

2 Experimental

2.1 Materials and methods

All chemical materials were utilized without further purification and purchased from Merck, Fluka, and Aldrich and. Melting points were measured on an Electrothermal 9100 apparatus (LABEQUIP LTD., Markham, Ontario, Canada) and are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ and DMSO-d_6 solvents on a Bruker DRX-250 Avance spectrometer at 250.13 and 62.90 MHz, respectively. FT-IR spectra were obtained on a Jasco 6300 FTIR spectrometer. Nanostructures were analyzed by X-ray powder diffraction (XRPD) with a X'Pert-PRO advanced diffractometer using Cu (Ka) radiation (wavelength: 1.5406 Å), operated at 40 kV and 40 mA at room temperature in the range of 2θ from 20° to 80°. The particle morphology of nanocatalyst was determined by FE-SEM (TE-SCAN, Brno Czech Republic). To measure the amount of coating, thermo gravimetric analyses were performed (TGA Q500) up to 800 °C in air at a ramp rate of 10 °C/min.



Scheme 1 Synthesis of 2-amino-4,6diarylnicotinonitrile in the presence of $CoFe_2O_4$@SiO_2-SO_3H

2.2 Preparation of catalyst ($CoFe_2O_4$@SiO_2-SO_3H)

This catalyst was obtained in three steps according to the presented procedure in our previous work including first step synthesis of $CoFe_2O_4$ MNPs; second step coating of SiO_2 on the $CoFe_2O_4$ MNPs and third step synthesis of SO_3H functionalized silica-coated magnetite nanoparticles [22].

2.3 General experimental approach for the preparation of 2-amino-4,6-diarylnicotinonitrile derivatives

In a 5 ml microwave reaction vessel, a mixture of aromatic aldehyde **1a-m** (1 mmol), acetophenone **2** (1 mmol), malononitrile **3** (1 mmol) and ammonium acetate **4** (1.5 mmol) and $CoFe_2O_4$@Silica sulfuric acid (0.012 g) were placed. Then, the mixture was heated in a microwave oven in 600 W of power for 2 min. The progress of the reaction was elucidated by TLC (*n*-Hexane: EtOAc, 10:6). The catalyst was separated from the mixture by an external magnet and washed several times with ethanol for use again. Ultimately, the pure product was obtained by recrystallization from hot ethanol. The structures of the products **5a-m** were determined by FTIR, ^{1}H-NMR and ^{13}C-NMR spectroscopic data. The structure of the product **5c** was also verified by the single-crystal X-ray analysis.

2.4 Spectral data of selected products

2.4.1 *2-amino-4,6-diphenylnicotinonitrile* (5a)

Mp 187–189 °C (Reported: 186–187 °C [23]). FTIR (KBr, cm^{-1}): 3463, 3303, 2205, 1637, 1585, 1549, 1495, 1451, 1369, 1075, 849, 775, 698; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.38 (s, 2H, NH_2), 7.20 (s, 1H, pyridine H-5), 7.25–7.99 (m, 10H, ArH).^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 111.12, 117.12, 127.32, 128.16, 128.80, 128.93, 130.19, 136.92, 137.93, 155.12, 159.82, 160.23.

2.4.2 *2-amino-4-(4-chlorophenyl)-6-phenylnicotinonitrile* (5b)

Mp 221–224 °C (Reported: 223–225 °C [23]). FTIR (KBr, cm^{-1}): 3484, 3362, 2215, 1631, 1574, 1546, 1493, 1450, 1362, 1259, 1091, 1013, 842, 778, 687; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.38 (s, 2H, NH_2), 7.21–8.00 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 110.98, 127.31, 128.83, 129.23, 129.51, 130.33, 160.21.

2.4.3 *2-amino-4-(3-chlorophenyl)-6-phenylnicotinonitrile* (5c)

Mp 168–170 °C. FTIR (KBr, cm^{-1}): 3469, 3305, 2205, 1635, 1578, 1547, 1479, 1369, 1258, 1159, 844, 793, 696; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.44 (s, 2H, NH_2), 7.16–8.00 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 110.99, 116.68, 126.38, 127.32, 128.22, 128.81, 129.84, 130.20, 130.35, 134.90, 137.66, 138.61, 153.51, 160.17.

2.4.4 *2-amino-4-(2-chlorophenyl)-6-phenylnicotinonitrile* (5d)

Mp 199–201 °C. FTIR (KBr, cm^{-1}): 3489, 3341, 2228, 1623, 1571, 1553, 1477, 1361, 1253, 1160, 844, 763, 687; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.36 (s, 2H, NH_2), 7.15–7.98 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 112.20, 127.08, 127.36, 128.79, 130.27, 130.64, 152.97, 159.62.

2.4.5 *2-amino-4-(4-fluorophenyl)-6-phenylnicotinonitrile* (5e)

Mp 164–166 °C. FTIR (KBr, cm^{-1}): 3474, 3393, 2206, 1644, 1574, 1553, 1452, 1368, 1233, 1158, 830, 767, 697; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.40 (s, 2H, NH_2), 7.16–8.00 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 111.09, 115.90 (d, $^2J_{CF}$ = 22.01 Hz), 117.01, 127.32, 128.81, 130.08, 130.22 (d, $^3J_{CF}$ = 08.80 Hz), 137.82, 154.01, 159.96, 160.25, 165.67 (d, $^1J_{CF}$ = 250.34 Hz).

2.4.6 *2-amino-4-(3-fluoroophenyl)-6-phenylnicotinonitrile* (5f)

Mp 162–165 °C. FTIR (KBr, cm^{-1}): 3473, 3311, 2206, 1645, 1575, 1511, 1453, 1369, 1234, 1159, 830, 767, 697; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.40 (s, 2H, NH_2), 7.16–7.99 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 111.08, 115.89 (d, $^2J_{CF}$ = 22.01 Hz), 116.24, 116.99, 127.32, 128.80, 130.08 (d, $^3J_{CF}$ = 08.80 Hz), 133.00, 137.82, 154.00, 159.96, 160.25, 161.69 (d, $^1J_{CF}$ = 250.97 Hz).

2.4.7 *2-amino-4-(2-fluorophenyl)-6-phenylnicotinonitrile* (5 g)

Mp 178–180 °C. FTIR (KBr, cm^{-1}): 3465, 3305, 2206, 1637, 1587, 1550, 1450, 1369, 1256, 1103, 860, 759, 706; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.39 (s, 2H, NH_2), 7.20–7.93 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 112.22, 116.26 (d, $^2J_{CF}$ = 21.38 Hz), 116.47, 124.59, 127.36, 128.79, 130.25, 130.55, 131.54 (d, $^3J_{CF}$ = 08.17 Hz), 137.79, 149.59, 159.86, 161.22.

2.4.8 *2-amino-4-(4-nitrophenyl)-6-phenylnicotinonitrile* (5 h)

Mp 216–218 °C. FTIR (KBr, cm^{-1}): 3489, 3375, 2210, 1636, 1571, 1518, 1495, 1348, 1261, 1106, 847, 753, 694; ^{1}H NMR (250.13 MHz, DMSO): δ_H 6.92–8.33 (m, 12 H, ArH); ^{13}C NMR (62.90 MHz, DMSO): δ_C 109.59, 118.90, 124.16, 127.37, 129.12, 130.01, 130.43, 130.64, 137.65, 154.47, 161.19.

2.4.9 *2-amino-4-(3-nitrophenyl) -6-phenylnicotinonitrile* (5i)

Mp 208–210 °C. FTIR (KBr, cm^{-1}): 3478, 3362, 2218, 1622, 1577, 1528, 1444, 1343, 1259, 1083, 769, 741, 691; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.44 (s, 2H, NH_2), 7.21–8.46 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 110.88, 123.28, 124.46, 127.37, 128.88, 130.09, 130.59, 134.11, 138.50, 160.20.

2.4.10 *2-amino-4-(4-bromophenyl)-6-phenylnicotinonitrile* (5j)

Mp 186–188 °C. FTIR (KBr, cm^{-1}): 3472, 3305, 2206, 1642, 1574, 1545, 1491, 1366, 1258, 1072, 833, 767, 699; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.38 (s, 2H, NH_2), 7.16–7.99 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 110.90, 116.88, 124.40, 127.32, 128.83, 129.74, 130.34, 132.20, 135.77, 137.73, 153.84, 160.07, 160.22.

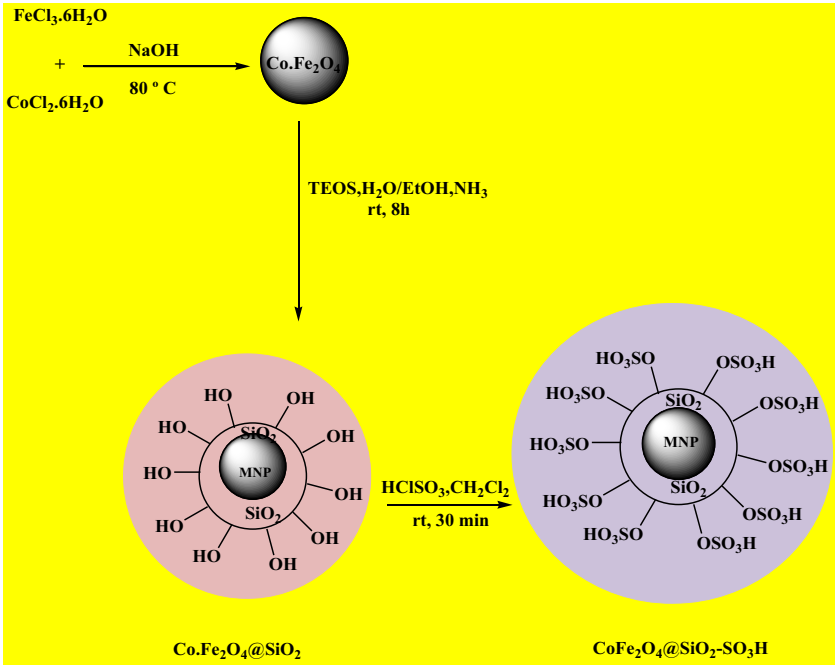
2.4.11 *2-amino-4-(4-cyanophenyl)-6-phenylnicotinonitrile* (5 k)

Mp 185–187 °C. FTIR (KBr, cm^{-1}): 3475, 3363, 2204, 1618, 1574, 1545, 1449, 1360, 1261, 1159, 826, 767, 688; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.47 (s, 2H, NH_2), 7.15–7.99 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 110.77, 113.63, 115.37, 116.45, 118.12, 119.67, 127.34, 128.33, 128.87, 128.99, 129.21, 129.99, 130.55, 132.69, 137.45, 141.29, 152.92, 160.23, 160.41.

2.4.12 *2-amino-4-(2,6-dichlorophenyl) -6-phenylnicotinonitrile* (5 l)

Mp 174–176 °C. FTIR (KBr, cm^{-1}): 3489, 3373, 2214, 1666, 1577, 1560, 1436, 1355, 1215, 1151, 843, 779, 693; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.34 (s, 2H, NH_2), 7.08–8.01 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 111.80, 115.56, 127.39, 128.39, 128.79, 130.35, 130.84, 134.05, 137.63, 150.77, 159.61, 160.22.

Scheme 2 Synthesis of $CoFe_2O_4$@SiO_2-SO_3H



2.4.13 *2-amino-4-(2,4-dichlorophenyl) -6-phenylnicotinonitrile* (5 m)

Mp 179–181 °C. FTIR (KBr, cm^{-1}): 3480, 3377, 2212, 1682, 1615, 1589, 1474, 1359, 1266, 1104, 868, 760, 691; ^{1}H NMR (250.13 MHz, $CDCl_3$): δ_H 5.46 (s, 2H, NH_2), 7.11–7.99 (m, 10 H, ArH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ_C 111.98, 116.05, 127.38, 127.55, 128.84, 130.16, 131.14, 133.23, 134.36, 136.11, 137.59, 151.87, 159.87.

2.5 Single crystal X-ray crystallography

Crystal of **5c** was obtained by dissolution of **5c** in hot ethanol and then slow evaporation of its solvent at room temperature.

The crystallographic measurement of **5c** was carried out on a Kuma KM4-CCD κ-geometry automated four-circle diffractometer equipped with a CCD camera Sapphire2 and graphite-monochromatized Mo Kα radiation ($\lambda = 0.71073$ Å). The data were collected at 102(2) K by using the *Oxford-Cryosystems* cooler. Data were corrected for the Lorentz and polarization effects. Data collection, cell refinement, data reduction and analysis were carried out with KM4-CCD software, CrysAlisPro [24]. Analytical absorption correction was applied. The structure was solved with direct methods using SHELXT-2014 [25] and refined by a full-matrix least squares technique with the anisotropic thermal parameters for non-H atoms with the use of SHELXL-2014 [25]. H atoms were found in difference Fourier maps and were refined isotropically. In the final refinement cycles, C-bound H atoms were repositioned in their calculated positions and refined using a riding model, with C–H = 0.95 Å, and with $U_{iso}(H) = 1.2U_{eq}(C)$. Amine H atoms were refined isotropically with $U_{iso}(H) = 1.2U_{eq}(N)$. Figures were made

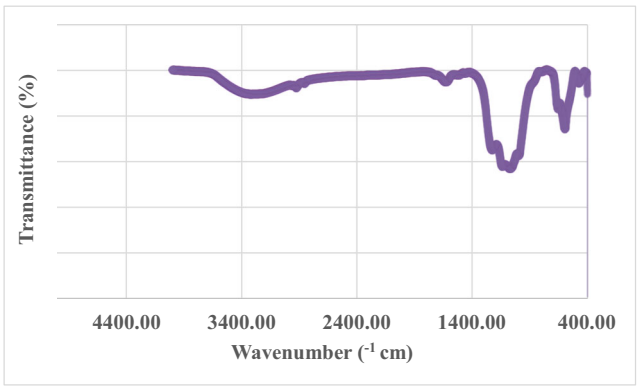


Fig. 1 FT-IR spectra of $CoFe_2O_4$@SiO_2-SO_3H MNPs

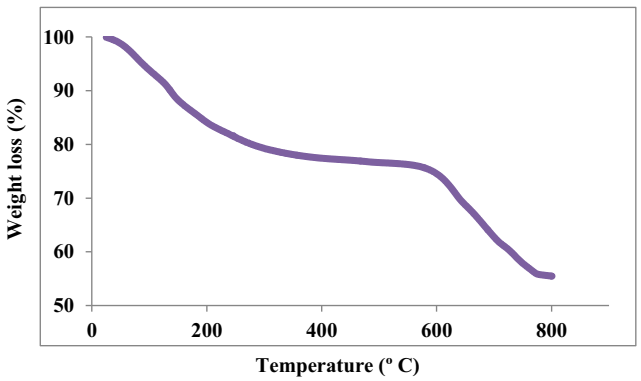


Fig. 2 TGA curves of $CoFe_2O_4$@SiO_2-SO_3H MNPs

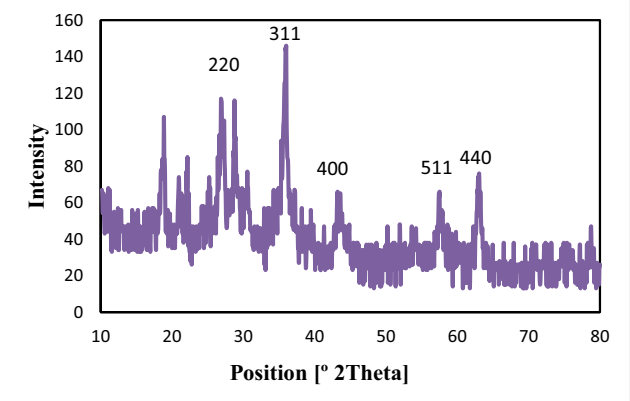


Fig. 3 XRPD pattern of $CoFe_2O_4$@SiO_2-SO_3H MNPs

using the DIAMOND program [26]. The crystallographic information file (CIF) was deposited with The Cambridge Crystallographic Data Centre (http://www.ccdc.cam.ac.uk/; deposition number CCDC 1587653 and provided as ESI.

Crystal data for ***5c***. $C_{18}H_{12}ClN_3$, $M_r = 305.76$, colorless block, crystal size 0.55 × 0.40 × 0.23 mm, triclinic, space group $P\bar{1}$, $a = 9.213(3)$, $b = 9.445(3)$, $c = 9.661(4)$ Å, $\alpha = 73.52(3)°$, $\beta = 61.69(4)°$, $\gamma = 85.13(3)°$, $V = 708.5(5)$ Å^3, $T = 102(2)$ K, $Z = 2$, $\mu = 0.27$ mm^{-1} (for Mo Kα, $\lambda = 0.71073$ Å), analytical absorption correction, $T_{min} = 0.883$, $T_{max} = 0.945$, 9961 reflections measured, 5131 unique ($R_{int} = 0.036$), 4595 observed ($I > 2\sigma(I)$), $(\sin\theta/\lambda)_{max} = 0.844$ Å^{-1}, 205 parameters, 0 restraints, $R = 0.052$, $wR = 0.150$ (observed refl.), GOOF = $S = 1.03$, $(\Delta\rho_{max}) = 0.56$ and $(\Delta\rho_{min}) = -0.48$ e Å^{-3}.

3 Results and discussion

3.1 Catalyst characterization

The details of the functionalized catalyst preparation approach are represented in scheme 2. First, the $CoFe_2O_4$ MNPs have been synthesized. Then, after coating of the $CoFe_2O_4$ MNPs with silica layers (using TEOS), the modification of facial hydroxyl groups with chlorosulfonic acid cause to $CoFe_2O_4$@Silica sulfuric acid [22]. The structure of catalyst was studied by FT-IR, TGA, XRD, and SEM.

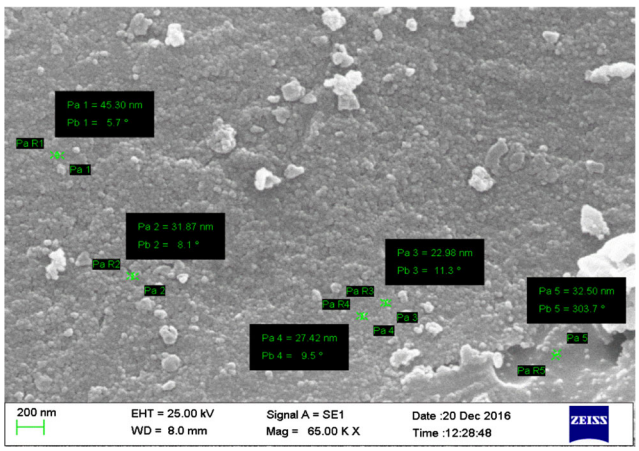


Fig. 4 SEM image of $CoFe_2O_4$@SiO_2-SO_3H MNPs

Table 1 The synthesis of 2-amino-4,6-diarylnicotinonitrile derivatives under a different amount of catalyst

Entry	Catalyst (g)	Time (min)	Yield [b] (%)
1	None	20	36
2	0.004	4	68
3	0.008	3	79
4	0.012	1.5	90
5	0.016	3	81

Figure 1 indicates the FT-IR spectra of $CoFe_2O_4$@Silica sulfuric acid. The band in the region of 591 cm^{-1} is attributed to the stretching vibration of the (M-O) band and the bands at about 1061 cm^{-1} and, 1073 cm^{-1} belong to (Si–O–Si) stretching vibrations. The presence of sulfuric acid is verified by peaks at about 3300 cm^{-1} (O–H stretching) and 1042 cm^{-1} and 1134 cm^{-1} (S–O) [27].

A thermogravimetric analysis (TGA) was also utilized to determine the percent of functional groups that are coated on to the surface of magnetic nanoparticles (Fig. 2). The TGA curve was separated into three areas according to three mass loss ranges. The first area, which occurred below 150 °C, showed a mass loss that was attributed to the loss of physically adsorbed solvent and surface hydroxyl groups (11.65%). The second region (150–600 °C) shows that the silica-coated MNPs are thermally stable. Finally, the third area that occurred between 600 and 800 °C belongs to the mass loss of SO_3H groups (32.81%) [28, 29].

Figure 3 displays the XRPD of $CoFe_2O_4$@SiO_2-SO_3H MNPs that matched well with standard XRD pattern of $CoFe_2O_4$ (card no. 00–001-1121). The diameter of the $CoFe_2O_4$@Silica sulfuric acid MNPs was determined by Debye-Scherrer equation with XRD data (D = 0.94 λ/B Cos θ) 33 nm [28, 30].

The size of the nanocatalyst was measured using scanning electron microscopy (SEM) (Fig. 4) that the $CoFe_2O_4$@Silica sulfuric acid MNPs are ranging from 22.98–45.30 nm and their shape is spherical.

Table 2 The synthesis of 2-amino-4,6-diarylnicotinonitrile derivatives under various microwave power

Entry	Catalyst (g)	Microwave power (W)	Time (min)	Yield [a] (%)
1	0.012	500	1.5	64
2	0.012	550	1.5	82
3	0.012	600	1.5	90
4	0.012	650	1.5	76

Table 3 Three-component condensation of aldehydes, acetophenone, malononitrile, and ammonium acetate for the synthesis of 2-amino-4,6-diarylnicotinonitrile

Entry	R	Product	Time (min)	Yield (%) [a]	M.P (° C)	References
1	H	**5a**	2	89	187–189	186–87 [23]
2	4-Cl	**5b**	1.5	90	180–182	221–24 [23]
3	3-Cl	**5c**	2	87	168–170	–
4	2-Cl	**5d**	2	90	199–201	–
5	4-F	**5e**	1.5	92	164–166	–
6	3-F	**5f**	2	88	162–165	–
7	2-F	**5 g**	2	85	178–180	–
8	4-NO_2	**5 h**	2	87	216–218	–
9	3-NO_2	**5i**	2	88	208–210	–
10	4-Br	**5j**	1.5	92	186–188	–
11	4-CN	**5 k**	1.5	92	185–187	–
12	2,6-$(Cl)_2$	**5 l**	2	86	174–176	–
13	2,4-$(Cl)_2$	**5 m**	1.5	89	179–181	–

3.2 Evaluation of the catalytic activity of $CoFe_2O_4$@Silica sulfuric acid in the preparation of 2-amino-4,6-diarylnicotinonitrile derivatives

In this research, green energy, eco-friendly and facile procedure for the preparation of 2-amino-4,6-diarylnicotinonitrile derivatives using $CoFe_2O_4$@Silica sulfuric acid are explained. First, to optimize the reaction conditions the efficiency and amount of the $CoFe_2O_4$@Silica sulfuric acid MNPs catalyst were investigated in a model reaction of 4-chlorobenzaldehyde **1b** (1 mmol), acetophenone **2** (1 mmol), malononitrile **3** (1.5 mmol) and ammonium acetate **4** (1 mmol) for the synthesis of compound **5b** under solvent-free conditions in the absence and presence of $CoFe_2O_4$@Silica sulfuric acid (Table 3, entry 2). It was proved that in the absence of a nanomagnetic solid acid catalyst, the only trace of the desired product was obtained. When the reaction was carried out in the presence of $CoFe_2O_4$@Silica sulfuric acid, it proceeded rapidly to give the desired product. The obtained results from the reaction to determine the optimum amount of catalyst represented in Table 1. As can be seen from this table, the best results were obtained using 0.012 g of catalyst. Ultimately, the effect of microwave power inputs from 500 to 650 W was evaluated (Table 2).

After optimization of the reaction conditions, the reaction of acetophenone, malononitrile and ammonium acetate with diverse aldehydes was performed in according to the general experimental method (Scheme 1). In all the cases, the

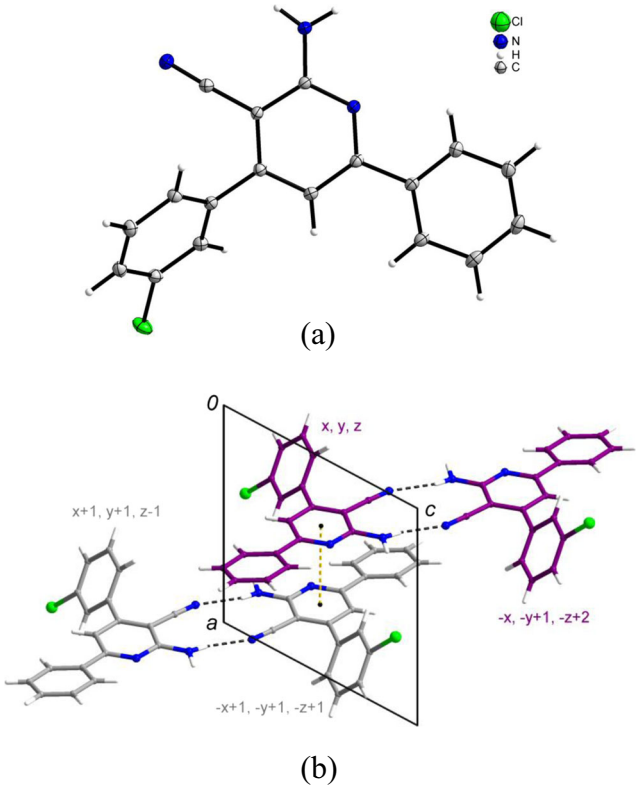


Fig. 5 X-ray crystal structure of **5c**: molecule (a) and packing diagram (b). Displacement ellipsoids in (a) are drawn at the 50% probability level. Black dashed lines represent N–H···N hydrogen bonds [N–H, H···N, N···N distances = 0.84(2), 2.18(2), 3.017(2) Å, N–H···N angle = 169(2)°]. Yellow dotted line – $\pi\cdots\pi$ stacking [centroid···centroid distance = 3.494(2) Å]

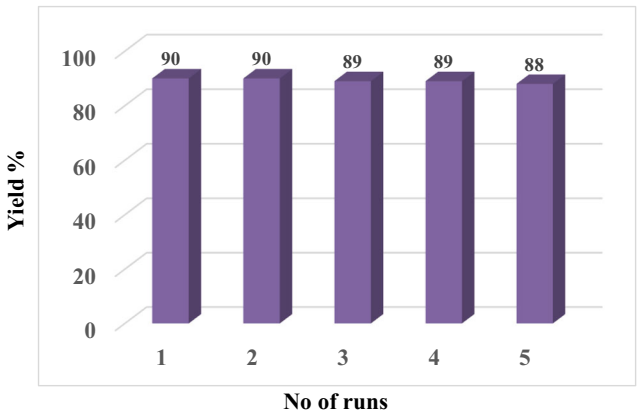


Fig. 6 Reusability and recovery of the $CoFe_2O_4$@SiO_2-SO_3H

corresponding 2-amino-4,6-diarylnicotinonitrile analogues were synthesized in high yields and short reactions times. The results of the transformation of differently substituted aryl aldehydes to 2-amino-4,6-diarylnicotinonitrile derivatives **5a-m** are summarized in Table 3.

Reaction conditions: 4-chlorobenzaldehyde **1** (1 mmol), acetophenone**2** (1 mmol) malononitrile**3** (1 mmol), ammonium acetate**4** (1 mmol) under microwave irradiation at 600 W in solvent-free conditions. [a] Isolated yield.

Reaction conditions: 4-chlorobenzaldehyde **1** (1 mmol), acetophenone**2** (1 mmol) malononitrile**3** (1 mmol), ammonium.

acetate**4** (1 mmol) with 0.012 g $CoFe_2O_4$@SiO_2-SO_3H in solvent-free conditions. [a] Isolated yield.

Reaction conditions: benzaldehyde **1a-m** (1 mmol), acetophenone**2** (1 mmol) malononitrile**3** (1 mmol), ammonium acetate**4** (1 mmol) with 0.012 g $CoFe_2O_4$@SiO_2-SO_3H under microwave irradiation at 600 W in solvent-free conditions.[a] Isolated yield.

The structure of compound **5c** was verified by single-crystal X-ray analysis. As shown in Fig. 5a, the phenyl ring is almost coplanar with the pyridyl ring (interplanar angle amounts to 11°), while the chlorophenyl ring is twisted relative to the central ring at about 56°. In the crystal lattice, the molecules of **5c** interact with each other via N–H···N hydrogen bonds giving rise to centrosymmetric dimers, which are further linked by $\pi\cdots\pi$ stacking interactions between the pyridyl rings (Fig. 5b).

Ultimately, the recyclability and reusability of the reaction catalyst were evaluated. After the removal of catalyst from the reaction mixture, the catalyst was washed with ethanol and dried to eliminate any remaining ethanol and reutilized in the further. As shown in Fig. 6, $CoFe_2O_4$@Silica sulfuric acid MNPs could be reutilized at least five times with little loss of activity.

4 Conclusion

In this research, we were represented using $CoFe_2O_4$@Silica sulfuric acid as a reusable, efficient and inexpensive catalyst for the one-pot preparation of 2-amino-4,6-diarylnicotinonitrile. Short reaction time, utilize of recyclable catalyst, simple, high yields, and inexpensive are significant features of this method.

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References

1. Ahankar H, Ramazani A, Joo SW (2016) Magnetic nickel ferrite nanoparticles as an efficient catalyst for the preparation of polyhydroquinoline derivatives under microwave irradiation in solvent-free conditions. Res Chem Intermed 42(3):2487–2500
2. Kiasat AR, Davarpanah J (2015) Fe_3O_4@ 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(5):2991–3001
3. Koesnarpadi S, Santosa SJ, Siswanta D, Rusdiarso B (2015) Synthesis and characterizatation of magnetite nanoparticle coated humic acid (Fe_3O_4/HA). Procedia Environ Sci 30:103–108
4. Aghahosseini H, Ramazani A, Ślepokura K, Lis T (2018) The first protection-free synthesis of magnetic bifunctional l-proline as a highly active and versatile artificial enzyme: Synthesis of imidazole derivatives. J Colloid Interface Sci 511:222–232
5. Malekzadeh AM, Ramazani A, Rezaei SJT, Niknejad H (2017) Design and construction of multifunctional hyperbranched polymers coated magnetite nanoparticles for both targeting magnetic resonance imaging and cancer therapy. J Colloid Interface Sci 490:64–73
6. Dayyani N, Ramazani A, Khoee S, Shafiee A (2017) Synthesis and characterization of the first generation of polyamino-ester dendrimer-grafted magnetite nanoparticles from 3-aminopropyltriethoxysilane (APTES) via the convergent approach. Silicon:1–7
7. Tarasi R, Ramazani A, Ghorbanloo M, Khoobi M, Aghahosseini H, Joo SW, Shafiee A Synthesis of Magnetic Fe3O4@ polyethyleneimine. Mn (II) from Fe3O4,[3-(2, 3-Epoxypropoxy) propyl] trimethoxysilane, Polyethyleneimine and Mn (II) Acetate as a Novel Silicon-Containing Polymeric Organic-Inorganic Hybrid Nanomaterial and Its Catalytic Investigation Towards the Oxidation of Cyclohexene, Ethyl Benzene and Toluene in the Presence of H_2O_2 as an Oxidant. Silicon:1–9
8. Sheldon RA (2007) The E factor: fifteen years on. Green Chem 9(12):1273–1283
9. Rezaei A, Ramazani A, Gouranlou F, Woo Joo S (2017) Silica Nanoparticles/Nanosilica Sulfuric Acid as a Reusable Catalyst for Fast, Highly Efficient and Green Synthesis of 2-(Heteroaryl) acetamide Derivatives. Lett Org Chem 14(2):86–92
10. Ahankar H, Ramazani A, Ślepokura K, Lis T, Joo SW (2016) Synthesis of pyrrolidinone derivatives from aniline, an aldehyde and diethyl acetylenedicarboxylate in an ethanolic citric acid solution under ultrasound irradiation. Green Chem 18(12):3582–3593
11. Zhang F, Zhao Y, Sun L, Ding L, Gu Y, Gong P (2011) Synthesis and anti-tumor activity of 2-amino-3-cyano-6-(1H-indol-3-yl)-4-phenylpyridine derivatives in vitro. Eur J Med Chem 46(7):3149–3157
12. Bekhit AA, Baraka AM (2005) Novel milrinone analogs of pyridine-3-carbonitrile derivatives as promising cardiotonic agents. Eur J Org Chem 40(12):1405–1413
13. Murata T, Shimada M, Sakakibara S, Yoshino T, Kadono H, Masuda T, Shimazaki M, Shintani T, Fuchikami K, Sakai K (2003) Discovery of novel and selective IKK-β serine-threonine protein kinase inhibitors. Part 1 Bioorg Med Chem Lett 13(5): 913–918
14. Mantri M, de Graaf O, van Veldhoven J, Göblyös A, von Frijtag Drabbe Künzel JK, Mulder-Krieger T, Link R, de Vries H, Beukers MW, Brussee J (2008) 2-Amino-6-furan-2-yl-4-substituted nicotinonitriles as A2A adenosine receptor antagonists. J Med Chem 51(15):4449–4455
15. Deng J, Sanchez T, Al-Mawsawi LQ, Dayam R, Yunes RA, Garofalo A, Bolger MB, Neamati N (2007) Discovery of structurally diverse HIV-1 integrase inhibitors based on a chalcone pharmacophore. Bioorg Med Chem Lett 15(14):4985–5002
16. Shishoo C, Devani M, Bhadti V, Ananthan S, Ullas G (1983) Reaction of nitriles under acidic conditions: a novel, direct

formation of condensed 4-chloropyrimidines. Tetrahedron Lett 24(42):4611–4612
17. Kambe S, Saito K, Sakurai A, Midorikawa H (1980, 1980) A simple method for the preparation of 2-amino-4-aryl-3-cyanopyridines by the condensation of malononitrile with aromatic aldehydes and alkyl ketones in the presence of ammonium acetate. Synthesis (05): 366–368
18. Maiti S, Biswas S, Jana U (2010) Iron (III)-catalyzed four-component coupling reaction of 1, 3-dicarbonyl compounds, amines, aldehydes, and nitroalkanes: a simple and direct synthesis of functionalized pyrroles. J Med Chem 75(5):1674–1683
19. Gu Y (2012) Multicomponent reactions in unconventional solvents: state of the art. Green Chem 14(8):2091–2128
20. Dömling A, Ugi I (2000) Multicomponent reactions with isocyanides. Angew Chem Int Ed 39(18):3168–3210
21. Gers CF, Nordmann J, Kumru C, Frank W, Müller TJ (2014) Solvatochromic fluorescent 2-substituted 3-ethynyl quinoxalines: Four-component synthesis, photophysical properties, and electronic structure. J org chem 79(8):3296–3310
22. Hosseinzadeh Z, Ramazani A, Ahankar H, Ślepokura K, Lis T (2018) Sulfonic acid-functionalized silica-coated magnetic nanoparticles as a reusable catalyst for the preparation of pyrrolidinone derivatives in a green solvent conditions. SILICON Accepted for publication. https://doi.org/10.1007/s12633-017-9737-4
23. Shah HC, Shah VH, Desai ND (2009) A novel strategy for the synthesis of 2-amino-4, 6-diarylnicotinonitrile. Arkivoc 2:76–87
24. CrysAlisPro in KM4-CCD software; Agilent Technologies: (2012). Yarnton, U.K.,
25. Sheldrick GM (2015) Acta Crystallogr Sect. C. Cryst, Struct. Commun 71:3–8
26. Brandenburg K (2014) DIAMOND Version 3.2k, Crystal Impact GbR. Bonn, Germany,
27. Kiasat AR, 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 373:46–54
28. Naeimi H, Nazifi ZS (2013) A highly efficient nano-Fe_3O_4 encapsulated-silica particles bearing sulfonic acid groups as a solid acid catalyst for synthesis of 1, 8-dioxo-octahydroxanthene derivatives. J Nanopart Res 15(11):2026
29. Nemati F, Heravi MM, Rad RS (2012) Nano-Fe_3O_4 encapsulated-silica particles bearing Sulfonic acid groups as a magnetically separable catalyst for highly efficient knoevenagel condensation and michael addition reactions of aromatic aldehydes with 1, 3-cyclic diketones. Chin J Catal 33(11):1825–1831
30. Sadri F, Ramazani A, Massoudi A, Khoobi M, Azizkhani V, Tarasi R, Dolatyari L, Min B-K (2014) Magnetic $CoFe_2O_4$ nanoparticles as an efficient catalyst for the oxidation of alcohols to carbonyl compounds in the presence of oxone as an oxidant. Bull Kor Chem Soc 35(7):2029