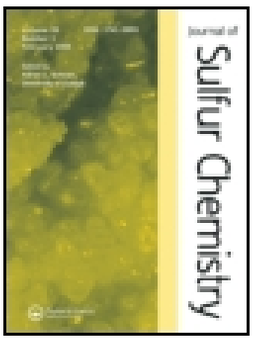

Journal of Sulfur Chemistry

ISSN: 1741-5993 (Print) 1741-6000 (Online) Journal homepage: http://www.tandfonline.com/loi/gsrp20

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To cite this article: Majid Ghashang, Syed Sheik Mansoor, Mohammad Reza Mohammad Shafiee, Mahboubeh Kargar, Mohammad Najafi Biregan, Fateme Azimi & Hadi Taghrir (2016): Green chemistry preparation of MgO nanopowders: efficient catalyst for the synthesis of thiochromeno[4,3-b]pyran and thiopyrano[4,3-b]pyran derivatives, Journal of Sulfur Chemistry, DOI: 10.1080/17415993.2016.1149856

To link to this article: http://dx.doi.org/10.1080/17415993.2016.1149856

Published online: 07 Mar 2016.

JOURNAL OF SULFUR CHEMISTRY, 2016
http://dx.doi.org/10.1080/17415993.2016.1149856

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Green chemistry preparation of MgO nanopowders: efficient catalyst for the synthesis of thiochromeno[4,3-b]pyran and thiopyrano[4,3-b]pyran derivatives

Majid Ghashang[a], Syed Sheik Mansoor[b], Mohammad Reza Mohammad Shafiee[a], Mahboubeh Kargar[a], Mohammad Najafi Biregan[a], Fateme Azimi[a] and Hadi Taghrir[a]

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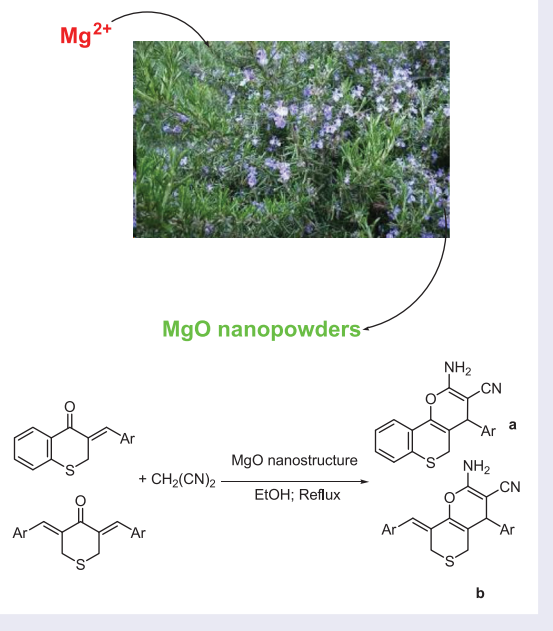
ABSTRACT

A mild and efficient method for the synthesis of thiochromeno[4,3-b]pyran and thiopyrano[4,3-b]pyran derivatives using MgO nanopowders as a catalyst is described. The MgO nanopowders were prepared *via* a green biosynthesis method using an extract of *Rosmarinus officinalis* leaves and were characterized by Field Emission Scanning Electron Microscopy and X-ray diffraction analyses.



ARTICLE HISTORY
Received 13 September 2015
Accepted 30 January 2016

KEYWORDS
Rosmarinus officinalis leaves; MgO nanopowders; 4H-pyran derivatives; thiochromeno[4; 3-b]pyran; thiopyrano[4; 3-b]pyran

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Supplemental data for this article can be accessed here. http://dx.doi.org/10.1080/17415993.2016.1149856

1. Introduction

Heterocyclic systems containing sulfur atoms have found broad application in the development of drugs such as antihyperglycemic,[1] pesticidal,[2] fungicides [3] and other compounds. In particular, sulfur-containing heterocycles such as thiopyrans and thiochromenes are of great interest because of their potent pharmacological and medicinal properties.[4] On the other hand, 4H-pyran fragments are well known for their potential pharmacological activities, such as antimicrobial,[5] antiflammatory,[6] and antiHIV.[7]

Having these results in hand, it occurred to us that incorporation of thiopyran and 4H-pyran moieties into a single molecule may impart drug potential that is absent in the parent substance. The first example of the synthesis of these types of compounds was done by Eiden and Felbermeir in 1984 *via* cycloaddition reactions of 3-benzylidenethiochroman-4-ones with enamines.[8] However, the simplest method for the synthesis of these molecules was introduced by Nakib *et al.* by applying piperidine as catalyst in the reaction of 3-benzylidenethiochroman-4-ones with malononitrile.[9] In the literature, only a few examples of these molecules have been synthesized. It is noticeable that the catalytic reaction of 3-benzylidenechroman-4-one or α,α'-bis (substituted-benzylidene) cycloalkanones with malononitrile is a well-known procedure similarly to the Nakib *et al.* reaction. However, the sulfur analogues of these compounds needed to construct thiochromeno[4,3-b]pyran and thiopyrano[4,3-b]pyran derivatives have not been investigated except for a few examples.[10–14]

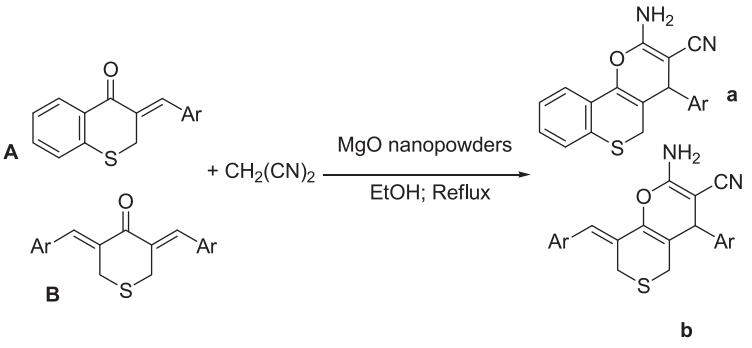
The exploration of these catalytic reactions depends on the preparation of metallic or nano-metallic heterogeneous catalysts. Heterogeneous catalytic reactions have emerged as green and environmentally friendly synthetic tools as they eliminate the need for multi-step purifications. Therefore, the preparation and application of heterogeneous catalyst are critical for the development of green synthesis technologies. In recent years, metal oxide catalysts have attracted increased interest for use in organic reactions since they are non-expensive and can be easily prepared in bulk and nanoscale. Most of them are insoluble in water or common organic solvents. Thus, they are utilized as heterogeneous catalysts in many organic transformations.[15–19] The MgO nanostructure is one of the basic metal oxides that finds excellent applications as an active catalyst for various organic transformations due to its high surface area combined with reactive morphologies.[20] Considering the importance of metal oxides for the preparation of organic compounds, it is surprising that the preparation of thiochromeno[4,3-b]pyran and thiopyrano[4,3-b]pyran derivatives using metal oxides has not yet been established.

In this article, we introduce MgO nanopowders as basic heterogeneous catalysts for the synthesis of thiochromeno[4,3-b]pyran and thiopyrano[4,3-b]pyran derivatives as a green, environmentally friendly catalyst prepared *via* a green biosynthesis method (Scheme 1).

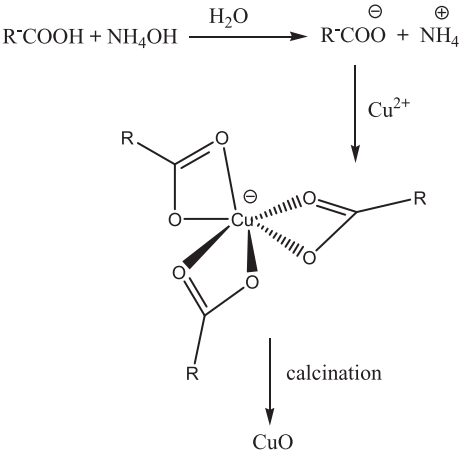
2. Results and discussion

2.1. MgO characterization

MgO nanopowders were synthesized *via* a convenient and green method using an extract of *Rosmarinus officinalis* leaves and $MgCl_2$ as starting materials. *R. officinalis* extract is known to be rich in carboxylic acids such as rosmarinic acid and carnosoic acid.[21] The



Scheme 1. Synthesis of 2-amino-4,5-dihydro-4-arylthiochromeno[4,3-b]pyran-3-carbonitrile and (8Z)-2-amino-8-arylidene-4,5,7,8-tetrahydro-4-arylthiopyrano[4,3-b]pyran-3-carbonitrile derivatives over MgO nanopowders.



Scheme 2. Proposed mechanism for the preparation of MgO nanopowders.

carboxyl group is converted to the carboxylic anion following the addition of ammonia solution. The presence of chelating agents such as carboxylic anions is the main reason for the preparation of MgO nanopowders.

The proposed mechanism for the preparation of MgO nanopowders is shown in Scheme 2.

The successful growth of MgO nanoparticles was first verified by a combination of Field Emission Scanning Electron Microscopy (FE-SEM) and X-ray diffraction (XRD) analysis. The XRD analysis of MgO nanopowders is shown in Figure 1. The XRD pattern indicates that the MgO appears as a single phase with cubic structure. The pronounced diffraction peaks related to the cubic phase of MgO are 43.0, 62.5, 74.9, and 78.9. The average crystal size of the MgO nanopowders was calculated according to the Scherrer equation as 69 nm.

FE-SEM was used to study the morphology of the surface of the MgO nanopowders (Figure 2). It was shown that the particles have a uniform and irregular morphology consisting of homogeneous agglomerated particles with sizes on the nanoscale scale. Figure 3 shows the size distribution of MgO nanopowders determined by statistical design from FE-SEM photographs. The average size of the nanoparticles was about 73 nm.

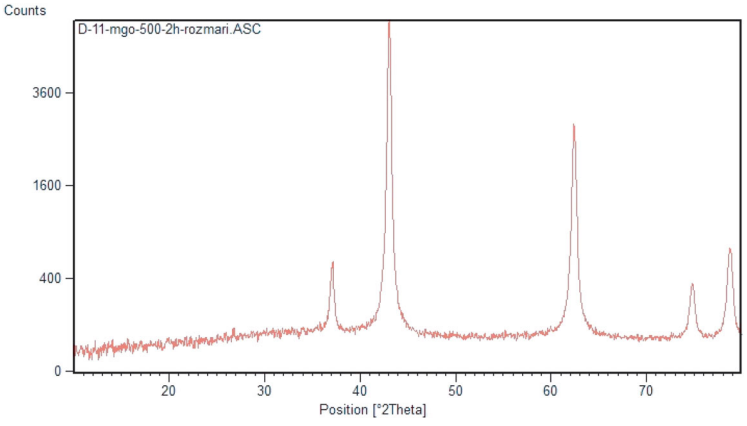


Figure 1. XRD pattern MgO nanopowders.

Table 1. Optimization of reaction conditions.

Entry	Catalyst (mmol)	*T* (°C)	Solvent (5 mL)	Time (h)	Yield (%)[a]
1	0.25	80	Solvent free	24	–
2	0.25	Reflux	*n*-Hexane	24	–
3	0.25	Reflux	CH_3CN	24	15
4	0.25	80	EtOAc	24	10
5	0.25	Reflux	CH_2Cl_2	24	–
6	0.25	80	H_2O	10	30
7	0.25	80	EtOH/H_2O (50%)	10	45
8	0.25	Reflux	EtOH	10	88
9	1	Reflux	EtOH	5	83
10	0.5	Reflux	EtOH	9	85
11	0.1	Reflux	EtOH	15	35
12	0.05	Reflux	EtOH	24	20

[a]Isolated yield (%).

2.2. Catalytic evaluation

Initially, the catalytic preparation of 2-amino-4,5-dihydro-4-arylthiochromeno [4,3-b]pyran-3-carbonitrile over MgO nanopowders was chosen as a model reaction for investigation. A variety of solvents including EtOH, H_2O, CH_2Cl_2, EtOAc, *n*-hexane, and CH_3CN as well as solvent-free conditions were screened and the results are summarized in Table 1. No yield of the product was obtained in nonpolar solvents under solvent-free conditions (Table 1, Entries 1, 2, and 5). However, the product was obtained in low yield in polar aprotic solvents and in aqueous media (Table 1, Entries 3, 4, and 6). Finally, the use of ethanol produced the highest product yield of 88% (Table 1, Entry 8). Changing the amount of catalyst produced no obvious experimental advantage. For example, a further increase in the catalyst loading did not improve the reaction yield (Table 1, Entries 9 and 10).

Using the optimized reaction conditions in hand (Table 1, Entry 8), a variety of 2-amino-4,5-dihydro-4-arylthiochromeno[4,3-b]pyran-3-carbonitrile derivatives (Scheme 1) were synthesized and the results are summarized in Table 2. A variety of 3-benzylidene-2,3-dihydrothiochromen-4-ones with *ortho*, *meta*, and *para* substitutions on the benzene ring

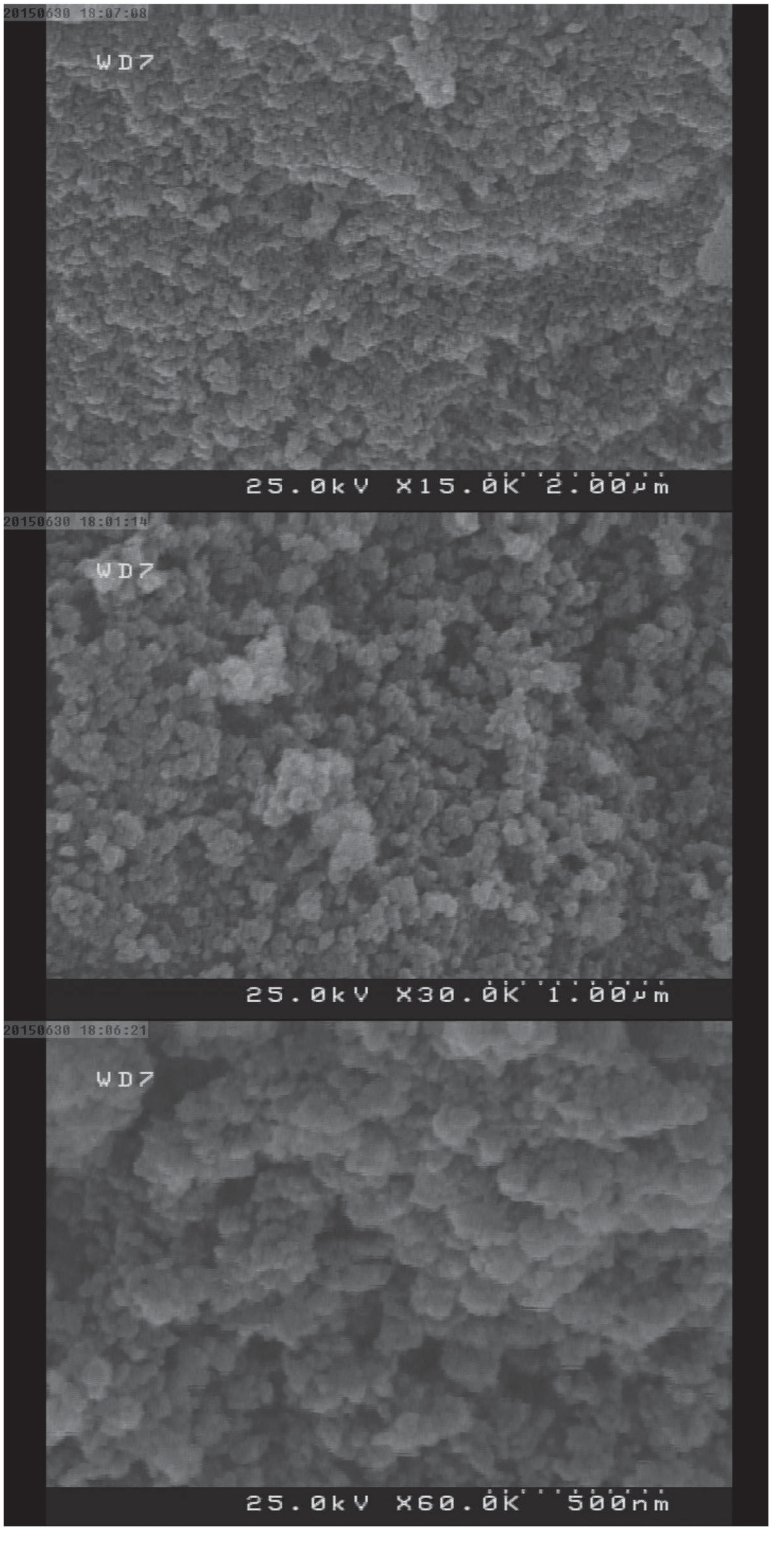


Figure 2. FE-SEM photographs of MgO nanopowders.

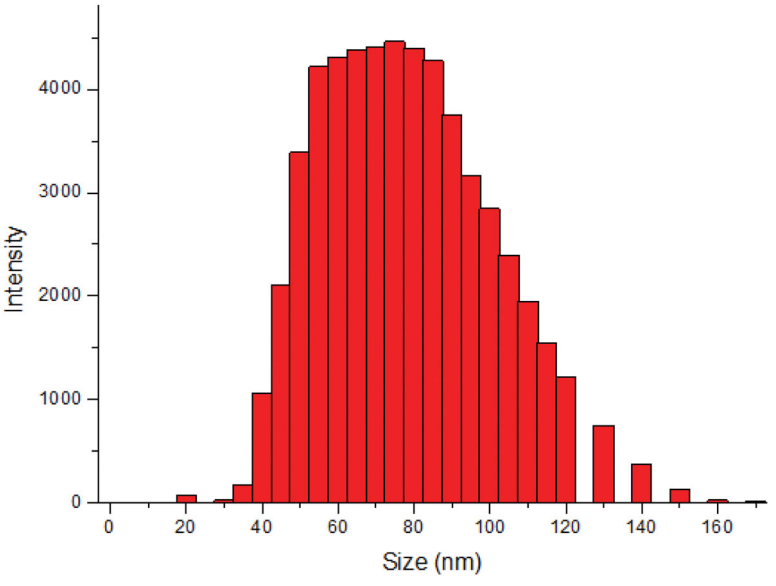


Figure 3. The size distribution of MgO nanopowders.

were examined. Substrates with nitro and halogen substituents tolerated the reaction conditions very well and gave excellent yields in shorter reaction times than those with methyl and methoxy groups (Table 2).

As a continuation of this study, the synthesis of (8Z)-2-amino-8-arylidene-4,5,7,8-tetrahydro-4-arylthiopyrano[4,3-b]pyran-3-carbonitrile derivatives over MgO nanopowders was also examined. The results showed good reactivity and provided the products in high yields (Table 2, Entries 11–15).

Based on the results and the reported literature,[10–14] a proposed mechanism for the preparation of the entitled compounds is shown in Scheme 3. Two sites may be activated by MgO; the carbonyl through the Lewis acid site (Mg atom) and the active methylene of malononitrile by deprotonation with basic sites (O atom). Michael addition of deprotonated active methylene to the activated α,β-unsaturated carbonyl compound generates the intermediate (**a**). The intramolecular cyclization and subsequent tautomerization of intermediate (**a**) afforded the targeted molecules.

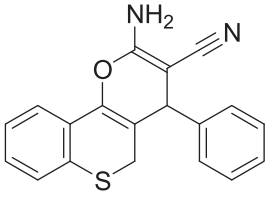
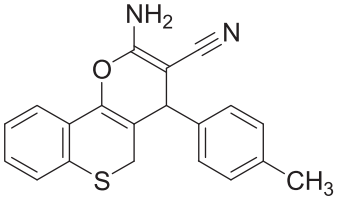
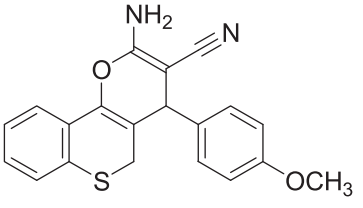
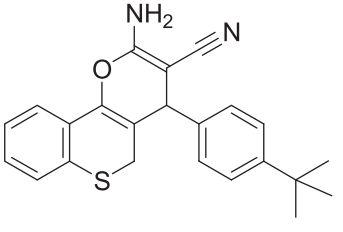
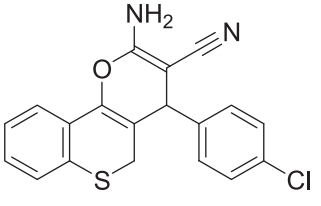
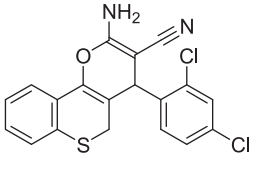
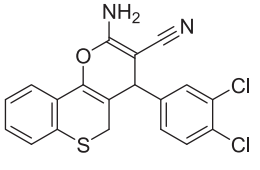
In conclusion, nanopowders of MgO were synthesized by a simple and cost-effective biosynthesis method using $MgCl_2$ and *R. officinalis* leaves extract solution. FE-SEM micrographs show the agglomeration of fine particles having crystalline sizes of about 73 nm.

MgO nanopowders showed a very high reactivity in the synthesis of thiochromeno[4,3-b]pyran and thiopyrano[4,3-b]pyran derivatives and provides good yields of pure products.

3. Experimental

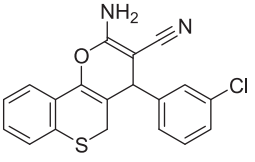
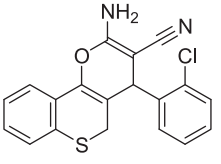
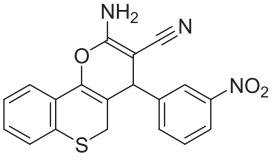
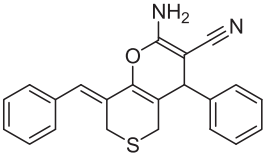
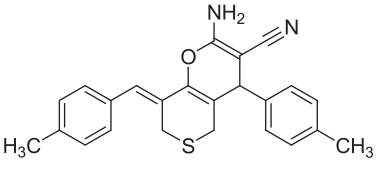
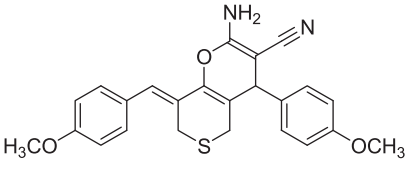
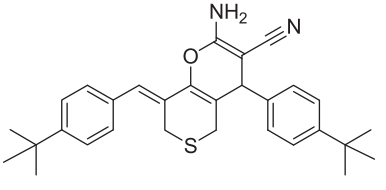
All reagents were purchased from Merck and Aldrich and used without further purification. All products were characterized using their spectral (^{1}H NMR, and ^{13}C NMR)

Table 2. Synthesis of 2-amino-4,5-dihydro-4-arylthiochromeno[4,3-b]pyran-3-carbonitrile and (8Z)-2-amino-8-arylidene-4,5,7,8-tetrahydro-4-arylthiopyrano[4,3-b]pyran-3-carbonitrile derivatives over MgO nanopowders.

Entry	Product structure	Product	Time (h)	Yield (%)[a]	M.p. (°C)
1		$\mathbf{a_1}$	10	88	193–195
2		$\mathbf{a_2}$	12	80	211–213
3		$\mathbf{a_3}$	15	75	207–209
4		$\mathbf{a_4}$	15	79	223–225
5		$\mathbf{a_5}$	12	82	214–216
6		$\mathbf{a_6}$	10	90	231–233
7		$\mathbf{a_7}$	9	86	224–226

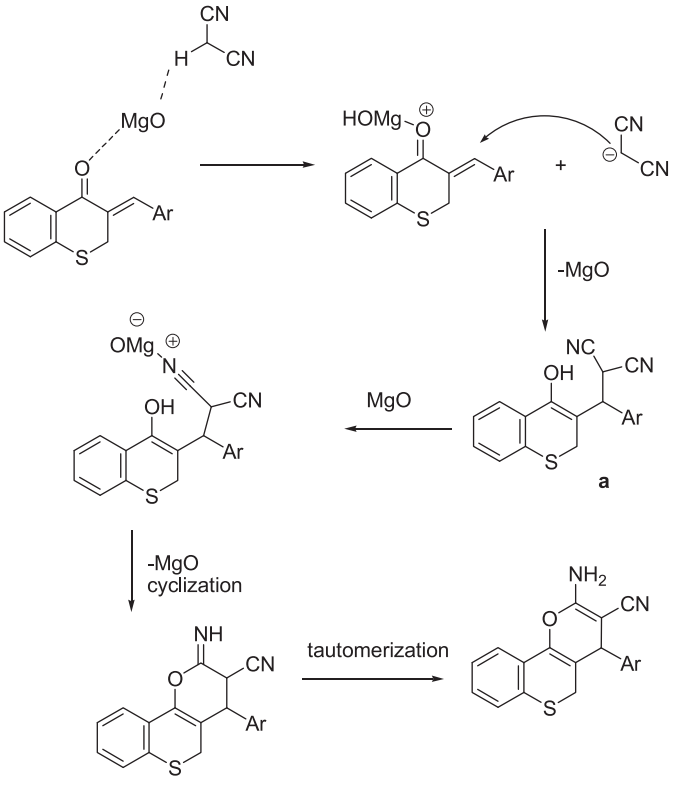
(*continued*).

Table 2. Continued.

Entry	Product structure	Product	Time (h)	Yield (%)[a]	M.p. (°C)
8		**a$_8$**	10	82	207–209
9		**a$_9$**	12	77	202–204
10		**a$_{10}$**	8	94	249–251
11		**b$_1$**	15	95	228–230
12		**b$_2$**	17	87	239–241
13		**b$_3$**	20	91	245–247
14		**b$_4$**	15	89	251–253

[a]Isolated yield.

data. The X-ray powder diffraction patterns were measured with D_8, Advance, Bruker, axs, diffractometer using Cu-Kα irradiation. FE-SEM was taken by a Hitachi S-4160 photograph to examine the shape and morphology of the samples. The NMR spectra were recorded on a Bruker Avance DPX 400 MHz instrument. The spectra were measured in



Scheme 3. Proposed mechanism for the preparation of thiochromeno[4,3-b]pyran derivatives.

DMSO-d_6 relative to TMS (0.00 ppm). TLC was performed on silica gel Polygram SIL G/UV 254 plates. *R. officinalis* leaves were collected from Esfahan province in Iran.

3.1. Preparation of MgO nanostructure

Initially, 20 g of *R. officinalis* leaves was washed in running tap water, ground and inserted into a 250 balloon flask containing 100 mL of de-ionized water and 50 mL of ethanol. The mixture was refluxed for 4 h and the extract was filtered to cut off the unrequited bodies. The extract was combined with 20 mL of aqueous ammonia (37%).

Next, to a solution of $MgCl_2$ (30 mmol) in 100 mL of water, plant extract (100 mL) was slowly poured drop-wise under vigorous magnetic stirring and the resulting precipitate was filtered, washed with water several times, dried, and calcinated at 500°C for 2 h.

3.2. Preparation of (Z)-3-arylidenethiochroman-4-one and (3Z,5Z)-3,5-diarylidene-tetrahydrothiopyran-4-one derivatives [22]

Tetrahydrothiopyran-4-one or thiochroman-4-one (1 mol) was dissolved in chloroform (20 mL), then the aromatic aldehyde (1 mol) and piperidine (0.5 mL) were added, and the

reaction mixture stirred and refluxed for 5 h. After completion of the reaction, the solvent was evaporated and the crude product was washed with water two times and finally crystallized in ethanol.

3.3. General procedure for preparation thiopyran derivatives

The starting materials **A** and **B** (Scheme 1) were prepared according to the reported literature.[22] A mixture of **A** or **B** (Scheme 1, 1 mmol), malononitrile (1.5 mmol), MgO (0.25 mmol), and 5 mL of ethanol was stirred magnetically under reflux conditions for the appropriate time as mentioned in Table 2. After completion of the reaction as detected by TLC, the reaction mixture was cooled to room temperature. After dissolving the crude product in boiling ethanol to separate the heterogeneous catalyst, the product was recrystallized from ethanol to yield a pure product.

3.3.1. Selected spectral data

3.3.1.1. 2-Amino-4,5-dihydro-4-phenylthiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_1). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 3.07 (d, J = 15.0 Hz, 1H), 3.31 (d, J = 15.0 Hz, 1H), 4.18 (s, 1H, CH|), 4.96 (s, 2H, NH_2), 7.17–7.53 (m, 9H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 27.1, 42.2, 60.8, 108.2, 119.3, 126.3, 127.1, 127.4, 128.4, 128.7, 129.2, 131.4, 132.3, 132.6, 137.5, 142.3, 159.1, 163.1 ppm. Found: C, 71.94; H, 4.67; N, 8.99; S, 10.16% $C_{19}H_{14}N_2OS$; requires: C, 71.67; H, 4.43; N, 8.80; S, 10.07%.

3.3.1.2. 2-Amino-4,5-dihydro-4-p-tolylthiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_2). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 2.27 (s, 3H, CH_3), 3.05 (d, J = 15.3 Hz, 1H), 3.29 (d, J = 15.3 Hz, 1H), 4.24 (s, 1H, CH), 5.21 (s, 2H, NH_2), 7.08 (d, J = 7.8 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 7.20–7.32 (m, 3H), 7.39 (d, J = 7.7 Hz, 1H), ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.6, 27.2, 42.1, 60.7, 108.3, 119.7, 126.1, 126.6, 127.5, 129.5, 131.5, 132.3, 132.7, 137.9, 140.2, 142.1, 159.2, 163.0 ppm. Found: C, 72.49; H, 5.05; N, 8.67; S, 9.79% $C_{20}H_{16}N_2OS$; requires: C, 72.26; H, 4.85; N, 8.43; S, 9.65%.

3.3.1.3. 2-Amino-4,5-dihydro-4-(4-methoxyphenyl)thiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_3). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 3.06 (d, J = 15.2 Hz, 1H), 3.30 (d, J = 15.2 Hz, 1H), 3.71 (s, 3H, OCH_3), 4.23 (s, 1H, CH), 5.68 (s, 2H, NH_2), 6.96 (d, J = 7.9 Hz, 2H), 7.20–7.32 (m, 5H), 7.38 (d, J = 7.7 Hz, 1H), ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 27.3, 42.2, 55.6, 60.3, 108.1, 114.9, 119.4, 124.9, 126.5, 127.9, 130.8, 132.4, 132.6, 138.1, 142.5, 159.3, 160.4, 163.1 ppm. Found: C, 69.21; H, 4.89; N, 8.34; S, 9.36% $C_{20}H_{16}N_2O_2S$; requires: C, 68.94; H, 4.63; N, 8.04; S, 9.20%.

3.3.1.4. 4-(4-tert-Butylphenyl)-2-amino-4,5-dihydrothiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_4). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 1.25 (s, 9H, $C(CH_3)_3$), 3.09 (d, J = 15.0 Hz, 1H), 3.31 (d, J = 15.0 Hz, 1H), 4.28 (s, 1H, CH), 6.21 (s, 2H, NH_2), 7.06 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 7.22–7.34 (m, 3H), 7.39 (d, J = 7.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 27.2, 31.4, 34.7, 42.3, 60.5, 108.6, 119.8, 123.4, 125.6, 126.1, 127.1, 131.4, 132.3, 132.5, 137.9, 142.2, 153.3, 159.1, 163.1 ppm. Found: C, 73.91; H, 6.11; N, 7.67; S, 8.74% $C_{23}H_{22}N_2OS$; requires: C, 73.76; H, 5.92; N, 7.48; S, 8.56%.

3.3.1.5. 2-Amino-4-(4-chlorophenyl)-4,5-dihydrothiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_5). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 3.08$ (d, $J = 15.2$ Hz, 1H), 3.29 (d, $J = 15.2$ Hz, 1H), 4.31 (s, 1H, CH), 6.35 (s, 2H, NH_2), 7.22–7.47 (m, 8H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 27.3, 42.2, 60.3, 108.6, 119.4, 125.8, 127.6, 128.1, 128.9, 131.4, 132.4, 132.7, 135.7, 137.9, 142.3, 159.0, 163.2$ ppm. Found: C, 64.92; H, 3.93; N, 8.14; S, 9.31% $C_{19}H_{13}ClN_2OS$; requires: C, 64.68; H, 3.71; N, 7.94; S, 9.09%.

3.3.1.6. 2-Amino-4-(2,4-dichlorophenyl)-4,5-dihydrothiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_6). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 3.12$ (d, $J = 15.6$ Hz, 1H), 3.37 (d, $J = 15.6$ Hz, 1H), 4.34 (s, 1H, CH), 6.89 (s, 2H, NH_2), 7.15–7.54 (m, 7H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 27.2, 42.5, 60.4, 108.7, 119.3, 125.9, 127.5, 127.8, 129.1, 128.5, 131.4, 132.3, 132.6, 133.2, 137.9, 135.3, 142.2, 159.2, 163.3$ ppm. Found: C, 59.12; H, 3.29; N, 7.40; S, 8.41% $C_{19}H_{12}Cl_2N_2OS$; requires: C, 58.92; H, 3.12; N, 7.23; S, 8.28%.

3.3.1.7. 2-Amino-4-(3,4-dichlorophenyl)-4,5-dihydrothiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_7). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 3.15$ (d, $J = 15.4$ Hz, 1H), 3.41 (d, $J = 15.4$ Hz, 1H), 4.37 (s, 1H, CH), 6.74 (s, 2H, NH_2), 7.21–7.50 (m, 7H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 27.2, 42.4, 60.3, 108.7, 119.4, 125.8, 127.3, 128.7, 129.3, 129.9, 131.4, 132.4, 132.7, 133.9, 133.8, 138.2, 141.9, 159.4, 163.2$ ppm. Found: C, 59.11; H, 3.31; N, 7.39; S, 8.38% $C_{19}H_{12}Cl_2N_2OS$; requires: C, 58.92; H, 3.12; N, 7.23; S, 8.28%.

3.3.1.8. 2-Amino-4-(3-chlorophenyl)-4,5-dihydrothiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_8). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 3.09$ (d, $J = 15.2$ Hz, 1H), 3.31 (d, $J = 15.2$ Hz, 1H), 4.32 (s, 1H, CH), 6.42 (s, 2H, NH_2), 7.21–7.48 (m, 8H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 27.2, 42.1, 60.1, 108.3, 125.7, 126.9, 127.5, 127.8, 128.4, 129.3, 130.6, 131.5, 132.4, 132.8, 138.3, 141.5, 159.1, 163.1$ ppm. Found: C, 64.89; H, 3.88; N, 8.15; S, 9.25% $C_{19}H_{13}ClN_2OS$; requires: C, 64.68; H, 3.71; N, 7.94; S, 9.09%.

3.3.1.9. 2-Amino-4-(2-chlorophenyl)-4,5-dihydrothiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_9). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 3.04$ (d, $J = 15.1$ Hz, 1H), 3.27 (d, $J = 15.1$ Hz, 1H), 4.32 (s, 1H, CH), 6.37 (s, 2H, NH_2), 7.21–7.47 (m, 8H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 27.1, 42.2, 60.3, 108.2, 119.2, 125.9, 127.1, 128.4, 129.0, 130.7, 130.8, 131.4, 132.4, 132.7, 132.9, 138.1, 142.2, 159.2, 163.1$ ppm. Found: C, 64.90; H, 3.86; N, 8.17; S, 9.23% $C_{19}H_{13}ClN_2OS$; requires: C, 64.68; H, 3.71; N, 7.94; S, 9.09%.

3.3.1.10. 2-Amino-4,5-dihydro-4-(3-nitrophenyl)thiochromeno[4,3-b]pyran-3-carbonitrile (Table 2, Product a_{10}). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 3.17$ (d, $J = 15.3$ Hz, 1H), 3.37 (d, $J = 15.3$ Hz, 1H), 4.48 (s, 1H, CH), 6.79 (s, 2H, NH_2), 7.21–7.32 (m, 3H) 7.39–7.46 (m, 2H), 7.79 (d, $J = 7.8$ Hz, 1H), 8.18–8.22 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 27.2, 42.3, 61.1, 108.8, 119.8, 122.7, 125.3, 126.1, 127.5, 129.9,$

131.5, 132.4, 132.6, 134.7, 138.1, 148.3, 148.7, 159.1, 163.4 ppm. Found: C, 63.09; H, 3.79; N, 11.74; S, 8.94% $C_{19}H_{13}N_3O_3S$; requires: C, 62.80; H, 3.61; N, 11.56; S, 8.82%.

3.3.1.11. (8Z)-2-amino-8-benzylidene-4,5,7,8-tetrahydro-4-phenylthiopyrano[4,3-b] pyran-3-carbonitrile (Table 2, Product b_1). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 2.97$ (d, $J = 15.7$ Hz, 1H), 3.25 (d, $J = 15.7$ Hz, 1H), 3.54 (d, $J = 15.8$ Hz, 1H), 3.69 (d, $J = 15.8$ Hz, 1H), 4.11 (s, 1H, CH), 6.56 (s, 2H, NH_2), 7.14 (s, 1H) 7.23–7.41 (m, 10H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 27.9, 28.7, 43.1, 56.5, 114.7, 120.2, 124.7, 126.8, 127.4, 127.6, 128.3, 128.9, 129.6, 129.9, 136.2, 142.1, 144.9, 159.2$ ppm. Found: C, 73.86; H, 5.17; N, 7.89; S, 9.07% $C_{22}H_{18}N_2OS$; requires: C, 73.71; H, 5.06; N, 7.82; S, 8.95%.

3.3.1.12. (8Z)-8-(4-methylbenzylidene)-4-(4-methylphenyl)-2-amino-4,5,7,8-tetrahydrothiopyrano[4,3-b]pyran-3-carbonitrile (Table 2, Product b_2). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 2.25$ (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 2.96 (d, $J = 15.9$ Hz, 1H), 3.22 (d, $J = 15.9$ Hz, 1H), 3.57 (d, $J = 16.1$ Hz, 1H), 3.75 (d, $J = 16.1$ Hz, 1H), 4.16 (s, 1H, CH), 6.83 (s, 2H, NH_2), 7.05–7.27 (m, 9H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 21.3, 21.5, 40.9, 43.7, 56.8, 113.9, 120.4, 121.4, 126.9, 127.6, 128.7, 129.1, 129.6, 132.7, 136.9, 140.1, 144.8, 145.1, 153.4, 160.1$ ppm. Found: C, 74.77; H, 6.02; N, 7.41; S, 8.49% $C_{24}H_{22}N_2OS$; requires: C, 74.58; H, 5.74; N, 7.25; S, 8.30%.

3.3.1.13. (8Z)-8-(4-methoxybenzylidene)-4-(4-methoxyphenyl)-2-amino-4,5,7,8-tetrahydrothiopyrano[4,3-b]pyran-3-carbonitrile (Table 2, Product b_2). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 2.97$ (d, $J = 15.8$ Hz, 1H), 3.24 (d, $J = 15.8$ Hz, 1H), 3.59 (d, $J = 15.9$ Hz, 1H), 3.78 (d, $J = 15.9$ Hz, 1H), 3.80 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.11 (s, 1H, CH), 6.85–6.98 (m, 6H), 7.14–7.22 (m, 5H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 41.2, 43.7, 55.8, 56.7, 56.9, 113.7, 120.5, 121.4, 124.8, 125.3.$ 127.6, 129.1, 129.6, 136.9, 140.1, 145.1, 153.4, 156.7, 157.9, 160.1 ppm. Found: C, 69.07; H, 5.52; N, 6.93; S, 7.84% $C_{24}H_{22}N_2O_3S$; requires: C, 68.88; H, 5.30; N, 6.69; S, 7.66%.

3.3.1.14. (8Z)-8-(4-tert-butylbenzylidene)-4-(4-tert-butylphenyl)-2-amino-4,5,7,8-tetrahydrothiopyrano[4,3-b]pyran-3-carbonitrile (Table 2, Product b_4). ^{1}H-NMR (400 MHz, DMSO-d_6): $\delta = 1.26$ (s, 9H), 1.37 (s, 9H), 3.00 (d, $J = 16.0$ Hz, 1H), 3.28 (d, $J = 16.0$ Hz, 1H), 3.55 (d, $J = 16.2$ Hz, 1H), 3.73 (d, $J = 16.2$ Hz, 1H), 4.17 (s, 1H, CH), 6.77 (s, 2H, NH_2), 6.99–7.14 (m, 7H), 7.23 (d, $J = 7.8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 28.1, 29.3, 31.2, 31.5, 34.7, 35.2, 43.4, 57.1, 115.1, 120.2, 125.4, 125.7, 126.8, 128.7, 129.2, 130.0, 131.9, 137.0, 140.2, 144.8, 145.1, 153.4, 159.2$ ppm. Found: C, 76.79; H, 7.56; N, 6.21; S, 6.99% $C_{30}H_{34}N_2OS$; requires: C, 76.56; H, 7.28; N, 5.95; S, 6.81%.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

We are thankful to the Islamic Azad University, Najafabad Branch research council for partial support of this research.

References

[1] Lee HW, Kim BY, Ahn JB, et al. Molecular design, synthesis, and hypoglycaemic and hypolipidemic activities of novel pyrimidine derivatives having thiazolidinedione. Eur J Med Chem. 2005;40:862–874.

[2] Eun JS, Kim KS, Kim HN, et al. Synthesis of psoralen derivatives and their blocking effect of hkv1.5 channel. Arch Pharm Res. 2007;30:155–160.

[3] Richardson K. GB Pat 2099818 and US Pat 4,404,216. 1982.

[4] Ward DE. The thiopyran route to polypropionates. Chem Commun. 2011;47(41):11375–11393.

[5] Morgan LR, Jursic BS, Hooper CL, Neumann DM, Thangaraj K, Leblance B. (1H-Imidazo[4,5-c]pyridin-2-yl)-1,2,5-oxadiazol-3-ylamine derivatives: further optimisation as highly potent and selective MSK-1-inhibitors. Bioorg Med Chem Lett. 2002;12:3407–3411.

[6] Moon DO, Kim KC, Jin CY, et al. Inhibitory effects of eicosapentaenoic acid on lipopolysaccharide-induced activation in BV2 microglia. Int Immunopharmacol. 2007;7:222–229.

[7] Flavin MT, Rizzo JD, Khilevich A, et al. Synthesis, chromatographic resolution, and anti-human immunodeficiency virus activity of (±)-calanolide A and its enantiomers. J Med Chem. 1996;39:1303–1313.

[8] Eiden F, Felbermeir G. 7-Phenyl[1]benzopyrano-(bzw. -thiopyrano)-pyrane aus 3-Benzylidenchromanonen (bzw. -thiochromanonen). Arch Pharm (Weinheim). 1984;317:861–867.

[9] Nakib TA, Bezjak V, Rashid S, Fullam B, Meegan MJ. The synthesis and antifungal activity of 2-amino-4-aryl-4H,SH-[1]benzothiopyrano[4,3-b]pyran-3-carbonitriles and 2-alkoxy-4-aryl-SH-[1]benzothiopyrano[4,3-b]pyridine-3-carbonitriles. Eur J Med Chem. 1991;26:221–230.

[10] Kumar RR, Perumal S, Senthilkumar P, Yogeeswari P, Sriram D. An atom efficient, solvent-free, green synthesis and antimycobacterial evaluation of 2-amino-6-methyl-4-aryl-8-[(E)-arylmethylidene]-5,6,7,8-tetrahydro-4H-pyrano[3,2-c]pyridine-3-carbonitriles. Bioorg Med Chem Lett. 2007;17:6459–6462.

[11] Kumar RR, Perumal S, Menéndez JC, Yogeeswari P, Sriram D. Antimycobacterial activity of novel 1,2,4-oxadiazole-pyranopyridine/chromene hybrids generated by chemoselective 1,3-dipolar cycloadditions of nitrile oxides. Bioorg Med Chem. 2011;19:3444–3450.

[12] Wang XS, Yang GS, Zhao G. Enantioselective synthesis of naphthopyran derivatives catalyzed by bifunctional thiourea-tertiary amines. Tetrahedron Asymmetr. 2008;19:709–714.

[13] Mobinikhaledi A, Foroughifar N, Moghanian H, Keshvarzi N. Piperazine catalyzed convenient synthesis of 4H-pyran derivatives from α,α'-bis(substituted-benzylidene) cycloalkanones and malononitrile under reflux conditions. J Saudi Chem Soc. 2015;19:399–403.

[14] Hu Z-P, Lou C-L, Wang J-J, Chen C-X, Yan M. Organocatalytic conjugate addition of malononitrile to conformationally restricted dienones. J Org Chem. 2011;76:3797–3804.

[15] Ghashang M. Preparation and application of barium sulfate nano-particles in the synthesis of 2,4,5-triaryl and *N*-aryl(alkyl)-2,4,5-triaryl imidazoles. Curr Org Synth. 2012;9:727–732.

[16] Ghashang M, Mansoor SS, Aswin K. Thiourea dioxide: an efficient and reusable organocatalyst for the rapid one-pot synthesis of pyrano[4,3-b]pyran derivatives in water. Chin J Catal. 2014;35:127–133.

[17] Mohammad Shafiee MR, Ghashang M, Fazlinia A. Preparation of 1,4-dihydropyridine derivatives using perchloric acid adsorbed on magnetic Fe_3O_4 nanoparticles coated with silica. Curr Nanosci. 2013;9:197–201.

[18] Ghashang M. 1-Butyl-1-methylpyrrolidinium hydrogen sulfate promoted preparation of 1,5-diaryl-3-(arylamino)-1H-pyrrol-2(5H)-one derivatives. Res Chem Intermed. 2013;39:2187–2195.

[19] Ghashang M. Aluminum hydrogen sulfate [$Al(HSO_4)_3$] as an efficient catalyst for the preparation of thioacetals. Res Chem Intermed. 2013;39:2837–2842.

[20] Das VK, Thakur AJ. Highly active nano-MgO catalyzed, mild, and efficient synthesis of amidines via electrophilic activation of amides. Tetrahedron Lett. 2013;54:4164–4166.

[21] Carvalho Jr RN, Moura LS, Rosa PTV, Meireles MAA. Supercritical fluid extraction from rosemary (*Rosmarinus officinalis*): kinetic data, extract's global yield, composition, and antioxidant activity. J Supercrit Fluids. 2005;35:197–204.
[22] Jegham N, Tka N, Kacem Y, Ben Hassine B. New N-substituted (E)-4-arylidene isoquinoline-1,3-dione derivatives: NMR spectroscopic investigation and antibacterial activity. Synth Commun. 2012;42:3328–3336.