Received: 27 March 2018 | Revised: 7 May 2018 | Accepted: 12 May 2018

DOI: 10.1002/aoc.4455

FULL PAPER

WILEY Applied Organometallic Chemistry

Butane-1-sulfonic acid immobilized on magnetic Fe_3O_4@SiO_2 nanoparticles: A novel and heterogeneous catalyst for the one-pot synthesis of barbituric acid and pyrano[2,3-*d*] pyrimidine derivatives in aqueous media

M. Pourghasemi-Lati[1] | F. Shirini[2] | M. Alinia-Asli[1] | M.A. Rezvani[1]

[1]University of Zanjan, Department of Chemistry, College of Science, Zanjan 45195-313, Iran

[2]University of Guilan, Department of Chemistry, College of Science, Rasht 41335, Iran

Correspondence
F. Shirini, Department of Chemistry, College of Science, University of Guilan, Rasht 41335, Iran.
Email: shirini@guilan.ac.ir
M. Alinia-Asli, Department of Chemistry, College of Science, University of Zanjan, Zanjan 45195-313, Iran.
Email: m_aliniaaslir@znu.ac.ir

Butane-1-sulfonic acid immobilized on magnetic Fe_3O_4@SiO_2 nanoparticles (Fe_3O_4@SiO_2-Sultone) was easily prepared via direct ring opening of 1,4-butanesultone with nanomagnetic Fe_3O_4@SiO_2. The prepared reagent was characterized and used for the efficient promotion of the synthesis of barbituric acid and pyrano[2,3-*d*] pyrimidine derivatives. All reactions were performed under mild and completely heterogeneous reaction conditions affording products in good to high yields. The catalyst is easily isolated from the reaction mixture by magnetic decantation and can be reused at least eight times without significant loss in activity.

KEYWORDS
aqueous media, barbituric acid, heterogeneous catalyst, magnetite nanoparticles, pyrano[2,3-*d*] pyrimidines

1 | INTRODUCTION

In recent years the use of magnetic nanoparticles (MNPs) for the preparation of supported heterogeneous catalysts has attracted significant attention.[1–12] This attention can be attributed to the unique properties of these types of compounds including high thermal and mechanical stability, large surface area to volume ratio, low toxicity, ease of recovery by use of an external magnetic field and well-defined pore size distribution.[13] In this regard magnetic metal oxide nanoparticles and especially Fe_3O_4 nanoparticles have been the focus of much research recently. This is because, among other advantages, the existence of many hydroxyl groups on the surface of Fe_3O_4 MNPs leads to a reaction with tetraethyl orthosilicate (TEOS) to form Si— O bonds and to provide reaction sites for further functionalization of Fe_3O_4@SiO_2 MNPs. Among various types of reagents that can be used for the functionalization of the surface of solid supports, 1,4-butanesultone is one of the most important. Sulfonation using this reagent leads to organic–inorganic hybrid materials that have been applied as impressive solid acid catalysts in organic transformations, a useful way to combine the advantageous characteristics of homogeneous protic acids and solid properties.[14]

Arylidene barbituric acids, as important heterocyclic compounds, can be obtained via the Knoevenagel condensation reaction between barbituric acid and its derivatives with aldehydes or ketones that do not contain α-hydrogen. For this purpose, a variety of catalysts and reagents have been used to facilitate this reaction including CuO nanoparticles,[15] $BiCl_3$,[16] [DABCO]$(SO_3H)_2Cl_2$,[17] $Ce_1Mg_xZr_{1-x}O_2$,[18] ZnO,[19] $CoFe_2O_4$,[20] $SiO_2 \cdot 12WO_3 \cdot 24H_2O$,[21] NH_2SO_3H[22] and $K_2NiP_2O_7$.[23]

The various biological properties of pyrano[2,3-*d*] pyrimidine derivatives[24–26] cause wide interest in the preparation of these compounds. For this reason a variety of methods using various catalysts such as Zn[(L)proline]$_2$,[27] DAHP,[28] SBA-Pr-SO_3H,[29] L-proline,[30] [BMIm]BF_4,[31] *N*-methylmorpholine,[32] 1,4-dioxane,[33]

$H_{14}[NaP_5W_{30}O_{110}]$[34] and $[KAl(SO_4)_2]$[35] have been reported for this purpose.

Although the methods mentioned above were accompanied by some improvements, most of them suffer from disadvantages such as harsh reaction conditions, use of harmful organic solvents, long reaction times, tedious work-up procedure, use of expensive and moisture-sensitive reagents, strongly acidic conditions, unsatisfactory yields, non-recoverability of the catalyst and environmental pollution. Thus, it is important to find more efficient catalysts and methods for the synthesis of arylidine barbituric acids and pyrano[2,3-*d*] pyrimidine derivatives.

2 | EXPERIMENTAL

2.1 | Chemicals

All chemicals, including iron (II) chloride tetrahydrate (99%), iron (III) chloride hexahydrate (98%) and aldehyde derivatives, were purchased from Merck or Fluka and were used without further purification. Water and other solvents were distilled before use. Yields refer to isolated products. The products were characterized by their physical constants, comparison with authentic samples and using FT-IR, ^{1}H NMR and ^{13}C NMR spectroscopies. Determination of the purity of the substrates and reaction monitoring were accomplished using TLC with silica-gel Polygram SILG/UV 254 plates. The FT-IR spectra were obtained with a VERTEX 70 (Bruker, Germany). Thermogravimetric analysis (TGA) was performed with a TG/DTA6300 (All-Nanotechnology Company, Japan). Samples were heated from 25 to 700 °C at 10 °C min^{-1} under nitrogen atmosphere. Scanning election microscopy (SEM) was conducted with a Philips XL30. Wide-angle X-ray diffraction (XRD) measurements were performed at room temperature with a Siemens D-500 X-ray diffractometer (Germany), using Ni-filtered Co-Kα radiation (λ = 0.15418 nm). The surface morphologies were characterized using atomic force microscopy (Ara Nanoscope, Iran).

2.2 | Catalyst Preparation

Firstly, Fe_3O_4 MNPs approximately 9–11 nm in size were synthesized using a reported chemical co-precipitation technique.[36]

Subsequently, the prepared Fe_3O_4 MNPs (4 g) were dispersed in a mixture of deionized water (48 ml) and ethanol (180 ml) by ultrasonication for 30 min. Then, ammonia (4.0 ml, 25%) and TEOS (2.4 ml) were charged to the reaction dish. After stirring at room temperature for 12 h, the silica-coated nanoparticles (Fe_3O_4@SiO_2-MNPs) were collected using a permanent magnet followed by washing three times with ethanol and diethyl ether and dried at 40 °C in vacuum for 24 h.

The sulfonation of the MNPs was conducted using the reaction of Fe_3O_4@SiO_2-MNPs with 1,4-butanesultone. For this purpose, Fe_3O_4@SiO_2-MNPs (4 g) were suspended in 100 ml of dry toluene containing 1,4-butanesultone (2.4 ml), and the colloidal solution was refluxed for 48 h to yield a magnetically separable reagent, namely butane-1-sulfonic acid immobilized on Fe_3O_4@SiO_2-MNPs (Fe_3O_4@SiO_2-Sultone), which was isolated and purified as described for Fe_3O_4@SiO_2-MNPs (Scheme 1).

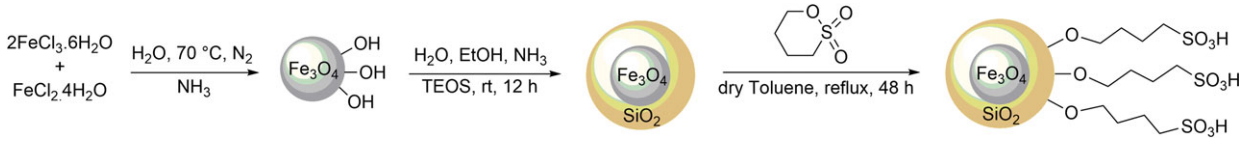
2.3 | Catalytic Activity

2.3.1 | General procedure for preparation of 5-arylidine barbituric acids

Aldehyde (1.0 mmol), barbituric acid (1.0 mmol) and Fe_3O_4@SiO_2-Sultone (25 mg) were added to a 25 ml round-bottomed flask in water and the resulting mixture was stirred at room temperature for the appropriate time. After completion of the reaction (monitored by TLC: *n*-hexane–ethyl acetate, 7:3), water was evaporated and the product dissolved in warm ethanol (5 ml). The catalyst was then separated using an external magnet. The solvent (ethanol) was evaporated to afford the pure product. If needed, for further purification, the product can be recrystallized from ethanol.

2.3.2 | General procedure for preparation of pyrano[2,3-*d*] pyrimidine derivatives

A mixture of aromatic aldehyde (1.0 mmol), barbituric acid (1.0 mmol), malononitrile (1.0 mmol) and Fe_3O_4@SiO_2-Sultone (25 mg) in water was stirred at 60 °C for the appropriate time. After completion of the reaction, water was evaporated, ethanol (5 ml) was added and the mixture was warmed to dissolve the product.



SCHEME 1 Preparation of Fe_3O_4@SiO_2-Sultone

Then the catalyst was separated using an external magnet. The solvent (ethanol) was evaporated to afford the pure product. If needed, for further purification, the product can be recrystallized from ethanol.

2.4 | Spectroscopic Data

2.4.1 | 5(4-Cl-Benzylidene) barbituric acid (4b)

FT-IR (KBr, ν_{max}, cm^{-1}): 3404, 3214, 2970, 1755, 1703, 1570. ^1H NMR (DMSO, δ, ppm): 7.53 (d, 2H, Ar— H), 8.08 (2d, 2H, Ar— H), 8.25 (s, 1H, HC= C), 11.25 (s, H, NH), 11.40 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ, ppm): 117.46, 127.76, 128.29, 133.25, 133.50, 148.70, 150.16, 165.10. EI-MS: m/z (%) 250 (M^+).

2.4.2 | 5(2-Cl-Benzylidene) barbituric acid (4c)

FT-IR (KBr, ν_{max}, cm^{-1}): 3460, 3120, 2981, 1754, 1569, 1454, 1079, 910, 782. ^{1}HNMR ($CDCl_3$, δ, ppm): 7.36 (t, 1H, H— Ar), 7.47 (t, 1H, H— Ar), 7.53 (d, 1H, H— Ar), 7.73 (d, 1H, Ar— H), 8.29 (s, 1H, HC= C), 11.25 (s, 1H, NH), 11.47 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ, ppm): 121.76, 126.29, 128.29, 131.88, 132.25, 133.15, 146.70, 150.16, 160.85, 162.60. EI-MS: m/z (%) 250 (M^+).

2.4.3 | 5(4-OH-Benzylidene) barbituric acid (4 h)

FT-IR (KBr, ν_{max}, cm^{-1}): 3420, 3214, 2970, 1755, 1703, 1570. ^1H NMR (DMSO, δ, ppm): 6.86 (d, 2H, Ar— H), 8.32 (2d, 2H, Ar— H), 8.24 (s, 1H, HC= C), 10.68 (S, 1H, OH), 11.13 (s, H, NH), 11.25 (S, 1H, NH). ^{13}C NMR ($CDCl_3$, δ, ppm): 115.60, 118.76, 128.70, 148.80, 150.20, 157.65, 165.10. EI-MS: m/z (%) 232 (M^+).

2.4.4 | 7-Amino-5-(4-methoxyphenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*] pyrimidine-6-carbonitrile (5i)

FT-IR (KBr, ν_{max}, cm^{-1}): 3317, 3282, 3145, 3063, 2215, 1743, 1668. ^1H NMR (DMSO, δ, ppm): 10.98 (s, 1H, NH), 10.80 (s, 1H, NH), 7.14 (d, J = 7.5 Hz, 2H, Ar= H), 6.86–6.82 (m, 4H, Ar= H and NH_2), 4.16 (s, 1H, CH), 3.81 (s, 3H, OCH_3). ^{13}C NMR (DMSO, δ, ppm): 161.99, 159.11, 155.61, 151.97, 151.36, 130.34, 129.50, 123.56, 113.14, 93.41, 58.66, 57.46, 53.46. MS (m/z) (%): 313.01 (M^+).

2.4.5 | Ethyl-7-amino-5-(4-chlorophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]pyrimidine-6-carboxylate (5n)

FT-IR (KBr, ν_{max}, cm^{-1}): 3311, 3188, 3091, 2228, 1899, 1648, 1543. ^1H NMR (400 MHz, DMSO, δ, ppm): 2.17 (3H, s, CH_3), 4.8 (2H, s, CH_2), 5.28 (s, 1H, H-5) 4.11 (2H, s, CH_2), 2.29 (3H, s, CH_3), 7.28 (m, H— Ar), 7.38 (m, 2H, H— Ar), 7.75 (s, 2H, NH_2), 10.99 (s, 1H, NH), 11.55 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ, ppm): 88.3, 98.5, 114.8, 126.9, 128.8, 129.0, 129.9, 130.5, 135.9, 150.1, 155.4, 155.8, 159.7, 160.9. MS: (M+) m/z, 313, 278, 188, 153, 111, 77, 57, 43.

2.4.6 | Ethyl-7-amino-5-(4-methoxyphenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]pyrimidine-6-carboxylate (5p)

FT-IR (KBr, ν_{max}, cm^{-1}): 3413, 3278, 2239, 2165, 1878, 1662, 1543. ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.32 (s, 3H, OCH_3), 4.41 (1H, s, H-5), 3.71 (s, 2H, CH_2), 2.49 (s, 3H, CH_3) 6.93 (m, 2H, H— Ar), 7.65 (m, 2H, H— Ar), 9.07 (2H, br, s, NH_2), 11.09–10.03 (s, br, 2H, NH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 33.03, 37.2, 55.8, 75.6, 114.2, 130.1, 134.1, 143.9, 150.5, 157.2, 162.4, 167.3. EI-MS: (m/z) = 89 (M+), 269, 232, 221, 201, 176, 149, 110.

3 | RESULTS AND DISCUSSION

In recent years, the introduction of new catalysts for the promotion of organic reactions has become an important part of our ongoing research programme.[37–39] Based on the above mentioned difficulties in the preparation of 5-arylidine barbituric acids and pyrano[2,3-*d*] pyrimidine derivatives and in continuation of our ongoing research programme on the introduction of new nanocatalysts for the promotion of organic reactions, we were interested in preparing, characterizing and studying the applicability of Fe_3O_4@SiO_2-Sultone in the synthesis of these compounds. After preparation of the reagent as described in Section 2, it was characterized using various methods, and the obtained results are summarized in the following sections.

3.1 | Characterization of Fe_3O_4@SiO_2-Sultone

3.1.1 | FT-IR analysis

FT-IR spectra of Fe_3O_4, Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2-Sultone are compared in Figure 1. These spectra showed

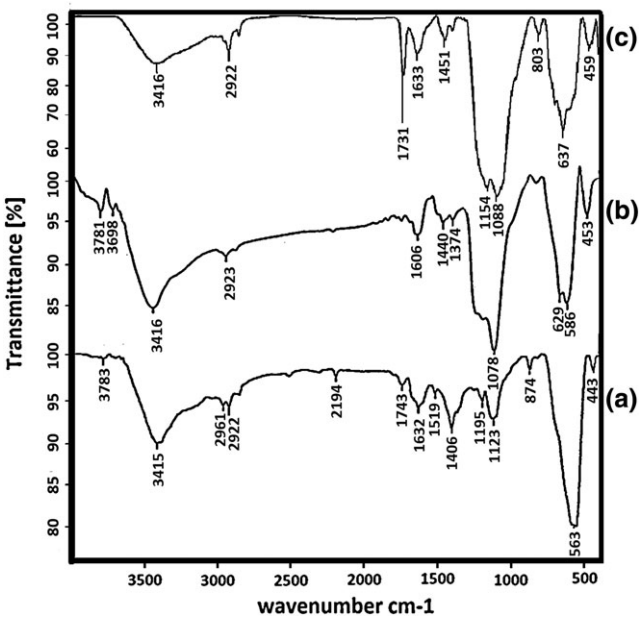


FIGURE 1 FT-IR spectra of (a) Fe_3O_4, (b) Fe_3O_4@SiO_2 and (c) Fe_3O_4@SiO_2-Sultone

broad bands at around 550–650 cm^{-1}, which were attributed to Fe— O vibrations.[40] In the spectra of Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2-Sultone, the strong bands observed at 1078 and 1088 cm^{-1} can be due to the Si— O— Si stretching modes of the silica shell. The peak at 1154 cm^{-1} is related to the stretching of S═ O bonds. The S— O stretching modes of sulfunic acid functional group lies at around 637 cm^{-1} proving the probable preparation of the catalyst.

3.1.2 | Powder XRD analysis

Figure 2 shows the XRD pattern of Fe_3O_4@SiO_2-Sultone. Diffraction peaks at 2θ= 30.4°, 35.8°, 43.3°, 54.0°, 57.6° and 63.2° corresponding to (2 2 0), (3 1 1), (4 0 0), (4 2 2), (5 1 1) and (4 4 0) are readily recognized in the XRD pattern. The observed diffraction peaks match with those of the standard Fe_3O_4 sample (JCPDS file no. 19–0629). The average crystallite size was calculated to be 10.7 nm using the Scherrer equation.

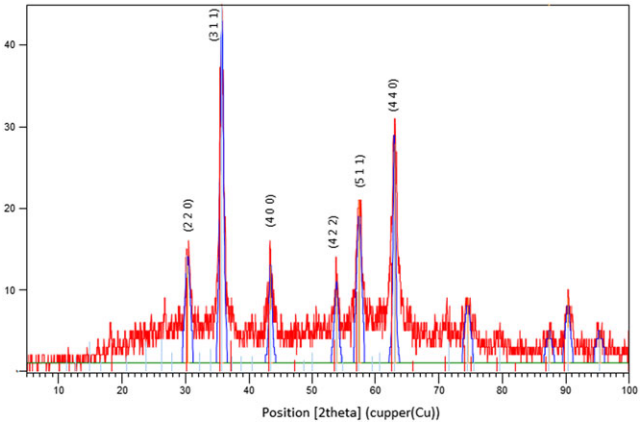


FIGURE 2 XRD pattern of Fe_3O_4@SiO_2-Sultone

3.1.3 | Thermal analysis

The thermal stability of Fe_3O_4@SiO_2-Sultone was determined using TGA (Figure 3). The weight loss of about 0.89% at a temperature below 130 °C can be related to desorption of water molecules from the catalyst surface. Also, another weight loss of 0.72% appears at around 240 °C due to decomposition of sulfuric acid and formation of sulfur dioxide. The complete loss of covalently attached organic moiety was observed in the range 420–600 °C. The amount of organic moiety was found to be about 12.12% against total solid catalyst.

3.1.4 | SEM analysis

Samples of Fe_3O_4 and Fe_3O_4@SiO_2-Sultone were also analysed using SEM for determining the size distribution, particle shape and surface morphology, as illustrated in Figure 4. The SEM images of Fe_3O_4 and Fe_3O_4@SiO_2-Sultone samples show that Fe_3O_4 has an amorphous morphology with particles of *ca* 10 nm in size and the synthesized Fe_3O_4@SiO_2-Sultone has nanometric dimensions ranging from *ca* 50 to 60 nm. It was also observed that all the supported particles have highly porous surfaces suitable for harbouring and shielding catalytic species and these particles are roughly globular in shape.

3.1.5 | Transmission electron microscopy analysis

Also, a study of the same region of Fe_3O_4@SiO_2-Sultone using transmission electron microscopy (TEM) confirmed that the magnetite particles were evenly distributed within this composite material (Figure 5). To our delight, TEM analysis of Fe_3O_4@SiO_2-Sultone showed a well-dispersed pattern of nanoparticles in a narrow size range of 50–60 nm.

3.1.6 | Energy-dispersive X-ray analysis

The energy-dispersive X-ray (EDX) spectrum of Fe_3O_4@SiO_2-Sultone is shown in Figure 6. This clearly shows the presence of Fe, N, O, C, Si and S in Fe_3O_4@SiO_2-Sultone.

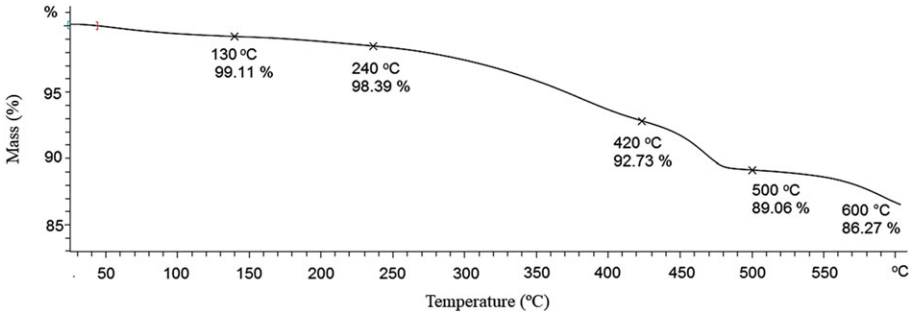


FIGURE 3 TGA curve of Fe_3O_4@SiO_2-Sultone

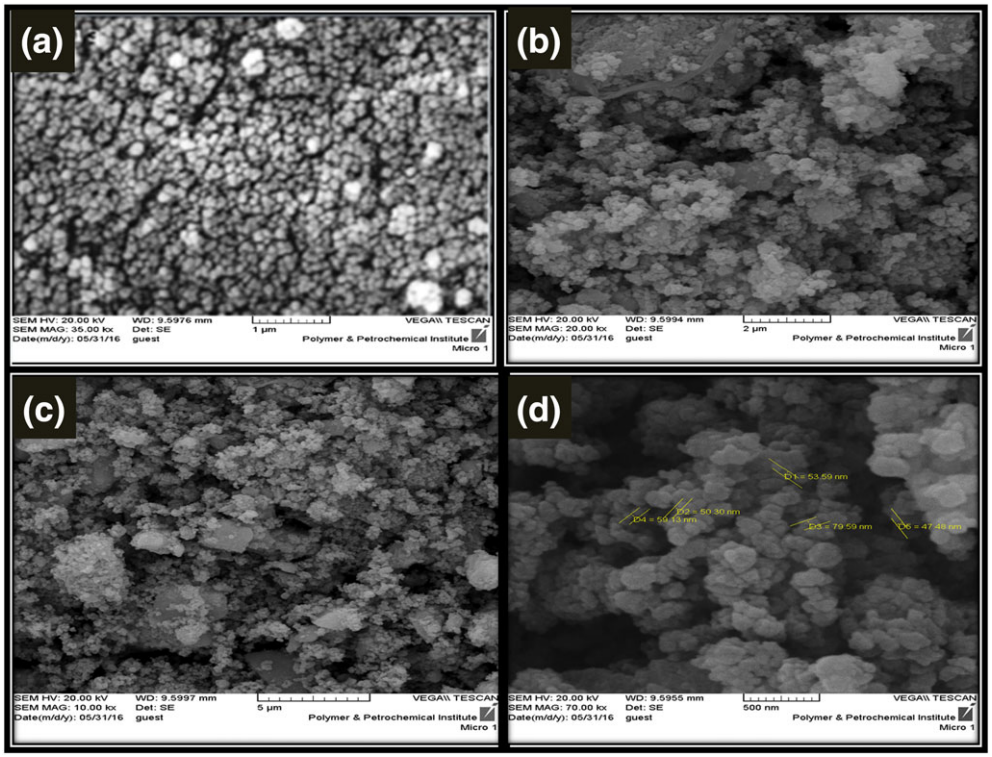


FIGURE 4 SEM images od (a) Fe_3O_4 and (b–d) Fe_3O_4@SiO_2-Sultone

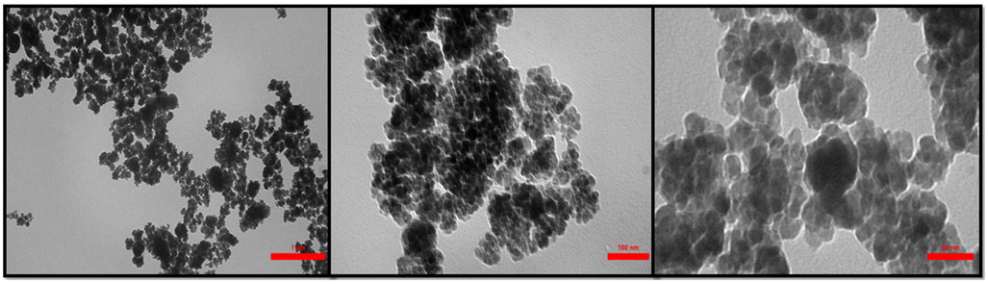


FIGURE 5 TEM images Fe_3O_4@SiO_2-Sultone

3.2 | Application of Fe_3O_4@SiO_2-Sultone

The results obtained from the structural studies directed us to accept that the prepared reagent can be formulated as Fe_3O_4@SiO_2-Sultone. On the basis of this structure, it is anticipated that this reagent may be able to catalyse the reactions which need acidic catalysts to increase their rate. In order to establish this suggestion, the catalytic effect of this reagent in the synthesis of 5-arylidine barbituric acids and pyrano[2,3-*d*]

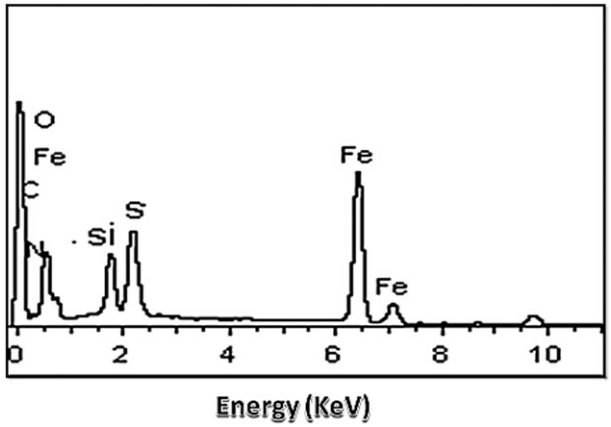


FIGURE 6 EDX spectrum of Fe_3O_4@SiO_2-Sultone

pyrimidine derivatives, as two model reactions, was studied.

First of all and in order to optimize the reaction conditions and the amounts of the catalyst, the reaction between 4-chlorobenzaldehyde and barbituric acid was studied in the presence of Fe_3O_4@SiO_2-Sultone. For choosing the reaction media, various solvents such as H_2O, EtOH, CH_2Cl_2 and CH_3CN and also solvent-free conditions were used and the best results were obtained in aqueous media. Moreover, the effects of the amount of the catalyst and temperature were examined in the model reaction (Table 1). Finally the best result was obtained using 25 mg of Fe_3O_4@SiO_2-Sultone at room temperature in water (Scheme 2).

After optimization of the reaction conditions, we scrutinized the efficiency of Fe_3O_4@SiO_2-Sultone in the preparation of 5-arylidine barbituric acid derivatives using various types of aldehydes containing electron-withdrawing as well as electron-donating groups. All the selected aldehydes gave the desired products in good to excellent yields during short reaction times (Table 2).

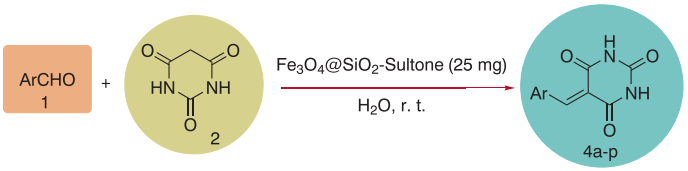
The proposed mechanism for the synthesis of 5-arylidine barbituric acid derivatives in the presence of the prepared catalyst is shown in Scheme 3. According to this mechanism and in the first step, the aldehyde is activated by a proton from Fe_3O_4@SiO_2-Sultone. Then, the carbonyl carbon is attacked by the nucleophilic compound to produce the Knoevenagel products.

Recyclability is an important factor for judging the sustainability of any catalyst. In this study, the recyclability of the catalyst was examined in the synthesis of 5-arylidine barbituric acid derivative obtained from the reaction of 4-chlorobenzaldehyde with barbituric acid under the optimized reaction conditions. When the reaction was completed, the catalyst was easily recovered by magnetic decantation. The recovered catalyst was washed with ethanol and diethyl ether (Figure 7), dried and reused over eight runs for the same reaction. Each time

TABLE 1 Optimization of reaction conditions for synthesis of 5-arylidene barbituric acid derivative of 4-chlorobenzaldehyde and barbituric acid catalysed by Fe_3O_4@SiO_2-Sultone[a]

Entry	Catalyst (mg)	Solvent	Temp. (°C)	Time (min)	Conversion (%)
1	20	EtOH	r.t.	60	20
2	25	EtOH	r.t.	60	20
3	35	EtOH	r.t.	60	20
4	25	—	Reflux	60	50
5	25	—	r.t.	60	10
6	25	—	60	60	20
7	25	H_2O	60	4	100
8	20	H_2O	r.t.	8	100
9	25	H_2O	r.t.	4	100
10	35	H_2O	r.t.	4	100

[a]Reaction conditions: 4-chlorobenzaldehyde (1 mmol), barbituric acid (1 mmol) and Fe_3O_4@SiO_2-Sultone.



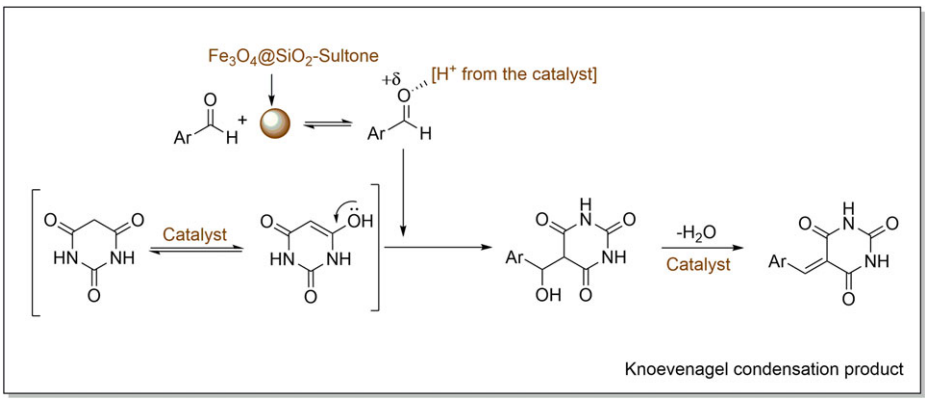
SCHEME 2 Synthesis of 5-arylidine barbituric acid derivatives catalysed by Fe_3O_4@SiO_2-Sultone

TABLE 2 Preparation of 5-arylidine barbituric acid derivatives catalysed by Fe_3O_4@SiO_2-Sultone[a]

Entry	ArCHO	Product	Time (min)	Yield (%)[b]	M.p. (°C)	
					Found	Reported
1	C_6H_4CHO	4a	5	98	257–259	255–256[17]
2	4-ClC_6H_4CHO	4b	4	98	295–297	298–300[22]
3	2-ClC_6H_4CHO	4c	5	95	265–266	268[41]
4	4-BrC_6H_4CHO	4d	6	92	292–293	288–290[15]
5	4-$NO_2C_6H_4CHO$	4e	5	93	269–272	268–270[15]
6	3-$NO_2C_6H_4CHO$	4f	8	92	239–240	242–243[42]
7	2-$NO_2C_6H_4CHO$	4 g	8	90	275–277	274–276[17]
8	4-OHC_6H_4CHO	4 h	10	94	>300	>300[42]
9	2-OHC_6H_4CHO	4i	12	90	246–248	249–250[17]
10	C_6H_5CH═ CHCHO	4j	7	95	267–269	266–268[43]
11	4-$MeOC_6H_4CHO$	4 k	5	95	295–297	296–298[15]
12	4-$CH_3C_6H_4CHO$	4 l	12	90	276–277	275–277[17]
13	3-$CH_3C_6H_4CHO$	4 m	8	95	208–209	210–214[17]
14	4-$CHOC_6H_4CHO$	4n	10	98	>300	>300[18]
15	3-$CHOC_6H_4CHO$	4o	10	98	>300	>300[18]
16	2-Naphthaldehyde	4p	6	95	263–264	266 (dec.)[44]

[a]Reaction conditions: benzaldehyde (1 mmol), barbituric acid (1 mmol) and Fe_3O_4@SiO_2-Sultone (25 mg); in H_2O at room temperature.

[b]Isolated yields.



SCHEME 3 Proposed mechanism for synthesis of 5-arylidene barbituric acid using Fe_3O_4@SiO_2-Sultone

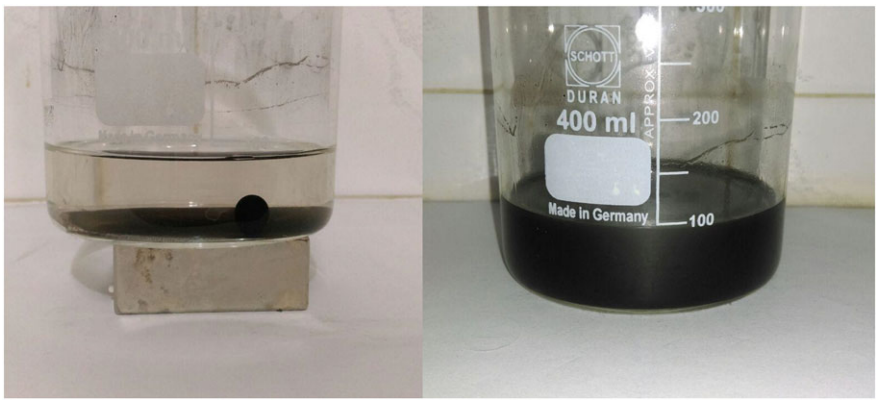


FIGURE 7 Separation of Fe_3O_4@SiO_2-Sultone in water using an external magnetic field

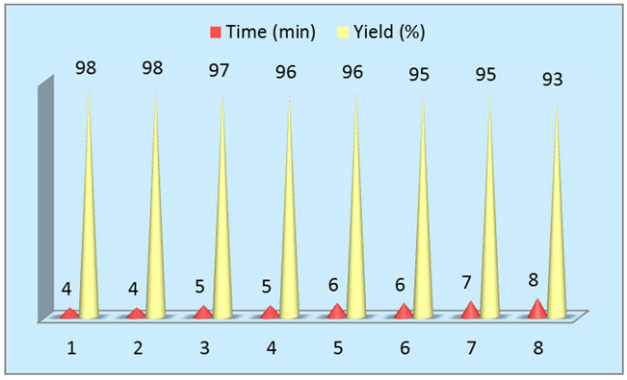


FIGURE 8 Reusability of Fe_3O_4@SiO_2-Sultone in the reaction of 4-chlorobenzaldehyde with barbituric acid

the product was obtained with the least change in the reaction time and yield (Figure 8).

5-Arylidene barbituric acid derivatives have previously been synthesized using various methods, but these methods either gave low yields or involved complex reaction conditions (Table 3). It is clear that the present method is superior in terms of reaction time and amount of catalyst.

After the successful application of Fe_3O_4@SiO_2-Sultone in the preparation of 5-arylidene barbituric acid derivatives from aldehydes and barbituric acid, we decided to prepare pyrano[2,3-*d*] pyrimidine derivatives in the presence of this reagent. The optimization studies

TABLE 3 Comparative performance of previously reported catalysts and Fe_3O_4@SiO_2-Sultone in the synthesis of 5-(4-chlorobenzylidene) pyrimidine-2,4,6(1*H*,3*H*,5*H*)trione

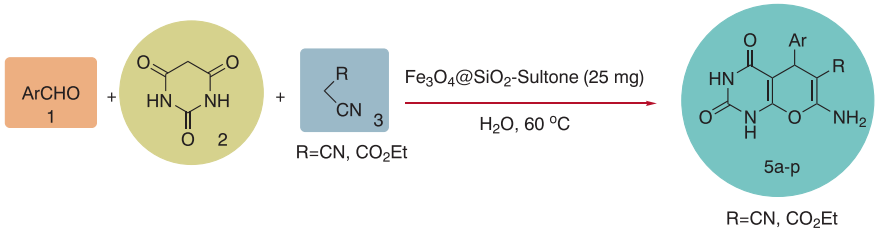
Entry	Catalyst/conditions	Time (min)	Yield(%)[a]	TOF (h^{-1})	Ref.
1	SiO_2.12WO_3.24H_2O/H_2O, r.t.	40	96	8000	[21]
2	1-*n*-Butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4)/grinding, r.t.	120	77.9	10.82	[42]
3	Aminosulfonic acid/grinding	180	96	77.5	[22]
4	$CoFe_2O_4$/water–ethanol/r.t.	2	91	15.16	[20]
5	PVP-Ni nanoparticles/ethylene glycol, 50 °C	5	93	6.88	[44]
6	CTAMB/H_2O, r.t.	30	82	91.11	[45]
7	[DABCO]$(SO_3H)_2Cl_2$/H_2O, 70 °C	5	94	15166	[17]
8	Fe_3O_4@SiO_2-Sultone/H_2O, r.t.	4	98	50	This work

[a]Isolated yields.

TABLE 4 Optimization of reaction conditions for synthesis of pyrano[2,3-*d*] pyrimidine derivatives catalysed by Fe_3O_4@SiO_2-Sultone[a]

Entry	Catalyst (mg)	Solvent	Temp. (°C)	Time (min)	Conversion (%)
1	15	H_2O	60	20	95
2	25	H_2O	60	12	100
3	35	H_2O	60	12	100
4	25	H_2O	r.t.	40	95
5	25	EtOH	60	60	50
6	25	CH_2Cl_2	60	120	20
7	25	CH_3CN	60	120	20
8	25	—	r.t.	60	20
9	25	—	100	60	40
10	25	H_2O/EtOH	60	20	100

[a]Reaction conditions: 4-chlorobenzaldehyde (1 mmol), barbituric acid (1 mmol), malononitrile (1 mmol) and Fe_3O_4@SiO_2-Sultone.



SCHEME 4 Synthesis of pyrano[2,3-*d*] pyrimidine derivatives catalysed by Fe_3O_4@SiO_2-Sultone

(Table 4) showed that the suitable conditions for the synthesis of pyrano[2,3-d] pyrimidines in the presence of Fe_3O_4@SiO_2-Sultone were as shown in Scheme 4.

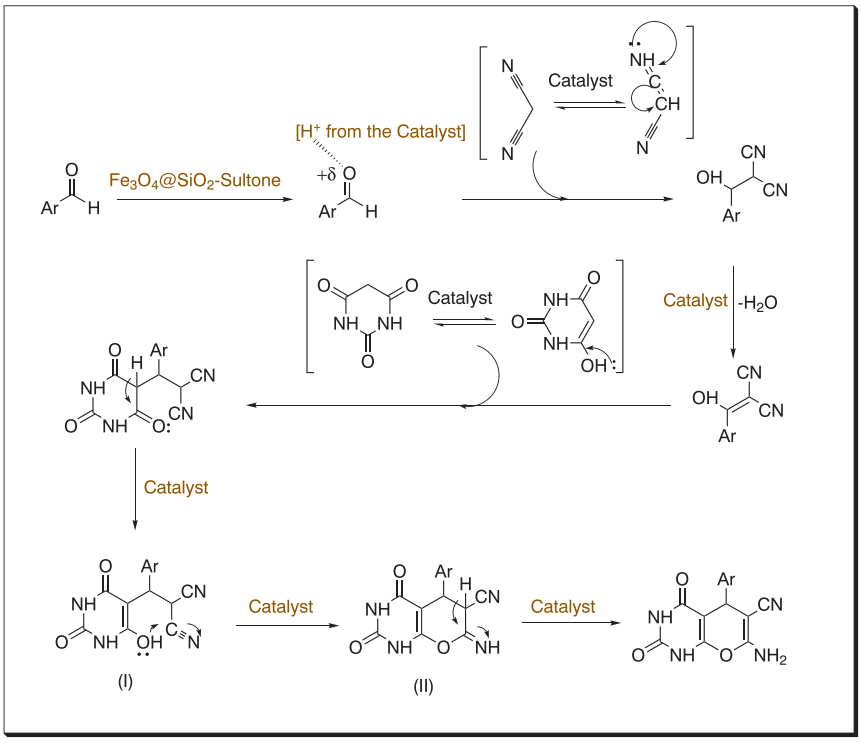
After optimization of the reaction conditions, various types of aromatic aldehydes were used in the same reaction under the determined conditions and the results

TABLE 5 Preparation of pyrano[2,3-*d*] pyrimidine derivatives catalysed by Fe_3O_4@SiO_2-Sultone[a]

Entry	ArCHO	R	Product	Time (min)	Yield (%)[b]	M.p. (°C)	
						Found	Reported
1	C_6H_4CHO	CN	5a	10	98	222–223	224–225[17]
2	4-ClC_6H_4CHO	CN	5b	12	97	295–297	298–300[46]
3	2-ClC_6H_4CHO	CN	5c	15	95	210–212	213–215[17]
4	4-BrC_6H_4CHO	CN	5d	20	92	237–239	235–236[29]
5	4-$NO_2C_6H_4CHO$	CN	5e	15	98	238–239	236–237[17]
6	3-$NO_2C_6H_4CHO$	CN	5f	17	95	262–264	266–268[17]
7	2-$NO_2C_6H_4CHO$	CN	5 g	25	90	253–255	254–256[17]
8	4-OHC_6H_4CHO	CN	5 h	20	95	>300	>300[46]
9	4-$MeOC_6H_4CHO$	CN	5i	12	97	277–278	280–284[29]
10	3-$MeOC_6H_4CHO$	CN	5j	10	95	207–209	200–206[29]
11	4-$CHOC_6H_4CHO$	CN	5 k	35	98	>320	>320[17]
12	4-$CH_3C_6H_4CHO$	CN	5 l	15	95	221–223	225[27]
13	C_6H_4CHO	CO_2Et	5 m	35	95	207–210	206–210[47]
14	4-ClC_6H_4CHO	CO_2Et	5n	30	95	>300	>300[48]
15	4-$NO_2C_6H_4CHO$	CO_2Et	5o	25	90	295–297	289–293[47]
16	4-$MeOC_6H_4CHO$	CO_2Et	5p	40	90	293–295	297–298[48]
17	4-MeC_6H_4CHO	CO_2Et	5q	50	87	220–222	225[27]

[a]Reaction conditions: benzaldehyde (1 mmol), barbituric acid (1 mmol), malononitrile (1 mmol) and Fe_3O_4@SiO_2-Sultone (25 mg); in H_2O at 60 °C.

[b]Isolated yields.



SCHEME 5 Proposed mechanism for synthesis of pyrano[2,3-*d*] pyrimidine derivatives using Fe_3O_4@SiO_2-Sultone

TABLE 6 Comparison of performance of previously reported catalysts with that of Fe_3O_4@SiO_2-Sultone in synthesis of 7-amino-6-cyano-5-(4-nitrophenyl)-5*H*-pyrano[2,3-*d*]pyrimidine

Entry	Catalyst/conditions	Time (min)	Yield(%)[a]	TOF (h^{-1})	Ref.
1	KAl $(SO_4)_2.12H_2O/H_2O$, 80 °C	45	92	0.34	[35]
2	Diammonium hydrogen phosphate/(H_2O, EtOH), r.t.	120	72	0.1	[28]
3	DABCO/(H_2O, EtOH), r.t.	120	92	0.13	[49]
4	Al-HMS-20/EtOH, r.t.	720	95	—	[46]
5	L-Proline/(H_2O, EtOH), r.t.	45	73	0.54	[30]
6	Tetrabutylammonium bromide (TBAB)/H_2O, reflux	35	80	0.38	[50]
7	[DABCO]$(SO_3H)_2Cl_2/H_2O$, reflux	25	83	1106	[17]
8	Fe_3O_4@SiO_2-Sultone/H_2O, 60 °C	15	98	13.3	This work

[a]Isolated yields.

are summarized in Table 5. Using this method, all reactions were performed under mild and completely heterogeneous reaction conditions with high yields and in short reaction times.

The proposed mechanism for the synthesis of pyrano[2,3-*d*] pyrimidine derivatives in the presence of the catalyst is shown in Scheme 5. According to this mechanism, the aldehyde is activated by a proton from Fe_3O_4@SiO_2-Sultone. Then, the carbonyl carbon is attacked by the nucleophilic compound to produce the Knoevenagel products. In continuation, a Michael addition occurs. The Michael adduct tautomerizes in the presence of acidic catalyst to generate intermediate I. This intermediate cyclizes to give the related intermediate II, which tautomerizes to produce the fully aromatized compound.

To investigate the reusability of the catalyst, the reaction of 4-chlorobenzaldehyde, barbituric acid and malononitrile under the optimized reaction conditions was studied. After the separation of the catalyst using an external magnet, the catalyst was washed with ethanol and diethyl ether, dried and reused for the same reaction. This process was carried out over seven runs and each time the product was obtained in high yields during short reaction times.

Table 6 presents a comparison of our results with those reported using other catalysts in the synthesis of pyrano[2,3-*d*] pyrimidine derivatives. This comparison indicates that in most cases, the reaction time is too long in the presence of the other nanocatalysts.

4 | CONCLUSIONS

We have introduced a novel and heterogeneous catalyst formulated as Fe_3O_4@SiO_2-Sultone as a highly powerful nanomagnetic catalyst for the synthesis of 5-arylidine barbituric acids and pyrano[2,3-*d*] pyrimidine derivatives in aqueous media. The procedure gave the products in excellent yields in very short reaction times. The most important advantages of the method include the simplicity in the preparation procedure, easy work-up, high reaction rates, excellent yields, recyclability of the catalysts using an external magnet and eco-friendly procedure. Further work to utilize this catalyst in other organic syntheses and transformations is in progress.

ACKNOWLEDGEMENTS

The authors are grateful to the Guilan and Zanjan Universities Research Councils for the partial support of this work.

ORCID

F. Shirini http://orcid.org/0000-0002-0768-3241

REFERENCES

[1] F. Kabiri Esfahani, D. Zareyee, R. Yousefi, *ChemCatChem* **2014**, *6*, 3333.

[2] F. Nemati, M. M. Heravi, R. Saeedi Rad, *Chin. J. Catal.* **2012**, *33*, 1825.

[3] M. Haghighat, F. Shirini, M. Golshekan, *J. Mol. Struc.* **2018**, *1171*, 168.

[4] A. R. Karimi, Z. Eekhari, M. Karimi, Z. Dalirnasab, *Synthesis* **2014**, *46*, 3180.

[5] H. Naeimi, S. Mohamadabadi, *Dalton Trans.* **2014**, *43*, 12967.

[6] L. Ghandi, M. K. Miraki, I. Radfar, E. Yazdani, A. Heydari, *ChemistrySelect* **2018**, *3*, 1787.

[7] M. A. El Aleem, A. A. El-Remaily, H. A. Hamad, *J. Mol. Catal. A* **2015**, *148*, 404.

[8] H. Veisi, P. Mohammadi, J. Gholami, *Appl. Organometal. Chem.* **2014**, *28*, 868.

[9] R. Ghorbani-Vaghei, N. Sarmast, *Appl. Organometal. Chem.* **2018**, *32*, e4003.

[10] H. Veisi, S. Taherib, S. Hemmati, *Green Chem.* **2016**, *18*, 6337.

[11] S. Mirfakhraei, M. Hekmati, F. Hosseini Eshbalab, H. Veisi, *New J. Chem.* **2018**, *42*, 1757.

[12] F. Bonyasi, M. Hekmati, H. Veisi, *J. Colloid Interface Sci.* **2017**, *496*, 177.

[13] J. Mondal, A. Biswas, S. Chiba, Y. Zhao, *Sci. Rep.* **2015**, *5*, 8294.

[14] A. Bamoniri, N. Moshtael-Arani, *RSC Adv.* **2015**, *5*, 16911.

[15] N. R. Dighore, P. L. Anandgaonker, S. T. Gaikwad, A. S. Rajbhoj, *Res. J. Chem. Sci.* **2014**, *4*, 93.

[16] K. M. Khan, M. Ali, T. A. Farooqui, M. Khan, M. Tahan, S. Perveen, *J. Chem. Soc. Pak.* **2009**, *31*, 823.

[17] N. Seyyedi, F. Shirini, M. S. N. Langarudi, *RSC Adv.* **2016**, *6*, 44630.

[18] S. B. Rathod, A. B. Ghamhire, B. R. Arbad, M. K. Lande, *Bull. Korean Chem. Soc.* **2010**, *31*, 339.

[19] M. T. Maghsoodlou, N. Hazeri, S. M. Habibi-Khorassani, Z. Shahkarami, N. Maleki, M. Rostamizadeh, M. Moradian, *Iran. J. Org. Chem.* **2010**, *2*, 391.

[20] J. R. Kaur, G. Kaur, *Chin. J. Catal.* **2013**, *34*, 1697.

[21] J. T. Li, M. X. Sun, *Aust. J. Chem.* **2009**, *62*, 353.

[22] J. T. Li, H. G. Dai, D. Liu, T. S. Li, *Synth. Commun.* **2006**, *36*, 789.

[23] E. A. Maadi, C. L. Matthiesen, P. Ershadi, J. Baker, D. M. Herron, E. M. Holt, *J. Chem. Crystallogr.* **2003**, *33*, 757.

[24] G. L. Anderson, J. L. Shim, A. D. Broom, *J. Org. Chem.* **1976**, *41*, 1095.

[25] D. Heber, C. Heers, U. Ravens, *Pharmazie* **1993**, *48*, 537.

[26] Y. Sakuma, M. Hasegawa, K. Kataoka, K. Hoshina, N. Kadota, *Chem. Abstr.* **1991**, *115*, 71646.

[27] M. M. Heravi, A. Ghods, K. Bakhtiari, F. Derikvand, *Synth. Commun.* **2010**, *40*, 1927.

[28] S. Balalaie, S. Abdolmohammadi, H. R. Bijanzadeh, A. M. Amani, *Mol. Diversity* **2008**, *12*, 85.

[29] G. M. Ziarani, S. Faramarzi, S. Asadi, A. Badiei, R. Bazl, M. Amanlou, *DARU J. Pharm. Sci.* **2013**, *21*, 3.

[30] M. Bararjanian, S. Balalaie, B. Movassagh, A. M. Amani, *J. Iran. Chem. Soc.* **2009**, *6*, 436.

[31] J. Yu, H. Wang, *Synth. Commun.* **2005**, *35*, 3133.

[32] A. A. Shestopalov, L. A. Rodinovskaya, A. M. Shestopalov, V. P. Litvinov, *Russ. Chem. Bull.* **2004**, *53*, 724.

[33] H. H. Zoorob, M. Abdelhamid, M. A. El-Zahab, M. Abdel-Mogib, *Arzneim. Forsch.* **1997**, *47*, 958.

[34] M. M. Heravi, A. Ghods, F. Derikvand, K. Bakhtiari, F. F. Bamoharram, *J. Iran. Chem. Soc.* **2010**, *7*, 615.

[35] A. Mobinikhaledi, N. Foroughifar, M. A. B. Fard, *Synth. React. Inorg. Met.-Org. Nano-Met. Chem* **2010**, *40*, 179.

[36] Z. Cheng, Z. Gao, W. Maa, Q. Sun, B. Wang, X. Wang, *Chem. Eng. J.* **2012**, *209*, 451.

[37] F. Shirini, M. Abedini, M. Seddighi, *J. Nanosci. Nanotechnol.* **2016**, *16*, 8208.

[38] F. Shirini, M. Abedini, S. Zarrabzadeh, M. Seddighi, *J. Iran. Chem. Soc.* **2015**, *12*, 2105.

[39] F. Shirini, M. Pourghasemi Lati, *J. Iran. Chem. Soc.* **2017**, *14*, 75.

[40] S. Sobhani, M. S. Ghasemzadeh, M. Honarmand, *Catal. Lett.* **2014**, *144*, 1515.

[41] S. Kamble, G. Rashinkar, A. Kumbhar, K. Mote, R. Salunkhe, *Arch. Appl. Sci. Res.* **2010**, *2*, 217.

[42] C. Wang, J. J. Ma, X. Zhou, X. H. Zang, Z. Wang, Y. J. Gao, P. L. Cui, *Synth. Commun.* **2005**, *35*, 2759.

[43] J. K. Rajput, J. Kaur, *Chin. J. Catal.* **2013**, *34*, 1697.

[44] J. M. Khurana, K. Vij, *Catal. Lett.* **2010**, *138*, 104.

[45] Z. Ren, W. Cao, W. Tong, X. Jing, *Synth. Commun.* **2002**, *32*, 1947.

[46] B. Sabour, M. H. Peyrovi, M. Hajimohammadi, *Res. Chem. Intermed.* **2015**, *41*, 1343.

[47] A. R. Bhata, A. H. Shallab, R. S. Dongrea, *JTUSCI* **2016**, *10*, 9.

[48] H. R. Safaei, M. Shekouhy, S. Rahmanpur, A. Shirinfeshan, *Green Chem.* **2012**, *14*, 1696.

[49] J. Azizian, A. Shameli, S. Balalaie, M. M. Ghanbari, S. Zomorodbakhsh, M. Entezari, S. Bagheri, G. Fakhrpour, *Orient. J. Chem.* **2012**, *28*, 327.

[50] A. Mobinikhaledi, M. A. Bodaghi-Fard, *Acta Chim. Slov.* **2010**, *57*, 931.

How to cite this article: Pourghasemi-Lati M, Shirini F, Alinia-Asli M, Rezvani MA. Butane-1-sulfonic acid immobilized on magnetic Fe_3O_4@SiO_2 nanoparticles: A novel and heterogeneous catalyst for the one-pot synthesis of barbituric acid and pyrano[2,3-*d*] pyrimidine derivatives in aqueous media. *Appl Organometal Chem*. 2018;e4455. https://doi.org/10.1002/aoc.4455