

RESEARCH PAPER

## A facile and efficient synthesis of indole and acridine derivatives using (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> nanostructure

Mahshid Abdoli, Navabeh Nami\*, Zinatossadat Hossaini

Department of Chemistry, Qaemshahr Branch, Islamic Azad University, Qaemshahr, Iran.

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### ABSTRACT

Acid functionalized multi-walled carbon nanotubes (MWCNTs)-COOH were reacted with La(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O in acetic acid by ultrasonication at 60°C to gain (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> hybrid. This nano-material was used as an efficient catalyst for the synthesis of some heterocycles containing nitrogen. Acridine and indole derivatives were obtained by the reaction of isatin or dimedone with some amino compounds such as thiosemicarbazone, amino acids, and anthranilic acid using (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> (5 mol%) in ethanol under reflux conditions. The products were gained in mild reaction conditions and good yields and identified by CHN analysis, NMR, and FT-IR spectra. The amount of La or La<sub>2</sub>O<sub>3</sub>-loading in (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> was measured using the inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis. The leaching of catalyst was measured using a hot filtration method. There was no leaching to confirm the stability of the catalyst. The catalyst was simply separated at the end of the reaction, washed, dried, and re-entered to a fresh reaction mixture 5 times without considerable loss of activity.

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### INTRODUCTION

Natural and synthetic heterocyclic compounds containing nitrogen are of considerable interest due to their technical properties and are widely used in medicinal chemistry [1,2]. Many compounds containing indole nucleus exhibit antiviral, anticancer, antitubercular, antimalarial, antibacterial, antioxidant, and antileishmanial activities. These properties of indoles have led to massive research and synthesis of a wide variety of structures [3,4]. Also, acridine derivatives are very important chemical compounds in biological and pharmacological properties such as antimicrobial and anticancer activities, due to their planar structure that can strongly link to the DNA [5,6]. Indeed, for the preparation of heterocyclic compounds containing nitrogen a huge variety of synthesis methods and analogs have been reported over the years [7-9].

Multi-walled carbon nanotubes (MWCNTs) are very attractive and well-known chemical compounds because of their special physical and chemical properties and a wide variety of industrial and biological activities such as drug delivery [10,11], electronics [12], catalysis [13-15], biosensors [16], biomedical [17], storage [18], and photovoltaic [19] activities.

Carbon nanotubes (CNTs) are effective supports for nanometal particles (NP) such as zinc oxide, rare metal oxide, or manganese oxide, and together they represent hybrid structures (NP-CNTs) that combine the unique properties of both [20]. Lanthanum oxide (La<sub>2</sub>O<sub>3</sub>) nanoparticles, one of the rare earth oxides, have attracted considerable attention due to their widely technical applications such as luminescence, magnetic, electronic, and catalytic properties, which are significantly different from those of bulk materials [21-23]. Nano-metal oxide particles and immobilized multi-walled

\* Corresponding Author Email: [navabehnami@yahoo.com](mailto:navabehnami@yahoo.com)

carbon nanotubes (MWNTs) have shown excellent catalytic properties in heterocyclic reactions [24]. Many metal oxides have been used to modify the surface of MWCNTs [25,26]. Due to the presence of very active sites on the large surface of (MWCNTs)-COOH/MxOy hybrid, it can be used as an effective catalyst in chemical reactions [27].

Because of the above reasons and based on our previous research [15], we present a simple method for the synthesis of some acridine and indole derivatives using (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> hybrid as an effective reusable catalyst under mild reaction conditions and good yields.

## EXPERIMENTAL METHOD

### Chemicals and Instrumentation

Solvents and chemicals were purchased from Aldrich and Merck. MWCNTs and (MWCNTs)-COOH (OD: 20-30 nm) were purchased from US Research Nanomaterials, Inc. (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> was distinguished by powder X-ray diffraction (XRD) PW 3040/60 X'Pert PRO diffractometer system, using Cu K $\alpha$  radiation with ( $\lambda = 1.5418 \text{ \AA}$ ) in the range of  $2\theta = 20\text{--}80^\circ$  at room temperature. The morphology and sizes of NPs were measured using a transmission electron microscope (TEM, 150 kV, and Philips-CM 10) and a scanning electron microscope (SEM) by Day Petronic Company-Iran. FT-IR measurements were recorded on a Shimadzu 8400s spectrometer with KBr plates. The NMR spectra were determined on Bruker XL 400 (400 MHz) instruments. Mass-spectrometric measurements were made on an Agilent 6890 N Network GC system. The elemental analysis was performed by the microanalytical service of Day Petronic Company. Melting points were obtained on an Electrothermal 9100 without further corrections.

### Synthesis and purification of (MWCNTs)-COOH

MWCNT (1 g) was added to 300 ml concentrated nitric acid and the mixture was refluxed for 8h, then centrifuged for 30 min at 10000 rpm. The functionalized MWCNTs were added in 800 ml redistilled water and filtered by a cellulose nitrate membrane filter (0.45  $\mu\text{m}$  pore size) using a vacuum filtration assembly. The product was frequently washed with distilled water to neutralize the pH of the filtrate. The filtered compound was dried in a vacuum oven at 80°C for 24 h and the obtained (MWCNTs)-COOH were characterized using different techniques [28].

### Preparation of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> hybrid

(MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> hybrid was prepared according to our previously reported procedures [15]. The functionalized (MWCNTs)-COOH (0.5 g) and La(NO<sub>3</sub>)<sub>3</sub>.6H<sub>2</sub>O (0.1 g) were added into 3 ml of acetic acid by ultrasonication at 60°C for 30 min. Then, under constant magnetic stirring, the reaction mixture was gently stirred for 24 extra hours. The solvent was evaporated, and the precipitate was then calcined at 200 °C for 2h.

### General procedure for the synthesis of some heterocycles containing nitrogen

Raw materials (1 mmol) and (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> (5 mol %) were mixed and reacted in ethanol (10 ml) under reflux conditions. The completion of the reaction was determined by TLC using *n*-hexane: ethyl acetate (1:1) and appeared by a UV lamp (254 & 366 nm). At the end, the reaction mixture was centrifuged and the catalyst was filtered and washed with ethanol (3 x 5 ml) and water (3 x 5 ml), dried at 100 °C for 2 h, and reused for the same reaction. The rest of the reaction mixture was evaporated, and the crude product was purified by recrystallization from ethanol/water or short-column chromatography on silica gel (*n*-hexane: ethyl acetate / 1:1). The products were determined by elemental analysis, NMR, and FT-IR spectra.

### 2-((*E*)-4-nitrobenzylidene)-*N*-((*Z*)-2-oxoindolin-3-ylidene)hydrazine-1-carbothioamide (1)

Reaction of 4-nitrobenzaldehyde thiosemicarbazone (2.24 g, 0.01 mol) and isatin (1.47 g, 0.01mol). Reaction time 90 min, Yield 3.32 g (94%), Yellow powder, mp > 300°C. FT-IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3424 (NH), 3015 (CH<sub>Aro</sub>), 2971 (CH<sub>Aliph</sub>), 1733 (C=O), 1617 (C=N), 1464 (NO<sub>2</sub>). <sup>1</sup>H NMR spectrum (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  ppm (*J*, Hz): 10.17 (1H, s, NH), 8.42 (2H, d, *J* = 8.8 Hz, CH<sub>Ar</sub>), 8.17 (1H, s, CH), 8.09 (2H, d, *J* = 8.8 Hz, CH<sub>Ar</sub>), 7.49 (1H, t, *J* = 7.6 Hz, CH<sub>Ar</sub>), 7.37 (1H, d, *J* = 7.6 Hz, CH<sub>Ar</sub>), 7.34(1H, d, *J* = 7.6 Hz, CH<sub>Ar</sub>), 7.28 (1H, t, *J* = 7.6 Hz, CH<sub>Ar</sub>). Found, %: C, 54.56; H, 3.09; N, 19.76. C<sub>16</sub>H<sub>11</sub>N<sub>5</sub>O<sub>3</sub>S. Calculated, %: C, 54.39; H, 3.14; N, 19.82.

### 3-(((*Z*)-*N*'-((*E*)-furan-2-ylmethylene)carbamohydrazonoyl)thio)-2-oxoindolin-3-yl (*Z*)-*N*'-((*Z*)-furan-2-ylmethylene)carbamohydrazonothioate (2)

Reaction of furfural thiosemicarbazone (3.38 g, 0.02 mol) and isatin (1.47 g, 0.01mol). Reaction

time 90 min, Yield 4.48 g (96%), Dark red powder, mp > 300°C. FT-IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3422.68 (NH), 3367.06 (NH<sub>2</sub>), 3267.63 (NH), 3162.20 (NH<sub>2</sub>), 3039.76 (CH<sub>Aro</sub>), 2924.70 (CH<sub>Aliph</sub>), 1729.12 (C=O), 1618.95 (C=N), 1597.58 (C=C), 1549.19 (C=C), 1503.80, 1466.20, 1272.98, 1222.05, 1190.65, 1148.83 (C-N), 1085.29 (C-O). <sup>1</sup>H NMR spectrum (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  ppm (*J*, Hz): 11.43 (1H, br, NH), 11.04 (1H, br, NH), 8.22 (2H, br, NH<sub>2</sub>), 7.96 (2H, s, N=CH), 7.81 (2H, d, *J* = 1.2, CH<sub>furan</sub>), 7.63 (2H, br, NH<sub>2</sub>), 7.58 (1H, t, *J* = 7.6, CH<sub>isatin</sub>), 7.50 (1H, d, *J* = 7.6, CH<sub>isatin</sub>), 7.06 (1H, t, *J* = 7.6, CH<sub>isatin</sub>), 6.96 (2H, d, *J* = 3.6, CH<sub>furan</sub>), 7.96 (1H, s, CH), 6.90 (1H, d, *J* = 11.2, CH<sub>isatin</sub>), 6.62 (2H, dd, *J* = 1.6, 3.4, CH<sub>furan</sub>). <sup>13</sup>C NMR spectrum (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$ , ppm: 184.87, 178.15, 159.65, 151.10, 149.70, 145.45, 138.91, 133.11, 125.20, 123.34, 118.21, 113.49, 112.81, 112.67. Found, %: C, 51.46; H, 3.59; N, 20.65. C<sub>20</sub>H<sub>17</sub>N<sub>7</sub>O<sub>3</sub>S<sub>2</sub>. Calculated, %: C, 51.38; H, 3.67; N, 20.97.

#### [1,4]oxazino[2,3-*b*]indol-3(5*H*)-one (3)

Reaction of glycine (750 mg, 0.01 mol) and isatin (1.47 g, 0.01 mol). Reaction time 90 min, Yield 1.59 g (86%), Yellow powder, mp > 300°C. <sup>1</sup>H NMR spectrum (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  ppm (*J*, Hz): 7.48 (2H, t, *J* = 7.6 Hz, CH<sub>Ar</sub>), 7.37 (1H, d, *J* = 7.6 Hz, CH<sub>Ar</sub>), 7.29 (1H, s, CH), 7.28 (1H, t, *J* = 7.6 Hz, CH<sub>Ar</sub>), 3.58 (s, 2H, CH<sub>2</sub>). Found, %: C, 64.65; H, 3.32; N, 15.15. C<sub>10</sub>H<sub>6</sub>N<sub>2</sub>O<sub>2</sub>. Calculated, %: C, 64.52; H, 3.25; N, 15.05.

#### 3-((5,5-dimethyl-3-oxocyclohex-1-en-1-yl)amino)piperidine-2,6-dione (4)

Reaction of glutamine (1.46 g, 0.01 mol) and dimedone (1.40 g, 0.01 mol). Reaction time 60 min, Yield 2.25 g (90%), Yellow powder, mp 258-260°C. FT-IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3429, 2959, 1650, 1616, 1581. <sup>1</sup>H NMR spectrum (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  ppm (*J*, Hz): 11.03 (1H, br, NH), 5.26 (1H, s, NH), 5.19 (1H, s, CH), 3.89 (1H, q, *J* = 7.2 Hz, CH), 3.43 (1H, q, *J* = 7.2 Hz, CH), 2.25 (1H, s, CH), 2.11 (4H, br, 2CH<sub>2</sub>), 2.08 (1H, s, CH), 1.26 (1H, t, *J* = 7.2 Hz, CH), 1.04 (1H, t, *J* = 7.2 Hz, CH), 0.97 (6H, s, 2CH<sub>3</sub>). Found, %: C, 62.56; H, 7.37; N, 11.21. C<sub>13</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>. Calculated, %: C, 62.38; H, 7.25; N, 11.19.

#### 1-(5,5-dimethyl-3-oxocyclohex-1-en-1-yl)-3-hydroxy-6,6-dimethyl-1,5,6,7-tetrahydro-4*H*-indol-4-one (5)

Reaction of glycine (750 mg, 0.01 mol) and dimedone (2.80 g, 0.02 mol). Reaction time 60

min, Yield 2.77 g (92%), Yellow powder, mp 146-148°C. FT-IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3434, 1639, 1633, 1291, 1210, 1162, 1026, 1000. <sup>1</sup>H NMR spectrum (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  ppm (*J*, Hz): 7.04 (1H, s, CH), 5.19 (1H, s, CH), 2.50 (2H, s, CH<sub>2</sub>), 2.23 (2H, s, CH<sub>2</sub>), 2.12 (2H, s, CH<sub>2</sub>), 1.95 (2H, s, CH<sub>2</sub>), 0.98 (6H, s, 2CH<sub>3</sub>), 0.96 (6H, s, 2CH<sub>3</sub>). <sup>13</sup>C NMR spectrum (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$ , ppm: 194.67, 171.51, 163.27, 139.34, 102.85, 94.59, 94.58, 50.72, 44.78, 44.77, 42.31, 42.30, 32.81, 32.80, 28.39, 28.38. Found, %: C, 71.85; H, 7.43; N, 4.74. C<sub>18</sub>H<sub>23</sub>N<sub>3</sub>O<sub>3</sub>. Calculated, %: C, 71.73; H, 7.69; N, 4.65.

#### 1-Hydroxy-3,3-dimethyl-3,10-dihydroacridin-9(4*H*)-one (6)

Reaction of anthranilic acid (1.37 g, 0.01 mol) and dimedone (2.10, 0.015 mol). Reaction time 80 min, Yield 560 mg (96%), Yellow powder, mp 218-220°C. FT-IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3428, 3010, 2958, 2304, 1903, 1679, 1615. <sup>1</sup>H NMR spectrum (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  ppm (*J*, Hz): 11.00 (br, 1H, OH), 9.41 (br, 2H, NH), 7.67 (1H, dd, *J* = 4, 8 Hz, CH<sub>Ar</sub>), 7.58 (1H, t, *J* = 8 Hz, CH<sub>Ar</sub>), 7.43 (1H, d, *J* = 8 Hz, CH<sub>Ar</sub>), 7.21 (1H, m, CH<sub>Ar</sub>), 6.72 (1H, d, *J* = 8 Hz, CH<sub>Ar</sub>), 6.49 (1H, t, *J* = 8 Hz, CH<sub>Ar</sub>), 5.19 (2H, s, 2CH), 2.39 (4H, s, 2CH<sub>2</sub>), 2.08 (4H, s, 2CH<sub>2</sub>), 1.03 (12H, s, 4CH<sub>3</sub>). <sup>13</sup>C NMR spectrum (100 MHz, DMSO-*d*<sub>6</sub>),  $\delta$ , ppm: 196.45, 170.08, 159.40, 151.95, 140.90, 134.17, 133.67, 131.93, 131.60, 124.04, 123.82, 122.49, 116.76, 115.00, 110.04, 102.88, 99.17, 50.58, 43.26, 32.78, 28.38, 28.31. Found, *m/z*: 241.10 [M]<sup>+</sup>. C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub>. Calculated, *m/z*: 241.11

## RESULTS AND DISCUSSION

The possible interaction between La(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O and (MWCNTs)-COOH was investigated using FT-IR spectroscopy, TGA/DTA, XRD, TEM, SEM, and EDX which leads to the preparation and stabilization of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> [15].

X-ray diffraction (XRD) is normally used to study and characterize the crystallization and average size of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>. In Fig. 1, the XRD pattern of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> shows seven intense peaks in the whole spectrum of 2 $\theta$  values ranging from 5° to 80°. The presence of six distinct high diffraction peaks at 2 $\theta$  values of 13.106°, 22.842°, 29.555°, 30.829°, 31.328°, 40.097°, 41.167° and 44.508° respectively, (JCPDS Number. (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>: 00-023-0322 [15, 29,30] confirmed that the (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> had been formed. The other diffraction

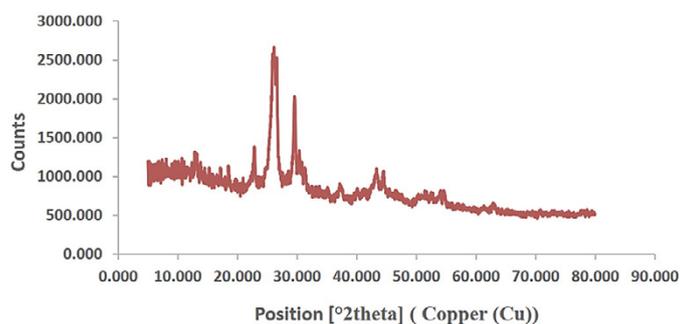


Fig. 1. XRD of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> nanocomposite [15]

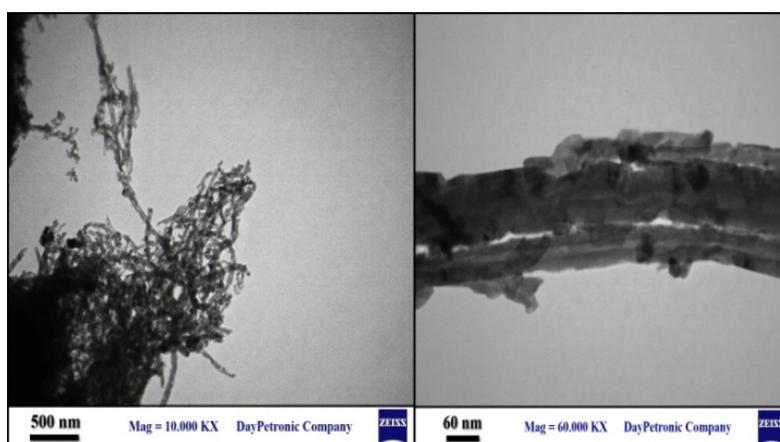


Fig. 2. TEM image of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> nanocomposite

peaks could be due to some chemical compounds and crystals on the surface of the nanoparticle. The wide X-ray diffraction peaks around their bases indicate that the (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> is in nano sizes. With the XRD pattern, the average diameter which can be calculated from Scherrer's equation [31] ( $D = K\lambda/\beta\cos\theta$ , where  $\beta$  is the peak width at half maximum,  $\lambda$  is X-ray wavelength, and  $K$  is constant) is obtained about 43.2 nm.

The morphology and size of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> were studied using transmission electron microscopy (TEM) in Fig. 2. The TEM image indicates that the La<sub>2</sub>O<sub>3</sub> nanoparticles are well bonded to the surface of multi-wall carbon nanotubes. In addition, the TEM values are in good agreement with the XRD's.

Fig. 3 shows the SEM images of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> and nanotubes outer diameter distribution. They indicate that La<sub>2</sub>O<sub>3</sub> nanoparticles have grown as nanoparticles on the surface of the (MWCNTs)-COOH.

The outside diameter (OD) of (MWCNTs)-COOH was 20-30 nm, but after modification it

was changed to 40-50 nm. It is shown that La<sub>2</sub>O<sub>3</sub> nanoparticles have grown as nanoparticles on the surface and inside of the (MWCNTs)-COOH.

In Fig. 4, EDX analysis was performed to confirm the elements presented in the resulted (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>, and the analysis revealed the presence of La, O, and C which demonstrates the success of the decoration process with La<sub>2</sub>O<sub>3</sub> nanoparticles.

(MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> (5 mol%) was used as an efficient catalyst for the synthesis of some heterocyclic compounds like acridine and indole derivatives with the reaction of isatin, dimedone, and amines or amino acids in ethanol. The structures were chemically characterized by elemental analysis, FT-IR, and NMR spectra. Because of its excellent capacity, exceedingly simple workup and satisfactory yields, (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> was proved to be a good catalyst for these reactions.

In the preliminary stage of the investigation, the model reaction of glycine and dimedone (Scheme 2) was carried out by using various

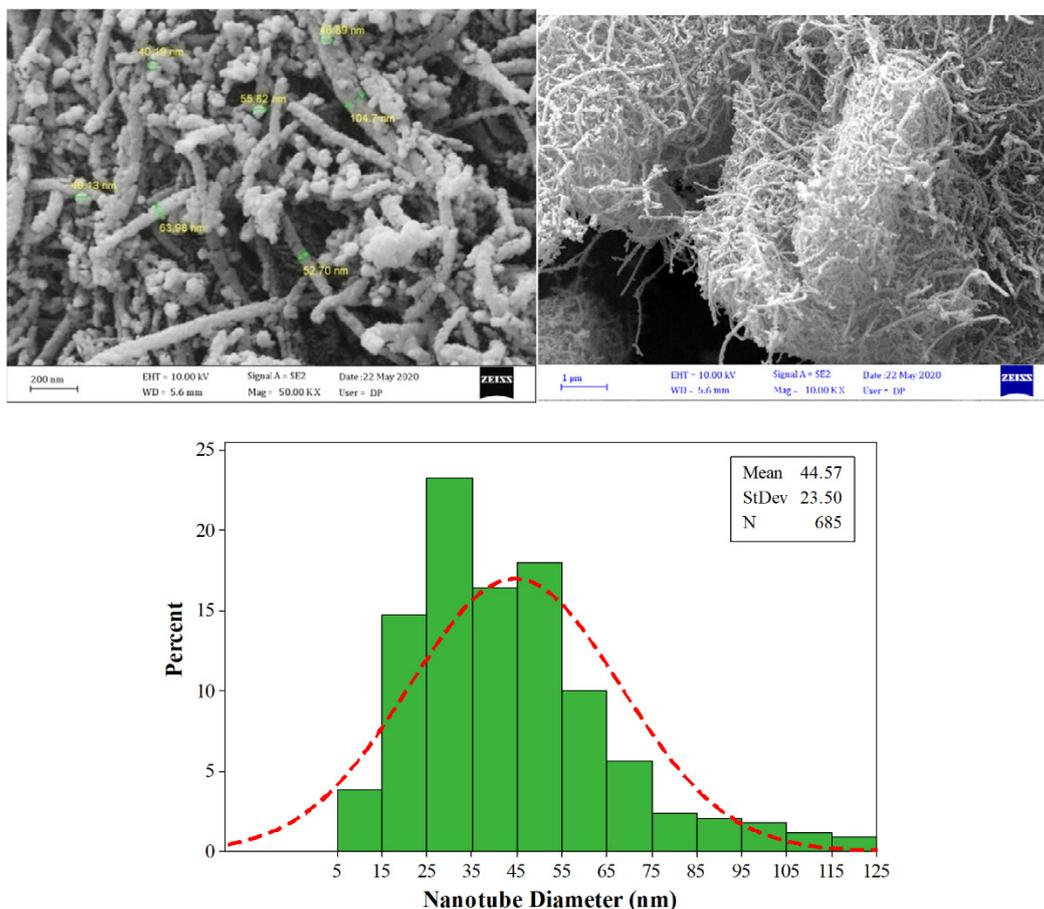


Fig. 3. (a,b) SEM micrograph of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> nanocomposite, (c) Nanotubes outer diameter distribution of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>

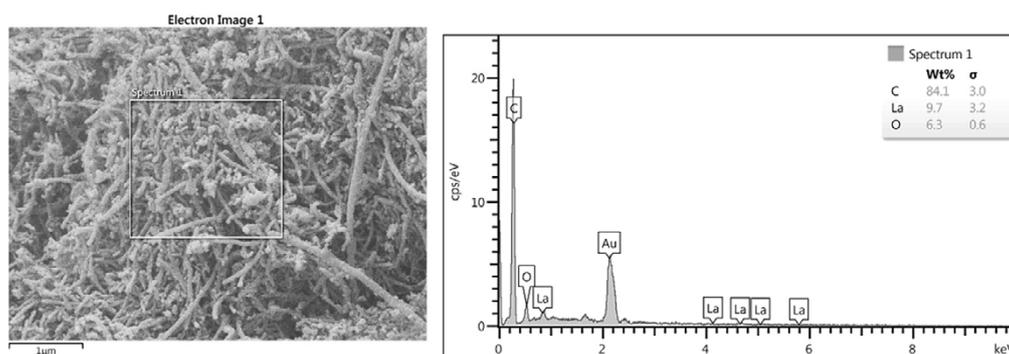
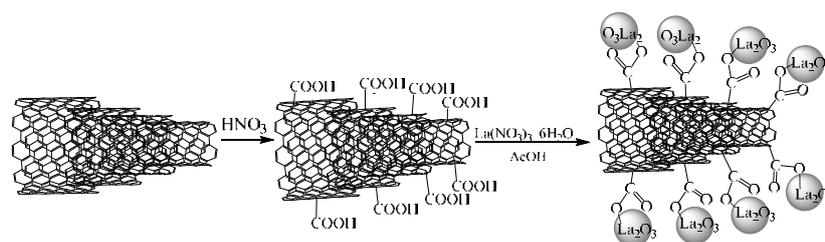


Fig. 4. EDX of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> nanocomposite [15]

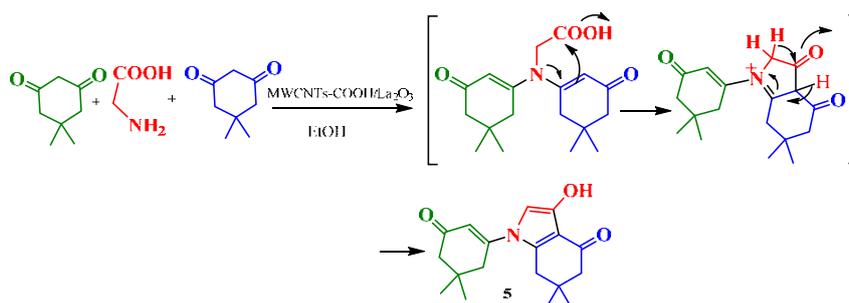
amounts of NPs in various solvents and solvent-free conditions. As shown in Table 1, the optimum amount of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> was 5 mol%. Decreasing the amount of the catalysts results in a decrease in the yield of the reaction, while increasing the amount of the catalysts does not improve the yield of the product any further.

In the absence of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>, the result of the reaction on the TLC plate even after 2h wasn't satisfactory. The best yield of the product was acquired with 5 mol% of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> in ethanol under mild reaction conditions (Table 1, Entry 14).

The structure of compound 5 was confirmed



Scheme 1. Preparation of (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> nanocomposite



Scheme 2. Synthesis of compound 5

Table 1. The reaction of glycine (1 mmol) and dimedone (1 mmol) under different conditions

Entry	Solvent	(MWCNTs)- COOH/La <sub>2</sub> O <sub>3</sub> (mol%)	Reaction Time (min)	Yield(%)
1	THF	-	120	trace
2	THF	3	60	45
3	THF	4	60	56
4	THF	5	60	78
5	THF	7	60	78
6	H <sub>2</sub> O	-	120	trace
7	H <sub>2</sub> O	3	60	36
8	H <sub>2</sub> O	4	60	43
9	H <sub>2</sub> O	5	60	57
10	H <sub>2</sub> O	7	60	58
11	EtOH	-	120	trace
12	EtOH	3	60	45
13	EtOH	4	60	80
14	EtOH	5	60	92
15	EtOH	7	60	93
16	CH <sub>2</sub> Cl <sub>2</sub>	-	120	trace
17	CH <sub>2</sub> Cl <sub>2</sub>	3	60	20
18	CH <sub>2</sub> Cl <sub>2</sub>	4	60	37
19	CH <sub>2</sub> Cl <sub>2</sub>	5	60	48
19	CH <sub>2</sub> Cl <sub>2</sub>	7	60	48
20	Solvent-free	-	120	trace
21	Solvent-free	3	120	33
22	Solvent-free	4	120	51
23	Solvent-free	5	120	60
24	Solvent-free	7	120	61

<sup>a</sup> Isolate Yield.

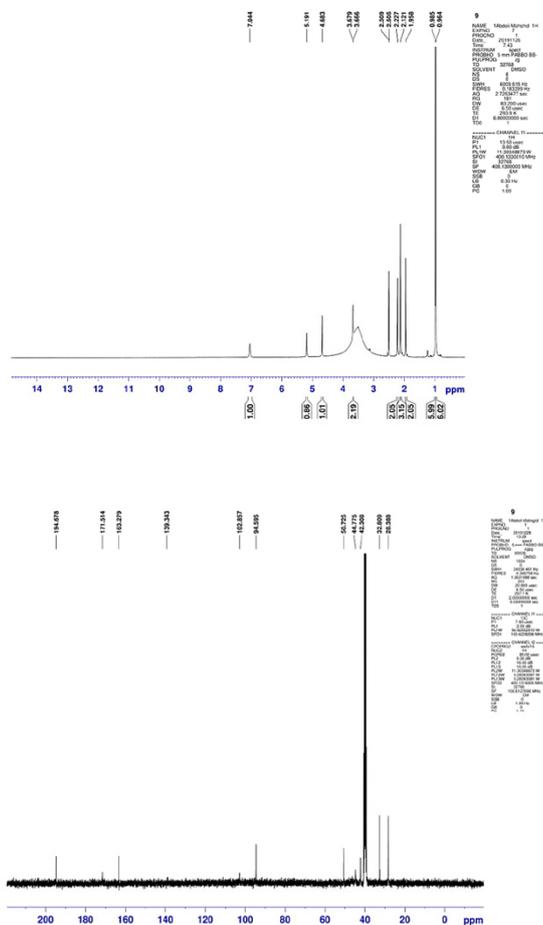


Fig. 5. <sup>1</sup>H NMR and <sup>13</sup>C NMR of compound 5

by IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, and elemental analysis data. The <sup>1</sup>H NMR spectrum of compound 5 exhibited two singlets at 0.96 and 0.98 ppm for methyl protons and four signals at 2.50, 2.23, 2.12, and 1.95 ppm for CH<sub>2</sub> protons. The =CH- and one aromatic proton were presented at 5.19 and 7.04 ppm, respectively. In the <sup>13</sup>C NMR spectrum, the resonances related to carbonyl groups of 5 were appeared at 194.67, 171.51 ppm. The signals attributed to unsaturated carbon double bonds (-CH=CH-) and (-N-CH=CH-) appeared at 163.27, 139.34, 102.85, and 94.59 ppm, respectively (Fig.5). The elemental analysis result of compounds 5 was satisfactory. The inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis was performed to determine the amount of La and La<sub>2</sub>O<sub>3</sub>-loading in (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> before (7.14 mg/g) and after (7.12 mg/g) the reaction.

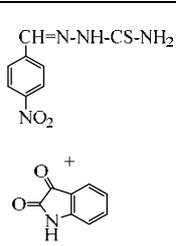
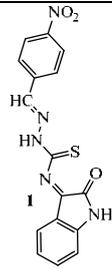
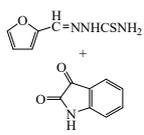
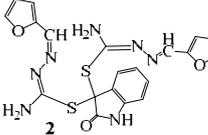
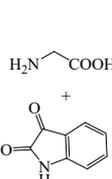
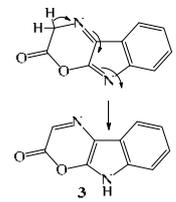
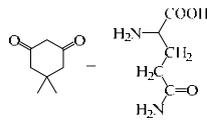
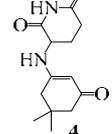
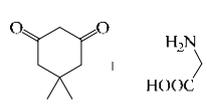
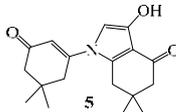
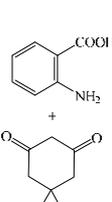
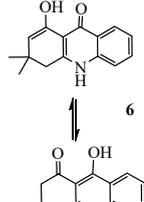
The leaching of catalyst has been measured

using a hot filtration method. The reaction mixture has been filtered out the catalyst ((MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>) from the reaction mixture at the stage of 50% conversion. We did not observe further progress of the reaction after filtration which indicates that there was no leaching to confirm the absence of La<sub>2</sub>O<sub>3</sub> NPs and stability of the catalyst.

We extended our studies on different amines with isatin and dimedone to evaluate the scope and potential limitations of this methodology (Table 2, entries 1–6). In almost all cases, the reactions proceeded smoothly within 60-90 min, providing the corresponding products in good isolated yields.

A plausible mechanism for the reaction is envisaged in Scheme 3. It is proposed that the carbonyl group of dimedone is primarily activated by (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>; NH<sub>2</sub> group attacks the carbonyl groups of two dimedones, and two molecules of water are removed and afforded

Table 2. Synthesis of some acridine and indole derivatives using (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>

Entry	Raw Materials	Product
1		
2		
3		
4		
5		
6		

intermediately. At least COOH groups forms a ring with one of dimedone to obtain 1-(5,5-dimethyl-3-oxocyclohex-1-en-1-yl)-3-hydroxy-6,6-dimethyl-1,5,6,7-tetrahydro-4H-indol-4-one 5.

To investigate the efficiency of the (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>, we compared some other metal oxide NPs for the synthesis of compound 5 and the results were summarized in Table 3. The metal oxide NPs were synthesized according to the previously reported procedures [32-36]. As shown in Table 3, the best catalyst for the synthesis of compound

5 is (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>. Using this metal oxide as a catalyst offers several advantages such as excellent yields, short reaction times, simplicity of the procedure, and using ethanol as a green solvent in contrast with other metal oxides.

The catalyst was simply separated by centrifugation, washed with ethanol and water, and dried at 100 °C for 2h. The recovered catalyst was then re-entered to a fresh reaction mixture under the same conditions and recycled 5 times without considerable loss of activity (Table 4).

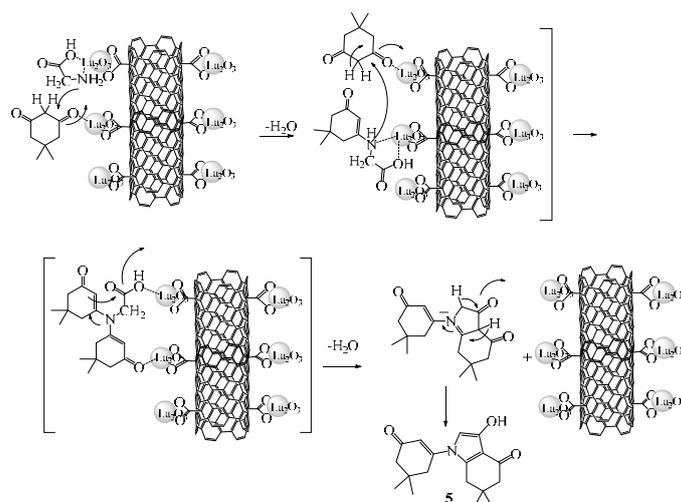
Scheme 3. A plausible mechanism for synthesis of compound 5 using (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>

Table 3. A comparison of different catalysts for the synthesis of compound 5 in ethanol

Entry	Catalyst	Amount of catalyst (mol%)	Time (hours)	Yield %
1	ZnO-CaO NPs	5	3	56
2	Fe <sub>3</sub> O <sub>4</sub> MNPs	5	3	47
3	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> -SO <sub>3</sub> H MNPs	5	3	65
4	La <sub>2</sub> O <sub>3</sub> NPs	5	2	71
5	(MWCNTs)-COOH/La <sub>2</sub> O <sub>3</sub>	5	1	92

Table 4. Recycling of the (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub>

Number of cycles	Yield <sup>a</sup> (%)
1	92
2	91
3	89
4	87
5	86

More recycling of the nanocatalyst led to a gradual reduction during the recovering and washing steps.

## CONCLUSION

In summary, (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> was used as an efficient reusable catalyst for the synthesis of some heterocyclic compounds containing nitrogen in ethanol. The reactions were accomplished in mild conditions and the products were obtained in high percentage yields. In addition to the intrinsic properties of nanocatalysts, (MWCNTs)-COOH/La<sub>2</sub>O<sub>3</sub> hybrid showed high catalytic activity in organic and heterocyclic chemistry and increased the rate of

the reaction without pollution. This method is less expensive and easier than other methods.

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## CONFLICTS OF INTEREST

There are no conflicts to declare.

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