Crumpled perovskite-type  $LaMo_xFe_{1-x}O_3$  nanosheets: a reusable catalyst for rapid and green synthesis of naphthopyranopyrimidine derivatives

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#### Crumpled perovskite-type LaMoxFe1-xO3 nanosheets: A reusable catalyst for rapid and green

### synthesis of naphthopyranopyrimidine derivatives

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#### Abstract

In this study, crumpled nanosheets of molybdenum-doped LaFeO<sub>3</sub> (LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub>) were prepared by the citric acid based sol-gel route. Characterization of the prepared LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> was carried out by Fourier transform infrared spectra (FT-IR), powder X-ray diffraction (XRD), energy dispersive spectroscopy (EDS), field emission scanning electron microscopy (FE–SEM). The catalytic performance of LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanostructures was evaluated in the green synthesis of naphthopyranopyrimidines from one-pot three-component reaction of 2-naphthol, different substituted aromatic aldehydes, barbituric acid and its derivatives under solvent-free conditions. This method provides several advantages such as mild conditions, operational simplicity, high yields, safety, easy workup and simple purification of products, little catalyst loading, and reusability of the catalyst.

*Keywords:* Heterogeneous catalysis, Crumpled nanosheets, LaMoFeO<sub>3</sub>, Naphthopyranopyrimidine, Nanostructures.

# 1. Introduction

Perovskite-type oxides with an ABO<sub>3</sub> structure (where A is rare earth and B is transition metal cations) have been applied as multifunctional metal oxide catalysts because of their high catalytic activity and thermal stability<sup>1</sup>. LaFeO<sub>3</sub> is a type of metal oxides with the perovskite structure that has various catalytic and electrical properties beside high stability over a wide temperature range, low thermal expansion coefficient, and nontoxicity<sup>2,3</sup>. These properties make them suitable as chemical sensors, electrodes materials for fuel cells, oxidation catalysts for air pollutants, photocatalyst, non-volatile magnetic memory devices, and oxygen permeation membranes<sup>2,4,5</sup>. Perovskite oxide LaFeO<sub>3</sub> has an orthorhombic structure and consists of FeO<sub>6</sub> octahedral units with La<sup>3+</sup> ions at the corners that can be modified with partial substitution of La by rare earth elements (i.e. Ba, and Ca) with general formula of La<sub>1-x</sub>A<sub>x</sub>FeO<sub>3</sub> and Fe by transition metal elements (e.g. Cr and Mn) with general formula of  $LaFe_{1-x}B_xO_3$ . The properties of the final product are controllable and depend on the nature and content of the dopant. Doping the catalysts with the metal nanoparticles increases the catalytic and electrochemical properties, the surface volume ratio of the catalyst, and the structural ability<sup>3, 6</sup>. Due to its high efficiency, the doped catalyst, has received increasing attention for various applications. For example Mg and Zn-doped LaFeO<sub>3</sub> have been applied as gas sensors, photocatalysts and oxidation catalysts<sup>1, 7</sup>. Metal-doped LaFeO<sub>3</sub> can be easily prepared by a sol-gel method.

Multicomponent reactions (MCRs), one-pot reactions that form products from more than two different starting compounds, are ideal reaction systems leading to high structural diversity and

molecular complexity through a single transformation<sup>8</sup>. A great variety of product can be prepared in a higher yield by multicomponent reactions. MCRs show outstanding features like high atom economy, less waste generation, and use of readily available starting materials<sup>9</sup>.

Pyran and pyrimidines are present in a number of natural products and many synthetic compounds and have lots of medicinal properties and therapeutic applications<sup>10,11</sup>. Multicomponent synthesis of pyran and pyrimidine derivatives has been developed using a variety of catalysts such as ZnFe<sub>2</sub>O<sub>4</sub>@alginic acid<sup>11</sup>, nano-Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-NH-gallic acid<sup>12</sup>, CoFe<sub>2</sub>O<sub>4</sub>@B<sub>2</sub>O<sub>3</sub>-SiO<sub>2</sub><sup>13</sup>, Fe<sub>3</sub>O<sub>4</sub>-halloysite-SO<sub>3</sub>H<sup>14</sup>, Fe<sub>3</sub>O<sub>4</sub>@HNTs-PEI<sup>15</sup>, Fe<sub>3</sub>O<sub>4</sub>@cellulose nanocomposite<sup>16</sup>, and MNPs@NHC(O)CH<sub>2</sub>CH<sub>2</sub>PPh<sub>2</sub><sup>17</sup>.

Pyranopyrimidines possess an array of biological and physiological properties such as antibacterial<sup>18</sup>, antifungal<sup>19</sup>, antimicrobial<sup>20</sup>, antitumor<sup>21</sup>, analgesic, anticonvulsant<sup>22</sup>, and antihypertensive<sup>23</sup>. Also, Mai et al. have reported that these compounds show SIRT1 inhibition activity<sup>24</sup> (Fig. 1).



Fig. 1. Some represented Sirtuin Inhibitors

A commonly applied method for the synthesis of naphthopyranopyrimidines relies on three component reaction of 2-naphthol, aldehyde and 1,3-dimethylbarbituric acid in the presence of catalysts such as  $I_2^{25}$ , InCl<sub>3</sub>,  $P_2O_5^{26}$ , lactic acid<sup>27</sup>, and KAl(SO<sub>4</sub>)<sub>2</sub>.12H<sub>2</sub>O<sup>28</sup>. Also, the synthesis of naphthopyranopyrimidines via the reaction of 2-naphthol, aldehyde and 6-amino-1,3-dimethyl uracil catalyzed by HPA<sup>29</sup>, Al(H<sub>2</sub>PO<sub>4</sub>)<sub>3</sub><sup>30</sup>, InCl<sub>3</sub><sup>31</sup>, and L-Proline<sup>32</sup> has been reported.

Herein, considering the importance of naphthopyranopyrimidine derivatives and with a purpose of developing a novel, efficient, reusable, cost-effective, non-toxic and environment-friendly catalyst for synthesis of these compounds, crumpled molybdenum-doped LaFeO<sub>3</sub> nanosheets were prepared and their ability as a catalyst was explored. To the best of our knowledge, this is the first report of preparing molybdenum-doped LaFeO<sub>3</sub> and investigation of its catalytic performance toward multicomponent synthesis of organic compounds.

#### 2. Experimental

#### 2.1. General

The required materials such as; La(NO<sub>3</sub>)<sub>3</sub>.6H<sub>2</sub>O, Fe(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O, (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>.4H<sub>2</sub>O, 2-naphthol, thiobarbituric acid, barbituric acid, ethanol, ethyl acetate, acetonitrile, dichloromethane, and aromatic aldehydes were purchased from Merck, Fluka, Aldrich companies in high purity and used without further purification. FT-IR spectra were obtained as KBr pellets with a Perkin Elmer 550 spectrometer in the range 400–4000 cm<sup>-1</sup>. <sup>1</sup>H NMR was recorded in DMSO-d<sub>6</sub> and CDCl<sub>3</sub> solvents on a Bruker DRX-400 spectrometer using tetramethylsilane as the internal reference. Field-emission scanning electron microscope (FT-SEM) and elemental analysis of nano catalysts were performed on TE-SCAN MIRA3 and AIS2100 instruments. X-ray diffraction patterns of nano-structures were recorded by using CuK $\alpha$  radiation ( $\lambda$ =1.5406A) on a Holland Philips XpertPro diffractometer. Melting points obtained with a Yanagimoto micro melting point apparatus and are uncorrected. The reaction monitoring was accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck Company).

#### 2.2. A procedure for the preparation of $LaFeO_3$ nanocatalyst (A)

At first, equimolar amounts of  $La(NO_3)_3 \cdot 6H_2O$  and  $Fe(NO_3)_3 \cdot 9H_2O$  were dissolved in deionized water. Then, 1 mole of citric acid per mole of metal ions was added. The resulting sol was evaporated at 80 °C under continuous stirring until a light brown gel was obtained. Then, the gel was dried overnight at 30 °C to obtain a dry gel. Finally, the (A) were prepared by calcination of the dry gel at 620 °C for 2 h<sup>33</sup>.

#### 2.3. A procedure for the preparation of $LaMo_{0.1}Fe_{0.9}O_3$ nanocatalyst (**B**)

Initially, 1 mmol of  $La(NO_3)_3 \cdot 6H_2O$  was dissolved in deionized water. 0.9 mmol of  $Fe(NO_3)_3 \cdot 9H_2O$  and 0.1 mmol of  $(NH_4)_6Mo_7O_{24}.4H_2O$  were added and stirred for 10 min. 1 mole of citric acid per mole of metal ions  $(La^{+3}, Fe^{+3}, Mo^{+6})$  was added. The resulting sol was evaporated at 80 °C under continuous stirring until a gel was obtained. Next, the obtained product was pre-calcined in a furnace at 400 °C for 2 h. Finally, the precursor was calcined at 750 °C for 3 h in air to obtain the perovskites phase of LaFeO\_3.

2.4. General procedure for the synthesis of naphthopyranopyrimidine derivatives catalyzed by LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanosheets

A mixture of aromatic aldehyde (1.0 mmol), cyclic-1,3-dicarbonyl compound (1.2 mmol) was treated with 2-naphthol (1.0 mmol) in the presence of LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> (8 mol%). The reaction mixture was heated in an oil bath at 100 °C. The progress of the reaction was monitored by TLC. At the end of the reaction, the mixture was cooled to room temperature, the product was extracted with EtOAc ( $3 \times 20$  mL) and the catalyst was filtered for recycling tests. After drying the product was recrystallized from ethanol to obtain the pure product. All of the products were identified by physical and spectroscopic data (see Supporting Information).

**12-(4-Fluoro-phenyl)-8,12-dihydro-9H-naphtho[1'**,**2':5,6]pyrano[2,3-d]pyrimidine-9,11-(10H)** -dione: White solid; m.p> 300 °C; IR (KBr)/ν (cm<sup>-1</sup>): 3366, 3077, 2932, 1711, 1657, 1567, 1535, 1505, 1360, 1274, 1219; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/δ (ppm): 5.59 (1H, s, CH), 6.99 (2H, t, *J*= 8.8 Hz, Ar), 7.30-7.34 (2H, m, Ar), 7.39-7.48 (3H, m, Ar), 7.90-7.96 (3H, m, Ar), 11.08 (1H, s, NH), 12.09 (1H, s, NH).

**12-(3-Bromo-phenyl)-8,12-dihydro-9H-naphtho**[**1**',**2**':**5,6**]**pyrano**[**2,3-d**]**pyrimidine-9,11-(10H)** -**dione**: White solid; m.p> 300 °C; IR (KBr)/ v (cm<sup>-1</sup>): 3493, 3191, 1716, 1645, 1596, 1510, 1358, 1264, 1239; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.61 (1H, s, CH), 7.14 (1H, t, *J*= 7.6 Hz, Ar), 7.22 (1H, d, *J*= 6.8 Hz, Ar), 7.29 (1H, d, *J*= 7.6 Hz, Ar), 7.42-7.54 (4H, m, Ar), 7.95 (1H, d, *J*= 8 Hz, Ar), 7.99 (2H, d, *J*= 8.8 Hz, Ar), 11.10 (1H, s, NH), 12.13 (1H, broad s, NH).

#### 12-(Phenyl)-8,12-dihydro-9-thioxo-9H-naphtho[1',2':5,6]pyrano[2,3-d]pyrimidine-11-(10H)-o

**ne**: White solid; m.p> 300 °C; IR (KBr)/ ν (cm<sup>-1</sup>): 3436, 3057, 2969, 1650, 1578, 1556, 1387, 1288, 1235; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.59 (1H, s, CH), 7.08 (1H, t, *J*= 7.2 Hz, Ar), 7.18 (2H, t, *J*= 7.2 Hz, Ar), 7.30 (2H, d, *J*= 7.6 Hz, Ar), 7.41-7.50 (3H, m, Ar), 7.93 (1H, d, *J*= 7.6 Hz, Ar), 7.98 (2H, t, *J*= 7.8 Hz, Ar), 12.44 (1H, s, NH), 13.60 (1H, s, NH).

**12-(4-Nitro-phenyl)-8,12-dihydro-9-thioxo-9H-naphtho[1'**,**2':5,6]pyrano[2,3-d]pyrimidine-11-**(**10H)-one:** White solid; m.p= 312-314 °C (decompose); IR (KBr)/ v (cm<sup>-1</sup>): 3437, 3064, 2971, 1649, 1550, 1518, 1391, 1345, 1291, 1236; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.79 (1H, s, CH), 7.44-7.48 (3H, m, Ar), 7.61 (2H, d, *J*= 7.6 Hz, Ar), 7.95-8.03 (3H, m, Ar), 8.06 (2H, d, *J*= 7.6

Hz, Ar), 12.49 (1H, s, NH), 13.68 (1H, s, NH).

**12-(3-Nitro-phenyl)-8,12-dihydro-9-thioxo-9H-naphtho**[**1**',**2**':**5**,**6**]**pyrano**[**2**,**3**-**d**]**pyrimidine-11-**(**10H**)**-one:** White solid; m.p= 290-292 °C (decompose); IR (KBr)/ ν (cm<sup>-1</sup>): 3159, 3076, 2872, 1690, 1667, 1558, 1528, 1350, 1205, 1116; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.83 (1H, s, CH), 7.44-7.50 (4H, m, Ar), 7.94-8.03 (5H, m, Ar), 8.18 (1H, s, Ar), 12.49 (1H, s, NH), 13.66-13.70 (1H, broad s, NH).

**12-(4-Fluoro-phenyl)-8,12-dihydro-9-thioxo-9H-naphtho**[**1**',**2**':**5**,**6**]**pyrano**[**2,3-d**]**pyrimidine-1 1-(10H)-one:** White solid; m.p> 300 °C; IR (KBr)/ v (cm<sup>-1</sup>): 3389, 3055, 2972, 1653, 1578, 1553, 1386, 1287, 1235; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.62 (1H, s, CH), 7.01 (2H, t, *J*= 8.4 Hz, Ar), 7.33 (2H, t, *J*= 6.4 Hz, Ar), 7.41-7.50 (3H, m, Ar), 7.93-7.98 (3H, m, Ar), 12.45 (1H, s, NH), 13.61 (1H, s, NH).

#### 12-(4-Bromo-phenyl)-8,12-dihydro-9-thioxo-9H-naphtho[1',2':5,6]pyrano[2,3-d]pyrimidine-1

**1-(10H)-one:** Pale yellow solid; m.p= 318 °C (decompose); IR (KBr)/ v (cm<sup>-1</sup>): 3472, 3056, 2875, 1658, 1594, 1561, 1457, 1209, 1127; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.60 (1H, s, CH), 7.26 (2H, d, *J*= 8.4 Hz, Ar), 7.36-7.50 (5H, m, Ar), 7.93-7.99 (3H, m, Ar), 12.47 (1H, s, NH), 13.61 (1H, s, NH).

#### 12-(3-Bromo-phenyl)-8,12-dihydro-9-thioxo-9H-naphtho[1',2':5,6]pyrano[2,3-d]pyrimidine-1

**1-(10H)-one:** White solid; m.p= 292 °C (decompose); IR (KBr)/ v (cm<sup>-1</sup>): 3450, 3076, 2886, 1691, 1667, 1593, 1564, 1208, 1130; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.62 (1H, s, CH), 7.13 (1H, t, *J*= 7.6 Hz, Ar), 7.21 (1H, d, *J*= 7.6 Hz, Ar), 7.28 (1H, d, *J*= 7.6 Hz, Ar), 7.40-7.51 (3H, m, Ar), 7.52 (1H, s, Ar), 7.92-7.99 (3H, m, Ar), 12.49 (1H, s, NH), 13.64 (1H, broad s, NH).

**12-(2,4-Dichloro-phenyl)-8,12-dihydro-9-thioxo-9H-naphtho**[**1'**,**2':5,6**]**pyrano**[**2,3-d**]**pyrimidin e-11-(10H)-one:** White solid; m.p> 300 °C; IR (KBr)/ v (cm<sup>-1</sup>): 3443, 3056, 2967, 1651, 1580, 1553, 1387, 1286, 1237; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz)/ δ (ppm): 5.74 (1H, s, CH), 7.05-7.18 (3H, m, Ar), 7.39 (1H, d, *J*= 8.80 Hz, Ar), 7.42-7.46 (2H, m, Ar), 7.53 (1H, t, *J*= 7.60 Hz, Ar), 7.92- 8.00 (2H, m, Ar), 12.43 (1H, s, NH), 13.61 (1H, s, NH).

# 3. Results and Discussion

# 3.1. Catalyst preparation and characterizations

Scheme 1 illustrates the process of preparation (**B**). Since the sol-gel process is a well-established synthetic approach<sup>34</sup>, Catalyst (**B**) was synthesized by the citric acid-assisted sol-gel method. La(NO<sub>3</sub>)<sub>3</sub>.6H<sub>2</sub>O, Fe(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O, and (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>.4H<sub>2</sub>O were used as starting materials.



Scheme 1. Schematic preparation of perovskite-type LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanostructures

After successful preparation of (**A**) and (**B**), the catalysts were characterized by FT-IR, XRD, SEM and EDX techniques.

The FT-IR spectra of the as-prepared (**A**) and (**B**) are shown in Fig. 2. In the spectrum of (A) (Fig. 2a) the vibrations at 3431 and 1629 cm<sup>-1</sup> are assigned to stretching and bending vibrations of water molecules<sup>4</sup>, respectively. In this spectrum a clear and strong peak at wave number about 561 cm<sup>-1</sup> is assigned to the Fe–O stretching vibrations in the octahedral FeO<sub>6</sub> groups in a perovskite-type structure and confirms the formation of typical perovskite structure<sup>35</sup>. In the FT-IR spectrum of (B) (Fig. 2b), the vibration at about 596 cm<sup>-1</sup> is related to the Fe–O stretching vibrations of the octahedral FeO<sub>6</sub> and are shifted toward higher wave number. This is probably related to a change in the bond distances<sup>36</sup>. A small peak at wave number about 796 cm<sup>-1</sup> reveals the presence of Mo-O bond which caused by replacing of Mo on Fe-site<sup>37</sup>.



Fig. 2. IR spectra of a) LaFeO<sub>3</sub> NPs, b) LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanosheets

X-ray diffraction patterns of the prepared (**A**) and (**B**) nanostuctures are shown in Figure 3. The main diffraction peaks in the XRD pattern of pure (**A**) (Fig. 3a) can be indexed to cubic perovskite crystal structure (JCPDS card No. 75-0541). According to the XRD data and using the Scherer equation<sup>38</sup>, the crystallite diameter of (**A**) nanostructures was calculated to be 35 nm. Also, the X-ray diffraction pattern of (**B**) (Fig. 3b) indicates the formation of a perovskite phase with slight changes in center values of XRD peak suggesting the incorporation of Mo into the structure. The main diffraction peaks in the XRD pattern of (**B**) can be indexed as the (100), (110), (111), (200), (210), (211), (220), (221) and (310), respectively. The presence of La<sub>2</sub>O<sub>3</sub> as a minor phase (marked with \*) is presented as a low level impurity phase.



Fig. 3. XRD patterns of the as-prepared a) LaFeO<sub>3</sub> and b) LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanostructures

Table 1 shows the lattice parameters, cell volumes and average crystallite sizes of (**A**) and (**B**). The structure of (**A**) is cubic (a=b=c=3.89,  $\alpha=\beta=\gamma=90^{\circ}$ ) which after Mo doping because of low content of Mo remains cubic. As can be seen, there was no change in cell volume with Mo doping. This is possibly due to the replacement of the Fe<sup>3+</sup> ions (0.65 Å) by the Mo<sup>6+</sup> ions with similar ionic radius (0.62 Å). The crystallite sizes of 35 and 18 were obtained for (**A**) and (**B**), respectively. Mo doping could cause slowing the crystal growth process and the suppress growth of large crystallites. The decrease in crystallite size increases the surface area which is favorable for the improvement of catalytic activity <sup>39</sup>.

Journal Pre-proofs <b>Table 1.</b> Crystallite size, cell volume and lattice parameters of LaFeO <sub>3</sub> and LaMo <sub>0.1</sub> Fe <sub>0.9</sub> O <sub>3</sub>								
Sample	Lattice constant (Å)		stant	Cell volume $(\lambda^3)$	Angle (°)	Crystallite size		
	а	b	c	$(A^{*})$		(1111)		
LaFeO <sub>3</sub>	3.89	3.89	3.89	58.86	$\alpha = \beta = \gamma = 90^{\circ}$	35		
LaMo <sub>0.1</sub> Fe <sub>0.9</sub> O <sub>3</sub>	3.89	3.89	3.89	58.86	$\alpha = \beta = \gamma = 90^{\circ}$	18		

The surface morphology of the prepared (**A**) and (**B**) were demonstrated using scanning electron microscopy (Fig. 4). According to the SEM micrograph of (**A**) (Fig. 4a) the average particle size of the semi sphere-shaped nanoparticles is 46 nm. The morphology of the doped sample (**B**) changed to crumpled nanosheets (Fig. 4b, c).



Fig. 4. FESEM images of a) LaFeO<sub>3</sub> nanoparticles, and crumpled LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanosheets (b) 1

#### μm (c) 3 μm

The energy dispersive X-ray (EDX) analysis was performed to determine the elements of the synthesized (**A**) and (**B**) nanostructures (Fig. 5). The EDX spectrum of (**A**) exhibited the peaks of La, Fe and O elements (Fig. 5a). Also, the EDX results show the elemental composition of (**B**) sample as displayed in Fig. 5b. The weight percentage of the elements (W %) and the theoretical values are in good agreement which confirms the purity of the as-synthesized catalyst.



Fig. 5. EDX spectrum of a) LaFeO<sub>3</sub>, b) LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanocatalyst

The specific surface area of (**B**) based on the Brunaure-Emmett-Taller (BET) analysis of the nitrogen absorption/desorption isotherms is 172.46 m<sup>2</sup>g<sup>-1</sup>. Total pore volume and pore size of (**B**) are 0.10 cm<sup>3</sup>g<sup>-1</sup> and 2.11 nm, respectively (Fig. 6a). The particles size distribution histogram of (**B**) is demonstrated in Fig. 6b. The average size of (**B**) nanosheets was determined about 166 nm.



Fig. 6. a) Nitrogen absorption/desorption isotherms of (B), b) particles size distribution

# 3.2. Catalytic activity of the prepared LaMoFeO<sub>3</sub> nanosheets in the synthesis of naphthopyranopyrimidines

The purpose of this work was evaluation of the activity of perovskite-type (**B**) nanosheets as a heterogeneous catalyst for synthesis of naphthopyranopyrimidine derivatives (Scheme 2). The reactions in the presence of (**B**) were completed within short times, and all products were obtained in excellent yields by a simple workup.



Scheme 2. Synthesis of naphthopyranopyrimidines in the presence of perovskite-type

LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> as a catalyst

In attempt develop optimal catalytic system for the synthesis of an to an naphthopyranopyrimidines, the reaction of 4-nitrobenzaldehyde (1 mmol), barbituric acid (1.2 mmol), and 2-naphthol (1 mmol) was selected as a model reaction and the effects of varying the catalyst amount and reaction time were studied. The results are summarized in Table 2. As can be seen in this Table show that in the absence of a catalyst, no conversion of the starting materials into the desired product occurs (Table 2, entry 1), confirming that the presence of a catalyst is necessary for this reaction. The model reaction was carried out in the presence of (A) as catalyst. The low yield of the product within 120 min was obtained (Table 1, entry 2). Therefore, in order to improve the yield and enhance the reaction rate, catalyst (B) was prepared and used as a reactive catalyst in this reaction. It was observed that using the prepared nanocatalyst led to decrease the reaction time and increase the yield of the desired product. The studies on the variation in the amounts of the catalyst, 5, 6, 8, and 10 mol%, suggest that product yield rises with increase of the catalyst amount which is due to the increasing number of active sites. However, the catalyst amount beyond 8 mol% showed no change in the yield (Table 2, entry 6). So, the optimum amount of the catalyst is 8 mol% of the nanosheets (Table 2, entry 5).

Since perovskites have significant physical and chemical properties like high thermal stability and oxygen mobility show catalytic activity for several reactions<sup>40</sup>. Catalytic activity of various types of perovskite oxides has been investigated due to their structural simplicity, diversity and flexibility<sup>41</sup>. Another advantage of these compounds is that their properties can be tuned by the partial or full substitution of the A or B cations<sup>42</sup>. The acid-base properties of multi-component

perovskites result in noteworthy catalytic activities of them. In perovskites, the basicity and acidity are related to the surface anions ( $O^{2-}$ ) and cations ( $M^{\delta^+}$ ), respectively. High specific surface area makes nanosheets favorable for many surface-active applications such as organic catalysis. Generally, the mixed metal oxide nanostructures have a large surface area that is responsible for enhanced active acidic and basic sites compared to the individual component oxides<sup>43,44</sup>.

In order to investigate the synergy effects of Fe, Mo, and La, the individual catalytic potential of La(NO)<sub>3</sub>.6H<sub>2</sub>O, (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>, and FeCl<sub>3</sub>.6H<sub>2</sub>O was investigated in the model reaction. The reaction by using these catalysts afforded the products in lower yields and longer reaction time in compare with our method (Table 2, entries 5, 7, 8 and 9). The results of Table 2 suggest a synergy effect in perovskites which is conducive to the enhancement of the catalytic activity of **(B)**. Doping of molybdenum can be enhancing the acidity of the catalyst, so, the high catalytic activity of **(B)** can be due to the presence of more surface acidic sites. Also, the **(B)** sample with a layered structure has larger specific areas than the **(A)** sample, which is a spherical particle, and it might be an advantageous feature providing more available Lewis acid sites for the catalytic reaction. So, here, the combination of synergy effects, large surface area and surface acidic properties of **(B)** lead to prominent catalytic performance.

	-OH + OH +	est e, 100 °C	O O NO2 O N O H
Entry	Catalyst/catalyst amount (mol%)	Time (min)	Yield (%) <sup>b</sup>
1	No catalyst	180	0
2	Nano LaFeO <sub>3</sub> (8 mol%)	120	35
3	LaFeMoO <sub>3</sub> (5 mol%)	20	67
4	LaFeMoO <sub>3</sub> (6 mol%)	20	80
5	LaFeMoO <sub>3</sub> (8 mol%)	20	92
6	LaFeMoO <sub>3</sub> (10 mol%)	20	92
7	La(NO) <sub>3</sub> . 6H <sub>2</sub> O (8 mol%)	120	21
8	(NH4)6M07O24 (8 mol%)	120	30
9	FeCl <sub>3</sub> . 6H <sub>2</sub> O (8 mol%)	120	26

**Table 2.** Effect of different amounts of catalyst on the synthesis of naphthopyranopyrimidines<sup>a</sup>

<sup>a</sup>General reaction conditions: 4-nitrobenzaldehyde (1 mmol), barbituric acid (1.2 mmol), and 2-naphthol (1 mmol).

<sup>b</sup>Isolated yields.

Also, in order to survey the effects of temperature and solvent, the reaction was performed in the presence of an optimum amount of (**B**) in CH<sub>2</sub>Cl<sub>2</sub>, CH<sub>3</sub>CN, H<sub>2</sub>O, and EtOH under reflux condition (Table 3 entries 1-4), and under solvent-free condition at 80, 90, 100, and 110 °C (Table 3, entries 5-8). The best results were obtained under solvent-free condition at 100 °C (Table 3, entry

7).

# **Table 3.** Effect of different solvents and temperatures on the synthesis of naphthopyranopyrimidines<sup>a</sup>

CC	$ \begin{array}{c} OH \\ \bullet \\ \bullet \\ H \end{array} \begin{array}{c} O \\ \bullet \\ \bullet \\ H \end{array} \begin{array}{c} O \\ \bullet \\ \bullet \\ H \end{array} \begin{array}{c} O \\ \bullet \\$	H Catalyst		
Entry	Solvent	Condition	Time (min)	Yield (%) <sup>b</sup>
1	CH <sub>2</sub> Cl <sub>2</sub>	Reflux	180	42
2	CH <sub>3</sub> CN	Reflux	120	57
3	H <sub>2</sub> O	Reflux	180	trace
4	EtOH	Reflux	90	79
5	Solvent-free	80 °C	20	76
6	Solvent-free	90 °C	20	87
7	Solvent-free	100 °C	20	92
8	Solvent-free	110 °C	20	92

<sup>a</sup>General reaction conditions: 4-nitrobenzaldehyde (1 mmol), barbituric acid (1.2 mmol), and 2-naphthol (1 mmol), LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> (8 mol%). <sup>b</sup>Isolated yields.

Thus, 8 mol% of the nanocatalyst, solvent-free condition, and 100 °C are found to be optimum conditions for the conversion of 4-nitrobenzaldehyde, barbituric acid, and 2-naphthol to the

corresponding naphthopyranopyrimidine. Adopting these optimized conditions, the scope of the present investigation is evaluated toward the synthesis of naphthopyranopyrimidine derivatives (Table 4). As shown in this Table, the reaction afforded the corresponding naphthopyranopyrimidines in high yields and short reaction times. The reactions were clean and did not require the chromatographic purification. The products were isolated by a simple work up and obtained in high purity. These results demonstrated that this method is an efficient approach for the one pot multi-component synthesis of naphthopyranopyrimidines. The structures of the products were characterized by spectroscopic data such as; IR, <sup>1</sup>H NMR and melting points.



$() \qquad \qquad$									
Entry	Y	v	D	Product	Time (min)	Vield <sup>b</sup> (%)	MI	P (°C)	
Entry	Λ		K	Troduct	Time (iiiii)	Tield (70)	Found	Reported	
1	0	CH <sub>3</sub>	Н	O V V V V V V V V V V V V V V V V V V V	30	84	226-228	223-225 <sup>25</sup>	
2	0	CH <sub>3</sub>	4-NO <sub>2</sub>	NO <sub>2</sub> O O N CH <sub>3</sub>	30	90	294-296	291-293 <sup>25</sup>	

				Journal Pre-	-proofs			
3	0	CH <sub>3</sub>	3-NO <sub>2</sub>	O O O O CH <sub>3</sub>	40	87	>300 °C	313-315 <sup>27</sup>
4	0	CH <sub>3</sub>	4-F	F O O N CH <sub>3</sub>	40	89	302-304	305-307 <sup>25</sup>
5	0	Н	Н	O O N O H	25	91	> 300	355-357 <sup>45</sup>
6	0	Н	4-NO <sub>2</sub>	NO <sub>2</sub> O O N H	20	92	> 300	371-373 <sup>45</sup>
7	0	Н	3-NO <sub>2</sub>		25	90	> 300	371-373 <sup>45</sup>
8	0	Н	4-F		20	91	> 300	-
9	0	н	4-Br	Br O N O H	20	90	> 300	297-299 <sup>45</sup>
10	0	Н	3-Br	O O N H	25	89	> 300	-

				Journal Pre-	oroofs			
11	S	Н	Н		30	87	> 300	-
12	S	Н	4-NO <sub>2</sub>	NO <sub>2</sub> O O N H	25	89	312-314	-
13	S	Н	3-NO <sub>2</sub>	NO <sub>2</sub> O N N S H	30	86	290-292	-
14	S	Н	4-F		25	88	> 300	-
15	S	Н	4-Br	Br O N S	30	87	318 °C	-
16	S	Н	3-Br	O O N H	35	84	292	-
17	S	Н	2,4-Cl		40	82	> 300	-

<sup>a</sup>General reaction conditions: aldehyde (1 mmol), 2-naphthol (1 mmol), cyclic-1,3-dicarbonyl compound (1.2 mmol), LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> (8 mol%). <sup>b</sup>Isolated yield.

To investigate the stability and reusability of the catalyst, after completion of the model reaction and separation of the catalyst from the reaction media, it was washed for several times with hot ethanol to remove adsorbed organic impurities from its surface, dried at 120 °C for 3 h and reused in next runs under the optimized reaction conditions. The catalyst could be recycled and reused at least for five runs without remarkable decrease in its catalytic activity (Figure 7a). The reused catalyst was analyzed using XRD pattern (Figure 7b). No significant difference between the XRD patterns of reused and the fresh catalyst confirms the stability of (**B**) nanocatalyst under the reaction conditions. Also, in order to investigate the catalyst leaching, the inductively coupled plasma (ICP) analysis was performed on the reaction mixture after separation of the catalyst. The results were shown that the leaching of the metal ions was negligible.



Fig. 7. The reusability study of LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanocatalyst for the model reaction

In order to show the merit of this study, the results of this research were compared with some reported literatures (Table 5)<sup>25,26,28</sup>. So, the reaction of 2-naphthol, 4-nitro benzaldehyde, and

1,3-dimethylbarbituric acid was chosen as a model reaction and the comparison was performed on the basis of reaction time and product yields. This methodology includes a number of advantages such as general applicability, applying a nontoxic and green catalyst, easy separation of product and nanocatalyst, reusability of the nanocatalyst for five times without considerable loss of catalytic activity, lower reaction times and higher yields.

	$\rightarrow OH \qquad $	р н		NO	2 O V V CH <sub>3</sub> CH <sub>3</sub>
Entry	Catalyst/	Catalyst amount	Time	Yield	Pof
Entry	conditions	(mol%)	(min)	(%)	Kel.
1	P <sub>2</sub> O <sub>5</sub> , solvent-free, 120 °C	20	80	58	26
2	InCl <sub>3</sub> , solvent-free, 120 °C	30	75	65	26
3	KAl(SO <sub>4</sub> ) <sub>2</sub> .12H <sub>2</sub> O, PEG-400, 60 °C	15	50	86	25
4	I <sub>2</sub> , solvent-free, 120 °C	10	55	86	28
5	LaMoFeO <sub>3</sub> , solvent-free, 100 °C	8	30	90	This work

Table 5. Comparison of the catalytic efficiency of LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> with other catalysts

Two probable mechanisms for the synthesis of naphthopyranopyrimidines in the presence of

(**B**) are proposed in Scheme 3. In Scheme 3a, the first step involves the formation of intermediate **4**, ortho-quinone methides, which was formed by the nucleophilic attack of 2-naphthol to aldehyde and elimination of one  $H_2O$  molecule. Adsorption of the aldehyde on the catalyst surface enhances the electrophilicity of the carbonyl group which is followed by the nucleophilic attack of 2-naphthol to them. Then, Michael addition of intermediate **4** with cyclic 1,3-dicarbonyl compound followed by cyclodehydration yield the desired product **8**.

The second probable mechanism (Scheme 3b) involves the activation of carbonyl group of aldehyde, nucleophilic attack of a 1,3-dicarbonyl compound to the aldehyde, Michael addition of intermediate **3** with 2-naphthol, and cyclodehydration.





Scheme 3. Two proposed reaction pathways for the synthesis of naphthopyranopyrimidines using perovskite-type  $LaMo_{0.1}Fe_{0.9}O_3$  nanosheets as catalyst

The proposed reaction mechanisms were supported by two control experiments that were performed in the presence of  $(\mathbf{B})$  under similar reaction conditions (Scheme 4). In both cases, the product formation was observed, which supports the proposed mechanisms.



Scheme 4. Control reactions catalyzed by LaFeMoO<sub>3</sub>

# 4. Conclusion

In this research, we have synthesized environmentally friendly, non-toxic, highly efficient, stable, separable and recyclable crumpled LaMo<sub>0.1</sub>Fe<sub>0.9</sub>O<sub>3</sub> nanosheets as a catalyst for the one pot three-component coupling of 2-naphthol, aromatic aldehydes, and cyclic-1,3-dicarbonyl compounds under solvent-free condition. In addition, the catalytic methodology offers advantages, such as short reaction times, high yields, avoidance of strong acid media, low catalyst requirement and very easy work up. Furthermore, the synthesized compounds are promising candidates for chemical biology and drug discovery.

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