



A microwave-assisted synthesis of 3,4-dihydropyrimidin-2(1H)-one/thione derivatives using nanocrystalline MgFe_2O_4 as catalyst

Chandrashekhar Arunrao Ladole, Nilesh Govindrao Salunkhe,
Ravindra Sakharam Bhaskar and Anand Shankarrao Aswar *

Department of Chemistry, Sant Gadge Baba Amravati University, Amravati, 444602, India

*Corresponding author at: Department of Chemistry, Sant Gadge Baba Amravati University, Amravati, 444602, India.
Tel.: +91.942.1790866. Fax: +91.721.2662135. E-mail address: anandaswar@yahoo.com (A. Aswar).

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ABSTRACT

3,4-Dihydropyrimidin-2(1H)-one/thione derivatives were synthesized in moderate to high yields via one-pot three component Biginelli reaction of aldehydes, ethyl acetoacetate and urea/thiourea in the presence of nanocrystalline MgFe_2O_4 as an efficient catalyst, in microwave irradiation under solvent free condition. This protocol offers several advantages including good yields of products, short reaction time and easy work-up procedure.

1. Introduction

Multicomponent reactions are very attractive tools to obtain the complex molecules from one-pot synthesis. Dihydropyrimidinones are vital synthons, pharmaceuticals, precursors, calcium-channel blockers and lead molecule for development of new anticancer drugs [1,2]. Some marine alkaloids containing dihydropyrimidine core unit possess interesting biological properties, e.g., batzelladine alkaloids have been found to be potent HIV gp-120-CD4 inhibitors [3]. Synthetic strategies for the dihydropyrimidine nucleus involves one-pot to multistep approaches. The classical Biginelli synthesis is a one-pot condensation using β -dicarbonyl compounds with aldehydes (Aromatic and aliphatic aldehydes) and urea or thiourea in ethanol solution containing catalytic amounts of acid. However, this method required longer reaction times, harsh reaction conditions and poor yields. Improvements in such syntheses have been sought continuously.

In recent years several methods and catalysts have been developed for synthesis of dihydropyrimidines. Few important catalysts are ionic liquids [4], H_3BO_3 [5], VCl_3 [6], $\text{Sr}(\text{OTf})_2$ [7], poly(4-vinylpyridinium)hydrogen sulphate [8], LaCl_3 -graphite [9], ZrO_2 [10], sulfated tungstate [11]. These processes are quite costlier, time consuming and environmental unfriendly.

Therefore, attempt has been made to develop mild, cheaper and eco-friendly process for their synthesis. Presently nanoparticles have attracted a great deal of attention as effective catalysts in synthetic organic chemistry. The Pd-nanoparticles are found to be efficient catalysts for the Mizoroki-Heck reaction [12], Suzuki cross-coupling [13], Stille type reactions [14], Sonogashira coupling reaction [15], Tsuji-Trost allylation [16], Pauson-Khand reactions [17] and azo-Michael reactions [18]. Cu-nanoparticles have proved to be good catalysts in the oxidative cyclization of Schiffs' bases [19] and for one-pot three-component synthesis of thiazolidine-2,4-dione derivatives [20]. A chemo selective reduction of aldehydes using Ni-nanoparticles as an efficient green catalyst is also recorded in the literature [21]. Very recently, metal oxides have been used in organic synthesis and these include copper(II) oxide in the synthesis of 1,4-dihydropyridines [22] and as an effective catalyst for the CO and NO oxidation, as well as in the oxidation of volatile organic pollutants [23]. Similarly, nano MgO in the synthesis of 2-amino-2-chromenes [24] have been reported. To the best of our knowledge, there are no reports on the synthesis of dihydropyrimidines using MgFe_2O_4 as catalyst. Some advantages of this catalyst are inexpensive, easy to prepare and insoluble in most of organic solvents, which could be recycled during work-up.

In view of the importance associated with this class of reaction here we report the performance of MgFe_2O_4 catalyst for the synthesis of dihydropyrimidines and predicts its reaction mechanism.

2. Experimental

2.1. Instrumentation

Analytical grade chemicals were used and distilled prior to use. Melting points were determined on a quality digital melting point apparatus. The IR spectra were recorded on Shimadzu FT-IR spectrometer. NMR spectra recorded on a Bruker Avance (300 and 400 MHz) spectrometer using CDCl_3 and $\text{DMSO-}d_6$ as a solvent. Chemical shifts (ppm) were referenced to the initial standard tetramethylsilane (TMS). The structural and phase purity of as prepared samples were characterized through XRD measurement using Bruker AXS-D8 advanced X-ray powder diffractometer with $\text{CuK}\alpha$ line ($\lambda = 1.54056 \text{ \AA}$) in the 2θ range from 10 – 90° . The morphology of prepared samples was examined by direct observation via Scanning Electron Microscope (SEM) model (JEOL Model JSM - 6390LV). The thermal analysis was performed by using thermo gravimetric-differential thermal analysis (TG/DTA) was carried out using a Perkin Elmer STA 6000 instrument in the nitrogen atmosphere with the flowing rate 20 mL/min in the range from room temperature to 720°C with the heating rate 10°C/min . Experiments under microwave irradiation were carried out in scientific microwave synthesizer system supplied by Ragatech Electronics India Pvt. Ltd., India having maximum power output of 700 W and 2450 MHz frequency with 10 power levels (140 to 700 W). Reactions were monitored by thin layer chromatography using silica gel 60F_{254} aluminum sheets (Merck).

Nanocrystalline MgFe_2O_4 (nc- MgFe_2O_4) was prepared by literature method with slight modification [25]. Magnesium ferrite powder was prepared in two steps. In first step the stoichiometric amount of magnesium chloride MgCl_2 dissolved in distilled water and allowed to react with sodium hydroxide (NaOH) solution dissolved in distilled water with vigorous stirring while in second step a solution of ferric chloride $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ prepared in HCl solution and mixed them and stirred for two hours and further heated for half an hour at 60°C . The mixture was allowed to settle and its pH adjusted to 7.5 with 2 N sodium hydroxide solution (NaOH). The product obtained was washed by repeated decantation till free from chloride ions. And then filtered it, dried at an oven at 120°C and calcinated at 500°C for five hours. The product obtained was investigated by Powder XRD, FT-IR, TG/DTA and SEM analysis.

2.2. General procedure for preparation 4a-r

A solution of aldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea or thiourea (1.5 mmol) and nc- MgFe_2O_4 ($10 \text{ mol}\%$) were placed in 100 mL round bottom flask without solvent and irradiated in microwave (350 W) for desired time. Upon completion of the reaction (Monitored by TLC using hexane:ethyl acetate ($6:4, v:v$) as eluent) the reaction mixture was diluted with ethanol (20 mL) and the reaction mass was stirred and allowed to cool, slurry was filtered to remove the catalyst and washed with ethanol ($3 \times 10 \text{ mL}$). Combined filtrates were concentrated under reduced pressure to obtain a solid residue. The solid residue was slurried in water ($3 \times 15 \text{ mL}$) and filtered, the cake was washed with hexane ($3 \times 15 \text{ mL}$) and recrystallized from ethanol to give pure product.

The all products are known compounds and were characterized by IR and ^1H NMR Spectroscopic data and melting points and compared with reported values.

Ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4a): M.p.: 201 – 202°C . ^1H NMR (300 MHz , CDCl_3 , δ , ppm): 1.14 (t, $J = 7.2 \text{ Hz}$, 3H , CH_3), 2.35 (s, 3H , CH_3), 4.04 , (q, $J = 7.2 \text{ Hz}$, 2H , CH_2), 5.41 (d, $J = 2.4 \text{ Hz}$, 1H , CH), 5.58 (s, 1H , NH), 7.26 – 7.33 (m, 5H , Ar-H), 7.71 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3246 , 2979 , 2937 , 1725 , 1649 , 1464 , 781 .

Ethyl 4-(4-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4d): M.p.: 229 – 230°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.09 (t, $J = 7.04 \text{ Hz}$, 3H , CH_3), 2.25 (s, 3H , CH_3), 3.95 (q, $J = 7.04 \text{ Hz}$, 2H , CH_2), 5.14 (d, $J = 3.04 \text{ Hz}$, 1H , CH), 7.23 (d, $J = 8.4 \text{ Hz}$, 2H , Ar-H), 7.30 (d, $J = 8.4 \text{ Hz}$, 2H , Ar-H), 7.71 (s, 2H , NH), 9.18 (s, 1H , OH). IR (KBr, ν , cm^{-1}): 3244 , 2980 , 2957 , 1723 , 1648 , 1461 , 781 .

Ethyl 4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4e): M.p.: 201 – 202°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.08 (t, $J = 7.04 \text{ Hz}$, 3H , CH_3), 2.23 (s, 3H , CH_3), 3.7 (s, 3H , O- CH_3), 3.93 (q, $J = 7.04 \text{ Hz}$, 2H , CH_2), 5.12 (d, $J = 2.7 \text{ Hz}$, 1H , CH), 6.74 (d, $J = 8.56 \text{ Hz}$, 2H , Ar-H), 7.13 (d, $J = 8.56 \text{ Hz}$, 2H , Ar-H), 7.42 (s, 1H , NH), 8.96 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3243 , 2956 , 2835 , 1706 , 1650 , 1461 , 785 .

Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4h): M.p.: 212 – 213°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.1 (t, 3H , CH_3), 2.24 (s, 3H , CH_3), 3.96 (q, 2H , CH_2), 5.16 (d, 1H , CH), 7.22 – 7.34 (m, 4H , Ar-H), 7.55 (s, 1H , NH), 9.04 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3244 , 2980 , 2957 , 1703 , 1649 , 1461 , 782 .

Ethyl 4-(furan-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4i): M.p.: 205 – 206°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.24 (t, $J = 7.04 \text{ Hz}$, 3H , CH_3), 2.32 (s, 3H , CH_3), 4.11 (q, $J = 7.32 \text{ Hz}$, 2H , CH_2), 5.19 (d, 1H , CH), 5.85 (s, 1H , furan-H), 5.94 (s, 1H , furan-H), 6.21 (s, 1H , furan-H), 7.21 (s, 1H , NH), 7.26 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3346 , 2984 , 2959 , 1650 , 1488 , 731 .

Ethyl 6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4j): M.p.: 209 – 210°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 0.91 (t, 3H , CH_3), 2.09 (s, 3H , CH_3), 3.13 (q, 2H , CH_2), 4.98 (d, 1H , CH), 7.03 – 7.09 (m, 5H , Ar-H), 9.39 (s, 1H , NH), 10.05 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3329 , 2980 , 1670 , 1574 , 1465 , 1196 .

Ethyl 4-(4-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4m): M.p.: 172 – 173°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.11 (t, $J = 6.9 \text{ Hz}$, 3H , CH_3), 2.24 (s, 3H , CH_3), 3.98 (q, $J = 6.7 \text{ Hz}$, 2H , CH_2), 5.08 (d, $J = 2.3 \text{ Hz}$, 1H , CH), 6.69 (d, $J = 8.1 \text{ Hz}$, 2H , Ar-H), 7.01 (d, $J = 8.1 \text{ Hz}$, 2H , Ar-H), 9.34 (s, 1H , NH), 9.5 (s, 1H , NH), 10.18 (s, 1H , OH). IR (KBr, ν , cm^{-1}): 3501 , 3184 , 3016 , 1686 , 1580 , 1482 , 1200 .

Ethyl 4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4n): M.p.: 153 – 154°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.13 (t, 3H , CH_3), 2.29 (s, 3H , CH_3), 3.73 (s, 3H , O- CH_3), 4.01 (q, 2H , CH_2), 5.03 (d, 1H , CH), 6.86 (d, $J = 6.7 \text{ Hz}$, 2H , Ar-H), 7.13 (d, $J = 6.7 \text{ Hz}$, 2H , Ar-H), 9.56 (s, 1H , NH), 10.24 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3314 , 2985 , 1667 , 1575 , 1461 , 1195 .

Ethyl 4-(furan-2-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4r): M.p.: 225 – 226°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.15 (t, 3H , CH_3), 2.29 (s, 3H , CH_3), 4.05 (q, 2H , CH_2), 5.25 (d, 1H , CH), 6.13 (s, 1H , furan-H), 6.35 (s, 1H , furan-H), 7.53 (s, 1H , furan-H), 9.62 (s, 1H , NH), 10.37 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3314 , 2987 , 1663 , 1574 , 1451 , 1188 .

Ethyl 4-(furan-2-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4r): M.p.: 225 – 226°C . ^1H NMR (400 MHz , $\text{DMSO-}d_6$, δ , ppm): 1.15 (t, 3H , CH_3), 2.29 (s, 3H , CH_3), 4.05 (q, 2H , CH_2), 5.25 (d, 1H , CH), 6.13 (s, 1H , furan-H), 6.35 (s, 1H , furan-H), 7.53 (s, 1H , furan-H), 9.62 (s, 1H , NH), 10.37 (s, 1H , NH). IR (KBr, ν , cm^{-1}): 3314 , 2987 , 1663 , 1574 , 1451 , 1188 .

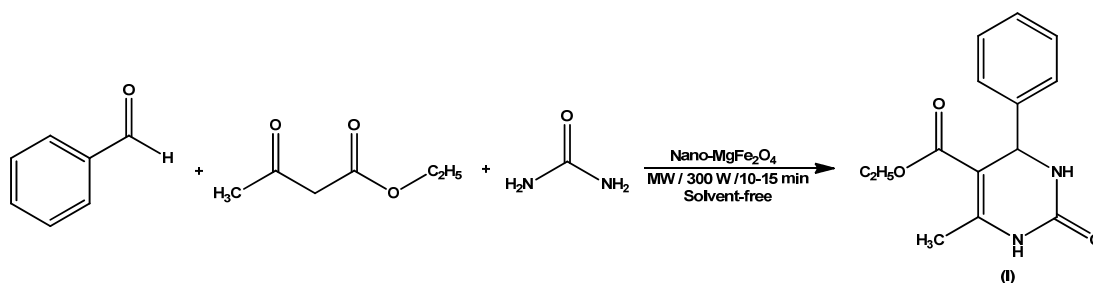
3. Results and discussion

The XRD pattern of the catalyst matches well with the reported JCPDS card No. JCPDS no. (8-1935) and confirm the phase purity of the material. The crystallite size was calculated using the Scherrer's formula and found to be 37.58 nm . The bands appeared in the region 500 – 650 cm^{-1} in the FT-IR spectrum of the catalyst can be ascribed to metal oxygen modes of tetrahedral and octahedral sites.

We used TG/DTA of MgFe_2O_4 , in order to study the changes occurred regarding the phase transition during heat treatment to the sample. According to the mass loss curve, the sample shows gradual continuous weight loss up to 100°C and heat flow endo down curve shows less significant peak assigned to

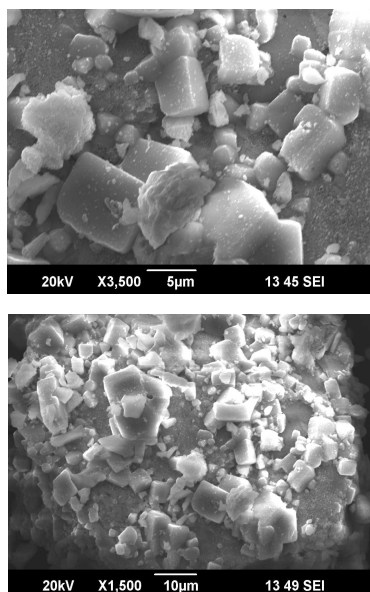
Table 1. Effect of different amounts of nc-MgFe₂O₄ and solvents on formation of compound **4a**^a

Entry	nc-MgFe ₂ O ₄ (mol%)	Condition / Solvents	Time (min) / Yield ^b (%)
1	-	Microwave/solvent free	20/18
2	3	Microwave/solvent free	18/38
3	6	Microwave/solvent free	15/62
4	10	Microwave/solvent free	7/95
5	10	Reflux/ethanol	120/62
6	10	Reflux/water	120/68
7	10	Reflux/toluene	120/35
8	10	Reflux/THF	120/54

^a Reactions carried out at 10 mmol scale with molar ratio of benzaldehyde: ethyl acetoacetate: urea=1:1:1.5.^b Isolated yield.

the evaporation of water and formation of Fe₂O₃ from Fe(OH)₃, respectively.

The weight loss curve shows further loss may be attributed to the evaporation of coordinated water. The total weight loss from room temperature to 720 °C was about 86.72%. The SEM images of MgFe₂O₄ are shown in Figure 1. The images show, tiny crystalline cubes of MgFe₂O₄ ferrite with agglomeration. Higher SEM particle size compared to XRD particle size can be attributed to agglomeration and different principal of the two techniques.

**Figure 1.** SEM image of the nc-MgFe₂O₄ ferrite.

To evaluate the feasibility of nc-MgFe₂O₄ for Biginelli reaction a model reaction (Scheme 1) with a building block ratio of 1:1:1.5 of benzaldehyde, ethyl acetoacetate and urea, respectively, to give 5-ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyridin-2 (1H)-one (**4a**) was conducted under different conditions both in the absence and in the presence of nc-

MgFe₂O₄ and results are given in (Table 1). In the absence of nc-MgFe₂O₄, only 18% yield of the product was obtained even after microwave irradiation for 20 min with recovery of starting material (Entry 1, Table 1) whereas in the presence of nc-MgFe₂O₄ (3 mol%), under the same conditions yield increased to 38% (Entry 2, Table 1). Building upon this result further studies were conducted and it was found that 10 mol% of nc-MgFe₂O₄ was optimum for this reaction and gave a product of 95% yield in just 7 min. (Entry 4, Table 1). Reaction got accelerated in presence of nc-MgFe₂O₄ (10 mol%) of catalyst to complete the reaction in just 7 minutes having 95% yield. Maintaining other conditions same, the catalyst amount was varied stepwise and was observed that for a reaction of 7 to 15 min. Duration of yield reached to maximum at 10 mol% and any further increase did not show any benefits (Figure 2).

The reaction was further examined in different solvents such as EtOH, toluene, H₂O and THF. In the presence of solvents was found to be reaction was sluggish and formation of by-products was observed (Entries 5-8, Table 1). The microwave irradiation below 350 W reaction proceeded slow giving a relatively low yield and no improvement was observed above 350 W microwave irradiation. All further studies were carried out under solvent free conditions with 10 mol% catalyst at 350 W microwave irradiation.

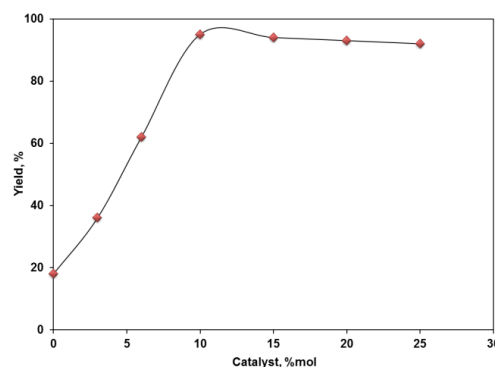
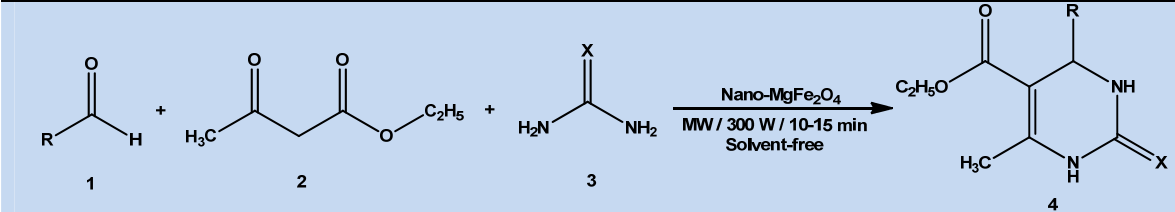
**Figure 2.** Graph of isolated yield of 5-ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyridin-2 (1H)-one versus mol% of nc-MgFe₂O₄ catalyst. Reaction conditions: benzaldehyde (10mmol), ethyl acetoacetate (10mmol), urea (15mmol) at 350 W microwave irradiation in solvent free condition for 7 min.

Table 2. comparative study with different catalyst.

Entry	Catalyst	Amount (mol%)	Molar Ratio ^a	Condition/Solvent	Time (min)/Yield ^b (%)	Reference
1	MgBr ₂	10	1:1:1.5	100 °C / solvent free	45/92	[26]
2	MgCl ₂ ·6H ₂ O	20	1:1:1.5	80 °C / solvent free	60/96	[27]
3	TiCl ₄ -MgCl ₂ /MgCl ₂ ·4CH ₃ OH	10	1:1:1.5	100 °C / solvent free	180/90	[28]
4	MgCl ₂	10	1:1:1.2	Reflux / acetic acid	45/90	[29]
5	AcOH	5	1:1:1.5	80 °C / water	30/58	[30]
6	nc-MgFe ₂ O ₄	10	1:1:1.5	Microwave / solvent free	7/95	This work

^a Molar ratio of benzaldehyde: ethyl acetoacetate: urea.^b Isolated yield.**Table 3.** Synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones using nc-MgFe₂O₄.


Product ^b	Substrate/ Product	X	Time/ min.	Yield %	M.p. (Lit. M.p.)/°C
4a	R: C ₆ H ₅	O	7	95	201 (200-202)
4b	R: 2-OH-C ₆ H ₄	O	14	86	202 (201-203)
4c	R: 3-OH-C ₆ H ₄	O	11	90	210 (210-212)
4d	R: 4-OH-C ₆ H ₄	O	9	92	229 (227-229)
4e	R: 4-OCH ₃ -C ₆ H ₄	O	12	89	201 (200-201)
4f	R: 3,4-OCH ₃ -C ₆ H ₃	O	14	87	205 (205-207)
4g	R: 2-OH,3-OCH ₃ -C ₆ H ₃	O	15	88	232(232-233)
4h	R: 4-Cl-C ₆ H ₄	O	10	90	212 (212-213)
4i	R: 2-Furyl	O	11	91	205 (203-205)
4j	R: C ₆ H ₅	S	10	92	209 (208-210)
4k	R: 2-OH-C ₆ H ₄	S	15	87	252(251-253)
4l	R: 3-OH-C ₆ H ₄	S	15	89	192 (191-193)
4m	R: 4-OH-C ₆ H ₄	S	9	91	172 (170-173)
4n	R: 4-OCH ₃ -C ₆ H ₄	S	14	86	153 (154-155)
4o	R: 3,4-OCH ₃ -C ₆ H ₃	S	15	87	153 (152-153)
4p	R: 2-OH,3-OCH ₃ -C ₆ H ₃	S	15	86	157 (156-159)
4q	R: 4-Cl-C ₆ H ₄	S	12	91	186 (184-186)
4r	R: 2-Furyl	S	10	90	225 (225-227)

^a Reaction conditions: aromatic aldehyde (10 mmol); β-ketoester (10 mmol); urea or thiourea (15 mmol); nc-MgFe₂O₄ (10 mol%).^b All products are known and were identified by their melting point, IR and ¹H NMR spectra according to literature.

Catalytic efficiency of nc-MgFe₂O₄ among the other solid catalysts for the preparation of the dihydropyrimidinone was evaluated and comparative data are presented in Table 2. Among the solid catalysts MgBr₂, MgCl₂·6H₂O, TiCl₄-MgCl₂/MgCl₂·4CH₃OH, MgCl₂, AcOH and MgFe₂O₄ was found to be superior in terms of catalyst amount as well as yield and reaction time. Results of MgCl₂·6H₂O were comparable and gave slightly higher yield however required reaction time was longer (Entries 2, Table 2).

Scope and generality of this protocol were demonstrated by subjecting a broad range of building block combinations such as aromatic aldehydes carrying either electron donating or electron withdrawing substituent, aliphatic aldehyde, different β-ketoesters and urea/thiourea. All the building block combination reacted very well, giving moderate to excellent yields of the desired products under optimized reaction conditions.

The structural variations in the aldehydes had no significant effect on the yields. Using aldehydes bearing sensitive functional groups like Cl, OH and OCH₃ the reaction proceeded smoothly to afford the corresponding products in excellent yields (product 4b-4h, and 4k-4q, Table 3). The reaction proceeded comparatively faster with aldehyde containing *p*-hydroxy group and required only 9 min to give corresponding dihydropyrimidinones in excellent yields (product 4d and 4m, Table 3). nc-MgFe₂O₄ also worked well even with an sensitive aldehyde such as furfural without leading to the formation of any side products (product 4i and 4r, Table 3). Longer reaction times (15 min) were needed for the reaction of 2-hydroxy, 3-methoxy benzaldehyde (product

4g and 4p, Table 3). Thiourea has been also used with success to provide the corresponding dihydropyrimidin-2-(1H)-thiones in high yields (product 4j-4r, Table 3). It is well known that for Biginelli reaction, aromatic aldehyde works very well.

Nanocrystalline-MgFe₂O₄ was easily separated from the reaction medium by adding ethanol to the stirred reaction mixture followed by filtration for reusability experiments. The recovered catalyst was dried in oven at 120 °C for 1 h. The recovered catalyst was reused four times under the same reaction conditions for preparation of compound 4a, as a model reaction, without any significant loss of activity (Table 4).

Table 4. Effect of recovered catalyst on the yield ^a.

Recycling	% Yield of catalyst (4a)
Fresh	95
First recycle	94
Second recycle	92
Third recycle	90
Fourth recycle	88

^a Loss of catalyst (<5%) during handling.

4. Conclusion

Nanocrystalline MgFe₂O₄ with high surface area has been synthesized by co-precipitation method and has been employed for the synthesis of dihydropyrimidines using a MW reactor under solvent-free condition. By this new procedure 3,4-dihydropyrimidin-2(1H)-ones/-thiones with varied substitution were synthesized. The attractive features of this protocol are its green-ness with respect to solvent free

reaction, recyclability of catalyst, mild reaction conditions, short reaction times and high yield.

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