MULTI-COMPONENT SYNTHESIS OF 2-AMINO-4*H*-CHROMENES CATALYZED BY NANO ZnO IN WATER

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Naphthalenediols, 1- and 2-naphthols, and phenols in the presence of nano ZnO as catalyst and water as green solvent react with methylenemalononitrile, generated in situ from aldehyde and malononitrile, to yield 2-amino-4*H*-chromenes.
Keywords: Heterocycles; Nanostructures; Heterogeneous catalysis; Green chemistry.

2-Amino-4*H*-chromene derivatives are an important class of organic compounds because of their uses as drugs, pesticides, analogs of natural compounds, dyes, and other materials with practical importance[1–6]. Substituted 2-amino-4*H*-chromenes have shown some biological activities, including antimicrobial[7], antiviral[8,9], cancer therapy[10–12] sex pheromone[13], mutagenicity[14] and central nervous system activity[15].

Chromen-4-one derivatives or their salts can be used as immune modulators and for the prophylaxis and treatment of different diseases of connective tissues, diabetes, psoriasis, pernicious anemia, ulcerous colitis, and chronic hepatitis[4]. In addition, many compounds containing enaminonitrile fragment are used as convenient synthons in the organic synthesis[1,4–6].

During the recent years, there are several reporting methods to synthesize of 2-amino-4*H*-chromene derivatives. The best method for synthesis of these compounds involves the three-component condensation of malonitrile, aldehyde, and a phenol or naphthol derivatives[16–25]. Recently, relatively benign reagents such as cetyltrimethylammonium chloride[20] basic alumina[19] nanosized MgO [24] and I_2/K_2CO_3 [23] have also been used. However, most of the reported methods for the synthesis of 2-amino-4*H*-chromenes require prolonged reaction time, reagents in stoichiometric amount, toxic organic solvents, and generate moderate yields of the product. The develop-

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ment of processes that are facile to carry out in the laboratory without recourse to inert atmosphere or limited solvents especially toxic organic solvents is an important goal in modern synthetic methodology. The identification of such processes can serve as a challenging goal that can lead to the discovery and development of new reaction chemistry. Therefore, the quest for cheap, environmentally friendly catalysts and mild reaction conditions is still a major challenge.

Zinc oxide (ZnO) is a versatile material that has key applications as an efficient catalyst in modern organic synthesis. ZnO nano particles can be active catalyst for different processes. Recently ZnO nano particle were described as catalysts for synthesis of β-phosphono malonates[26], Knoevenagel condensation[27], synthesis of tetrazoles[28], β-acetamido ketones[29], coumarines[30], dimethyl carbonates[31] and ferrocenyl phosphonates[32]. Herein we wish to report the novel synthesis of 2-amino-4*H*-chromenes by a multi-component condensation of an aldehyde, malononitrile and naphthols or phenols in water as a green solvent. The first step in this multi-component condensation is the Knoevenagel condensation of an aldehyde and malononitrile to produce the corresponding aryl methylene malononitrile. Recently, we have shown that a mixture of malononitrile and arylaldehydes, catalyzed by nano flake ZnO, is a synthetic method of aryl methylene malononitriles[27]. By this way, a variety of none readily obtained heterocyclic could be synthesized.

RESULTS AND DISCUSSION

Structural Properties and Characterization of the Nano ZnO

In this work, the structural properties of nano ZnO was analyzed by X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), and FTIR spectroscopy. Figure 1 shows XRD pattern of the nano ZnO, which is a typical zincite peak pattern with lattice constants a = 3.249 Å and c = 5.206 Å [33]. According to this pattern, no impurities could be find in the powder, indicating that they have been completely removed using the washing procedure. The mean particle size was calculated for the crystallized ZnO using the Scherrer equation using the corresponding peaks[34]. The (002) peak at $2\theta = 34°$ was used for particle size measurement. The average crystallite size was determined of about 25–50 nm.

SEM and TEM determined the morphology of the nano ZnO. Figure 2 shows SEM and TEM images of nano ZnO prepared with the sol method.

It was observed that the synthesized product was ZnO nano-flake and the wall of the flake is about 20–30 nm, thickness as shown in Fig. 2b.

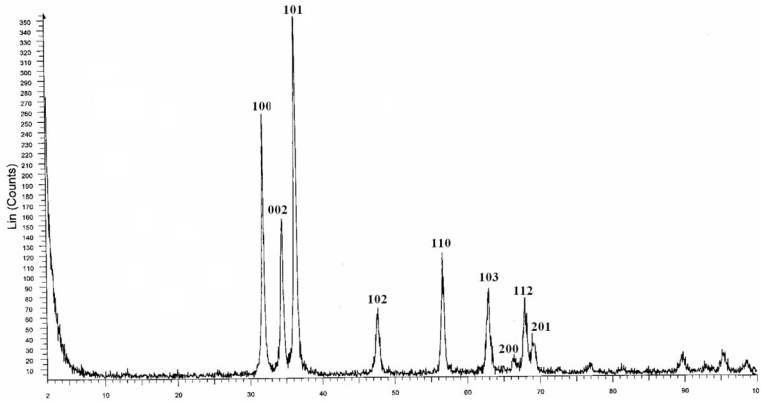


FIG. 1
XRD patterns of nano ZnO

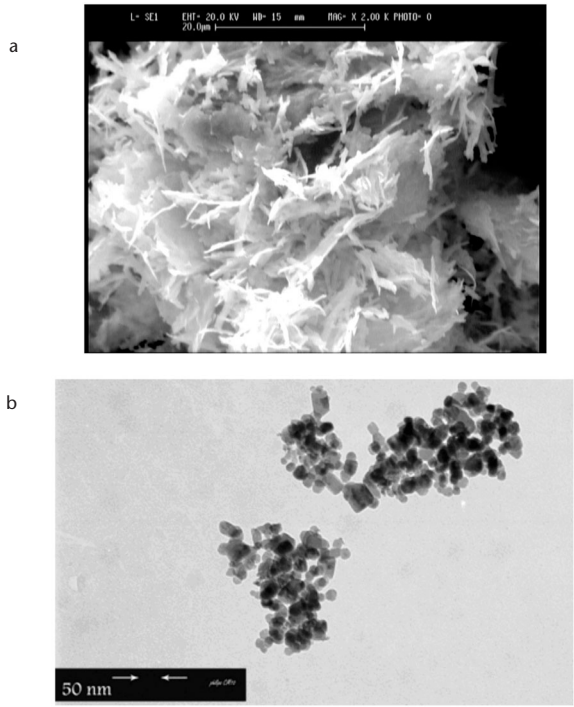


FIG. 2
SEM (a) and TEM (b) images of nano ZnO

In this work, the FTIR spectroscopy is also adopted as an applicable technique for further structural properties of nano ZnO. Infrared transmission spectrum of nano ZnO was recorded to be in the range of 4500–400 cm^{-1}. The adsorption band at 463 cm^{-1} is the stretching mode of ZnO [35]. In addition, the peak at 3421 cm^{-1} is due to the stretching of –OH groups present on the surface of the catalyst, caused during the absorption of water (Fig. 3). In this study, the adsorption of water molecules was also approved using thermo gravimetric (TG) analysis. The thermal behavior of nano ZnO and commercial ZnO (which was purchased from Merck Company) are shown in Fig. 4. A significant decrease in the weight percentage of the nano ZnO at temperatures to ~100 °C is related to the desorption ion of water

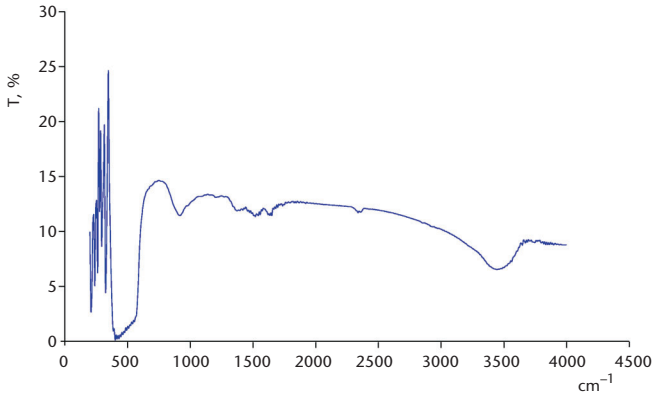


FIG. 3
FTIR spectrum of nano ZnO

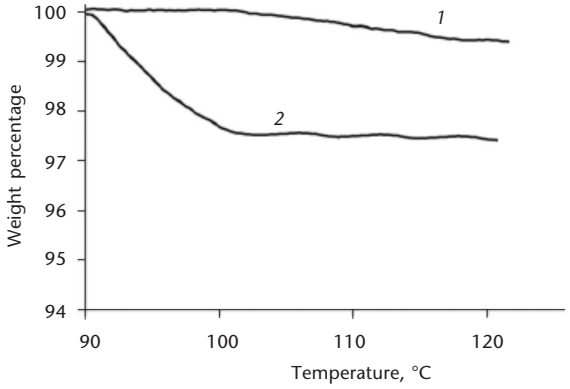


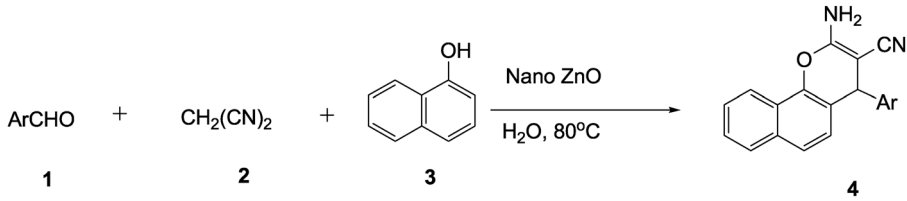
FIG. 4
Thermograms revealing the thermal stability of commercial ZnO (*1*) and nano ZnO (*2*)

molecules from the catalyst substrate. This was evaluated to ~0.7% according to the TG analysis. The catalyst surface is so much reactive that gain water from the air after calcinated.

Evaluation of Catalytic Activity of Nano ZnO for Synthesis of Chromene Derivatives

In conjunction to this work, we report results of our investigations on reactivity of nano ZnO as a perfect catalyst in the synthesis of some 2-amino-4*H*-chromenes.

Thus, it has been found that 1-naphthol reacts with arylaldehydes and malononitrile to yield 2-amino-4*H*-chromenes **4a**–**4i** (Scheme 1). These compounds are assumed to be formed via addition of 1-naphthol to aryl methylene malononitrile, generated in situ from aldehyde and malononitrile. Then the resulting acyclic Michael adducts spontaneously cyclized into the final isolable products **4**. The results are summarized in Table I.

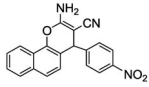
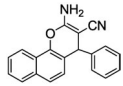
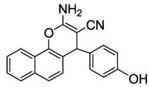
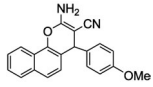
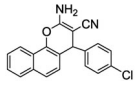
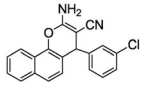
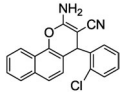
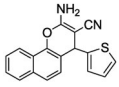
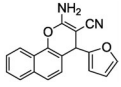


SCHEME 1
2-Amino-4*H*-chromene synthesis catalyzed by nano ZnO

It is important to note that in all cases, the formation of 4*H*-pyran **4** structures were preferred over a possible 2*H*-pyran structure. The former might result from the addition of the naphthol oxygen atom to the double bond in aryl methylene malononitriles (Knoevenagel adduct) and subsequent cyclization. ^{1}H NMR shows methylene proton signal at δ 4–5.5 ppm which is comparable with the expected one for 4*H*-pyran derivative. In addition, if the reaction product was 2*H*-pyran derivative, signals would appear at lower δ values, δ 3–4 ppm [36].

As indicated in the Table I, wide range of aromatic aldehydes bearing both electron-donating and electron-withdrawing substituents, afforded the corresponding 2-amino-4*H*-chromenes in good yields. Aromatic aldehydes carrying electron-withdrawing substituents reacted well with high yields. Mention must be made here that *para*-substituted aromatic aldehydes gave higher yields of 2-amino-4*H*-chromenes than *ortho*- and *meta*-

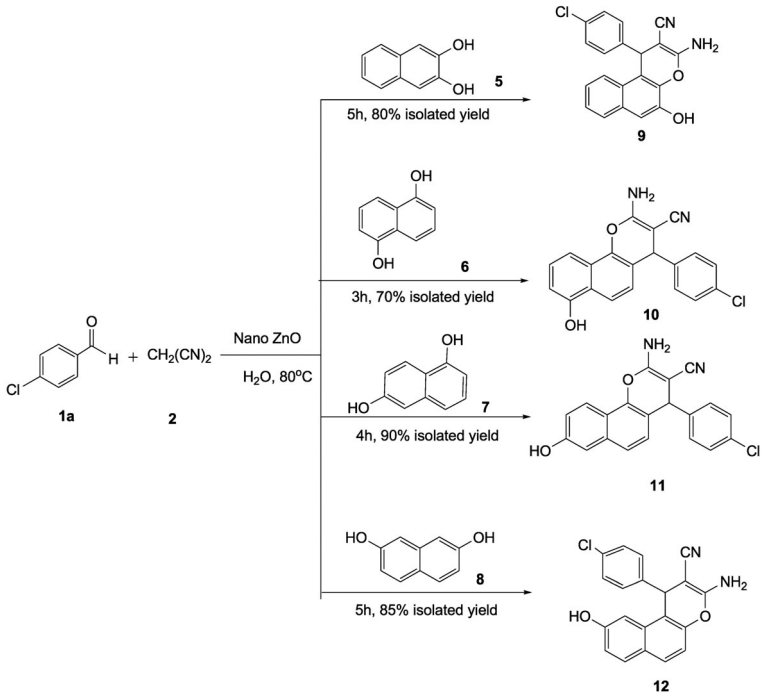
TABLE I
Three-component condensation of various aldehydes (1 mmol) with malononitrile (1 mmol) and 1-naphthol (1 mmol) catalyzed by nano ZnO (0.5 mmol) at 80 °C in water

Entry	Ar	Product **4**		Time, h	Yield, %[a]
1	4-NO_2-C_6H_4- **1a**		**4a**	0.5	98
2	C_6H_5- **1b**		**4b**	3	85
3	4-HO-C_6H_4- **1c**		**4c**	5	85
4	4-MeO-C_6H_4- **1d**		**4d**	12	50
5	4-Cl-C_6H_4- **1e**		**4e**	1.5	95
6	3-Cl-C_6H_4- **1f**		**4f**	5	75
7	2-Cl-C_6H_4- **1g**		**4g**	4	80
8	2-thiophenyl **1h**		**4h**	6	90
9	2-furan **1i**		**4i**	10	60

[a] Isolated yield.

substituted aromatic aldehydes did. However, aromatic aldehydes with electron-donating substituents give the expected compounds in a longer time and lesser yields. We propose, as an explanation for the result, that electron-donating substituents on the aromatic ring develop the electron density of C=C double bond in the intermediate (Knoevenagel adduct), which may be disadvantageous to the reaction of the phenol *ortho* C-alkylation with electrophilic C=C double bond.

The use of naphthalenediols attracted our attention because the reactions of these compounds with aromatic aldehydes **1** and malononitrile **2** can afford various naphthopyrans. In addition, to our knowledge, the synthesis aspect of such naphthopyrans was only partially exploited[37–41]. Previous attempt[37–41] to synthesize benzochromenes from 2,7- 2,3- 1,5- and 1,6-naphthalenediols **5–8** by a three-component reaction has failed. Herein, using nano ZnO in water as solvent in very mild and efficient reaction conditions, we succeeded in synthesis of 2-amino-4*H*-chromenes **9**–12 by three-component condensation (Scheme 2). In addition, we found that the

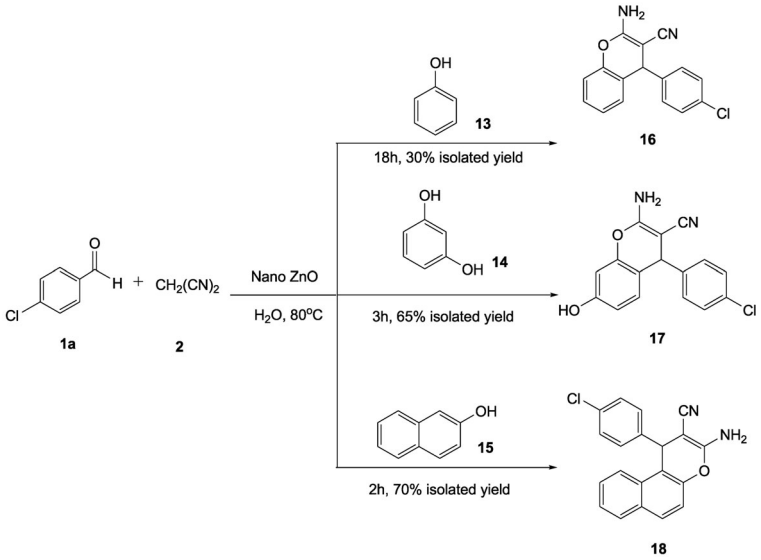


SCHEME 2
Synthesis of 2-amino-4*H*-chromenes **9–12** by three-component condensation catalyzed by nano ZnO

reaction of naphthalenediols **5–8** with 4-chlorobenzaldehyde **1e** and malononitrile **2** afforded only benzochromenes **9–12** regardless of the substrates ratio (1:1:1 or 1:2:2). The addition of double amounts of 4-chlorobenzaldehyde and malononitrile to these naphthalenediols yielded only 2-amino-4*H*-chromenes **9–12** and the corresponding naphthalene dipyrans was not observed.

It has been shown that 1,6-naphthalenediol **7** reacted with 4-chlorobenzaldehyde **1e** and malononitrile **2** in a molar ratio of 1:2:2 or 1:1:1 to give the benzochromene **11** regioselectively. The ^{1}H and ^{13}C NMR spectra of **11** are in good agreement with this structure (see Experimental).

To assess the efficiency of nano sized ZnO as catalyst in inducing these reactions, the reactions of phenol **13**, resorcinol **14** and 2-naphthol **15** with 4-chlorobenzaldehyde **1e** and malononitrile **2** were also studied. Phenol **13** reacted smoothly in the presence of nano ZnO to afford the corresponding 2-amino-4*H*-chromene **16** in moderate yield, while the reactions of resorcinol **14** and 2-naphthol **15** were good in time and yields that, afforded selectively 2-amino-4*H*-chromenes **17** and **18**, respectively (Scheme 3). We propose, as an explanation for the selectivity of these reactions, that benzopyrans **17** and **18** were formed by addition of the more anion of phenolic C-2 with electrophilic C=C double bonds.



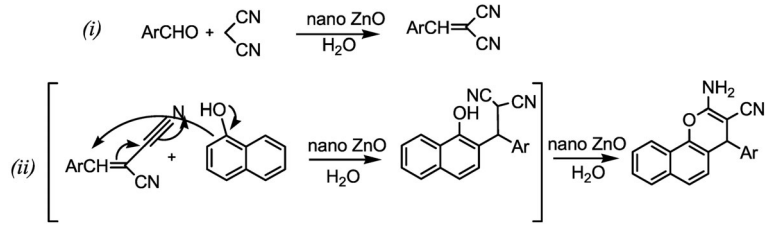
SCHEME 3
Synthesis of 2-amino-4*H*-chromenes **16–18** by three-component condensation catalyzed by nano ZnO

Structures of all compounds were characterized by ^{1}H NMR, FTIR, microanalysis, and mass spectroscopy.

A mechanistic proposal for the formation of 2-amino-4*H*-chromenes from the reaction of aldehyde, malononitrile, and a naphthol was proposed to involve through a two-step process: (i) The nucleophilic addition of the malononitrile to the carbonyl group of aldehyde forming a Knoevenagel product followed by (ii) the nucleophilic addition of the naphthol to the Knoevenagel product. The nano ZnO has Lewis acid sites (Zn^{2+}) and Lewis basic sites (O^{2-})[42]. A number of methods for determining acidity and acid strength of ZnO as well as nano sized ZnO have been reported[43]. Tanabe et al.[44] was shown that ZnO has a slight acidity of 0.004 mmol/g at acid strength $H_o < +6.8$, and ca. 0.010 mmol/g at the same acid strength when heated in air or in vacuum. Therefore we concluded that ZnO has a slight acidity properties and it could act as an acid catalyst.

In the first step (i) the Lewis base sites (O^{2-}) of nano ZnO takes up a proton of the malononitrile, and the resulting carbanions form a complex with the Zn^{2+} sites (Lewis acid-type) and the Lewis acid sites (Zn^{2+}) of nano ZnO is coordinated to the oxygen of the carbonyl group, resulting in the increased reactivity of aldehyde. To argument with this step, Knoevenagel product formation was observed (IR, NMR, MS) when aldehyde was treated with malononitrile in the presence of nano ZnO (10 mole %) at 80 °C for 1 h. In the second step (ii), we propose that the Lewis basic sites of nano ZnO (O^{2-}) coordinate to the –OH group of naphthol and then it could be attack to the electrophilic C=C double bond (Scheme 4).

Reactions were carried out under the same reaction conditions to obtain a comparative evaluation of the efficacy of nano ZnO with that of other catalysts reported recently for the synthesis of 2-amino-4*H*-chromenes

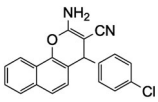
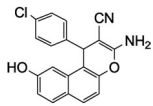


SCHEME 4
Proposed mechanism

(Table II). The Table shows that the yield of desired product in the presence of nano ZnO is comparably higher than other catalysts used. Consequently, our method can be certainly considered as a convenient alternative to the other eco-friendly catalytic methods used for one-pot three-component synthesis of 2-amino-4*H*-chromenes, specially, hydroxyl-2-amino-4*H*-chromenes.

Finally, in order to correlate between the catalyst properties and its activity, the reactions were carried out under the same reaction conditions to obtain a comparative evaluation of the efficacy of nano flake ZnO with that of other metal oxide catalysts for the synthesis of **4e** (Table III). Nano particles ZnO, nano-TiO_2, and nano-MgO, were simply prepared according to the literature or in our laboratory[27]. Our studies showed that nano-flake ZnO is an efficient catalyst and is more reactive than other commercial and nano metal oxides in the synthesis of **4e** (Table III). The catalytic activity was observed in the following order: nano-flake ZnO > nano-particles ZnO > commercial ZnO > different metal oxides with bulky and nano dimensions. The observed trend could be explained in terms the sized of the catalyst that, also contribute in making the reaction more feasible due to easy diffusion of reactants and product molecules. Nano-flakes ZnO used in the

TABLE II
Comparison of catalytic activity of nano ZnO catalyst with several other catalysts

Entry	2-amino-4*H*-chromenes	Reaction conditions	Time h	Yield %[a]
1		Nano ZnO (0.5 mmol)/H_2O/80 °C	1.5	95
		Bulky ZnO (0.5 mmol)/H_2O/80 °C	3	52
		Et_3N (0.5 mmol)/EtOH (25 ml)/reflux[29]	2	72
		Piperidine (0.02 mol)/EtOH (50 ml)/reflux[32]	3	59
		KF/Al_2O_3/EtOH (15 ml)/80 °C[31]	5–6	93
		I_2/K_2CO_3/H_2O/100 °C[23]	1	97
2		Nano ZnO/80 °C	5	85
		Bulky ZnO	24	trace
		Et_3N (0.5 mmol)/EtOH (25 ml)/reflux[29]	3	74
		Piperidine (0.02 mol)/EtOH (50 ml)/reflux[32]	3	0
		KF/Al_2O_3/EtOH (15 ml)/80 °C[31]	5–6	0
		I_2/K_2CO_3/H_2O/100 °C[23]	4–6	0

[a] Isolated yields.

present study is found to have large surface area (380 ± 0.8 m^2/g), compared to the other nano metal oxides.

TABLE III
Comparison of catalytic activity of nano-flake ZnO catalyst with other nano and bulky ZnO and several other catalyst for the synthesis of **4e**[a]

Yield of **4e** %[b]	Time h	Surface area m^2/g	Crystal size nm	Catalyst	Entry
95	1.5	380±0.8	20–30	Nano-flake ZnO	1
70	2	420±0.5	35±5	Nano-particles[c] ZnO	2
52	3	2.5–12	1500–2000	Commercial ZnO	3
40	4	250±0.6	18–30	Nano MgO[d]	4
40	4	35	122	Nano TiO_2[d]	5
40	5	10–40	500–700	Commercial MgO	6
45	5	5–20	1000	Commercial TiO_2	7

[a] Reaction condition: 4-Chlorobenzaldehyde (1 mmol), malononitrile (1 mmol), 1-naphthol (1 mmol), Catalyst (0.5 mmol), 80 °C, water. [b] Isolated yield. [c] Nano particles ZnO were synthesized as described previously[27]. [d] Nano MgO and TiO_2 were synthesized in our laboratories.

CONCLUSION

In conclusion, nano ZnO can serve as an efficient catalyst for the synthesis of 2-amino-4*H*-chromenes. In addition, various naphthalenediols can be reacted with aldehydes and malononitrile to produce various naphthopyranes. Finally, this procedure offers several advantages such as using water as a green and economical solvent, simple reaction set up, easy work up and crystallization, and good yields.

EXPERIMENTAL

^1H and ^{13}C NMR spectra (δ, ppm; *J*, Hz) were measured on Bruker Advance DPX FT 250 and 62.9 MHz spectrometer with TMS as an internal standard. IR spectra (ν, cm^{-1}) were obtained on a Perkin–Elmer or FTIR-800 instrument. Mass spectra were obtained on a Shimadzu GCMS0QP 1000EX at 20 and/or 70 eV. Elemental analyses were performed on Thermo Finnigan, Flash EA 1112 series microanalyzer by the head of the CHN laboratory.

Preparation of the Catalyst

In a typical experiment for the synthesis of nano ZnO, $Zn(OAc)_2{\cdot}2H_2O$ (10 mmol) and $CO(NH_2)_2$ (0.2 mol) were dissolved in 200 ml deionized water at room temperature to form a transparent solution. Then the mixture was refluxed for 12 h. It was cooled by cold water

to stop the reaction. The product was centrifuged and washed with deionized water and absolute ethanol, and dried at 80 °C for 8 h. The nano ZnO was obtained by calcining the precursor in a furnace in air at 400 °C for 2 h [27].

Synthesis of Chromene Derivatives by Nano ZnO. General Procedure

A mixture of aromatic aldehyde (1 mmol), malonitrile (1 mmol), phenol or naphthol derivative (1 mmol) and nano ZnO (0.5 mmol, 0.04 g) was added to a test tube and heated in an oil bath at 80 °C in water (2 ml). The progress of the reaction was monitored by TLC. After the reaction was completed, the catalyst was filtered off and the precipitate was recrystalized by EtOH. All synthesized compounds were stable as colorless to yellowish powders. Their structures were confirmed by spectroscopic methods and elemental analyses. It is worth to note that this conclusion is significant since there is no literature precedence for the syntheses of compounds **4h** and **9–12**. The structures of products were confirmed by NMR, elemental analyses and compared with authentic samples obtained commercially or prepared by reported methods. Products **4a–4g** and **16–18** are known and were characterized by ^{1}H, ^{13}C NMR and HRMS spectral data found to be identical with those described in refs[16–25]. For new compounds, the complete spectroscopic data are described bellow.

2-Amino-4-(thiophen-2-yl)-4H-benzo[h]chromene-3-carbonitrile (**4h**). Yellow powder (yield 90%); m.p.193–194 °C. IR (KBr): 3440, 3328, 1670, 2194. ^{1}H NMR (DMSO-d_6, 250 MHz): 8.19 (d, J = 8.50, 1 H), 7.85 (d, J = 8.20, 1 H), 7.13–7.57 (m, 8 H, Ar-H, NH_2), 6.88 (m, 1 H, Ar-H), 4.99 (s, 1 H, CH-Ar). ^{13}C NMR (DMSO-d_6, 62.9 MHz): 36.03, 55.78, 117.60, 120.56, 120.63, 121.40, 122.69, 123.81, 126.04, 126.59, 126.69, 126.83, 126.94, 127.59, 132.64, 142.60, 146.22, 160.26. ESI-MS m/z: $[M + H]^+$ 304. For $C_{18}H_{12}N_2OS$ (304.37) calculated: 71.03% C, 3.97% H; found: 70.93% C, 3.90% H.

2-Amino-4-(furan-2-yl)-4H-benzo[h]chromene-3-carbonitrile (**4i**). Yellow powder (yield 60%); m.p. 168–170 °C. IR (KBr): 3440, 3328, 1658, 2202. ^{1}H NMR (DMSO-d_6, 250 MHz): 8.28 (d, J = 8.30, 1 H), 7.95 (d, J = 8.40, 1 H), 7.49–7.72 (m, 4 H, Ar-H), 7.29 (m, 3 H, Ar-H, NH_2), 6.41 (m, 1 H, Ar-H), 6.31 (m, 1 H, Ar-H), 5.10 (s, 1 H). ^{13}C NMR (DMSO-d_6, 62.9 MHz): 34.5, 53.1, 106.0, 110.3, 115.3, 120.2, 120.5, 122.6, 123.8, 125.7, 126.6, 126.8, 127.6, 132.8, 142.6, 143.0, 156.2, 160.8. ESI-MS m/z: $[M + H]^+$ 288. For $C_{18}H_{12}N_2O_2$ (288.09) calculated: 74.99% C, 4.20% H; found: 74.87% C, 4.13% H.

3-Amino-1-(4chlorophenyl)-5-hydroxy-1H-benzo[f]chromene-2-carbonitrile (**9**). Yellow powder (yield 80%); m.p. 208–210 °C. IR (KBr): 3475, 3359, 3257, 1649, 2185. ^{1}H NMR (DMSO-d_6, 250 MHz): 10.28 (s, 1 H, OH), 7.93 (d, J = 8.10, 1 H), 7.63–7.71 (m, 2 H), 7.19–7.32 (m, 6 H), 6.93 (s, 2 H, NH_2), 5.29 (s, 1 H). ^{13}C NMR (DMSO-d_6, 62.9 MHz): 37.4, 57.3, 109.9, 116.6, 120.2, 123.2, 123.7, 124.0, 125.1, 126.4, 128.6, 128.6, 129.6, 130.0, 131.0, 131.2, 132.0, 139.0, 144.5, 160.0. ESI-MS m/z: $[M + H]^+$ 348. For $C_{20}H_{13}ClN_2O_2$ (348.78) calculated: 68.87% C, 3.76% H; found: 68.80% C, 3.71% H.

2-Amino-4-(4-chlorophenyl)-7-hydroxy-4H-benzo[h]chromene-3-carbonitrile (**10**). Yellow powder (yield 70%); m.p. 223–225 °C. IR (KBr): 3508–3208, 1660, 2200. ^{1}H NMR (DMSO-d_6, 250 MHz): 10.23 (s, 1 H, OH), 7.77 (m, 1 H), 7.63 (m, 1 H), 7.26 (m, 7 H, Ar-H, NH_2), 6.92 (m, 2 H), 4.89 (s, 1 H). ^{13}C NMR (DMSO-d_6, 62.9 MHz): 37.9, 55.7, 109.2, 111.3, 117.4, 118.3, 120.4, 124.0, 124.3, 127.4, 128.6, 129.4, 131.5, 142.5, 144.5, 153.0, 160.2. ESI-MS m/z: $[M + H]^+$ 348. For $C_{20}H_{13}ClN_2O_2$ (348.78) calculated: 68.87% C, 3.76% H; found: 68.81% C, 3.70% H.

2-Amino-4-(4-chlorophenyl)-8-hydroxy-4H-benzo[h]chromene-3-carbonitrile (**11**). Yellow powder (yield 90%); m.p. 194–196 °C. IR (KBr): 3500–3200, 1660, 2192. ^{1}H NMR (DMSO-d_6, 250 MHz): 9.93 (s, 1 H, OH), 8.28 (d, J = 8.66, 1 H), 8.07 (d, J = 9.01, 1 H), 7.36 (m, 2 H), 7.07–7.29 (m, 6 H, Ar-H, NH_2), 6.94 (d, J = 8.50, 1 H), 4.83 (s, 1 H). ^{13}C NMR (DMSO-d_6, 62.9 MHz): 14.0, 55.9, 108.9, 114.0, 116.9, 118.8, 120.4, 122.4, 126.3, 127.9, 128.3, 128.5, 129.4, 130.8, 131.3, 134.6, 142.6, 142.9, 144.8, 156.1, 160.1. ESI-MS *m/z*: $[M + H]^+$ 348. For $C_{20}H_{13}ClN_2O_2$ (348.78) calculated: 68.87% C, 3.76% H; found: 68.84% C, 3.70% H.

3-Amino-1-(4-chlorophenyl)-9-hydroxy-1H-benzo[f]chromene-2-carbonitrile (**12**). Yellow powder (yield 85%); m.p. > 280 °C. IR (KBr): 3402, 3305, 1647, 2190. ^{1}H NMR (DMSO-d_6, 250 MHz): 9.59 (s, 1 H, OH), 7.77 (d, J = 9.20, 1 H), 7.69 (d, J = 10.36, 1 H), 7.31 (d, J = 8.35, 2 H), 7.14 (d, J = 8.35, 2 H), 7.06 (s, 1 H), 6.92–6.95 (m, 4 H, Ar-H, NH_2), 5.03 (s, 1 H). ^{13}C NMR (DMSO-d_6, 62.9 MHz): 37.7, 57.4, 105.5, 113.0, 117.0, 120.3, 125.1, 128.6, 128.7, 129.38, 129.6, 130.1, 131.0, 131.9, 132.0, 144.4, 147.2, 156.3, 159.5, 160.03. ESI-MS *m/z*: $[M + H]^+$ 348. For $C_{20}H_{13}ClN_2O_2$ (348.78) calculated: 68.87% C, 3.76% H; found: 68.79% C, 3.71% H.

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REFERENCES

1. Mohr S. J., Chirigios M. A., Fuhrman F. S., Pryor J. W.: *Cancer Res.* **1975**, *35*, 3750.
2. Dell C. P., Smith C. W.: EP 537949; *Chem. Abstr.* **1993**, *119*, 139102d.
3. Panda D., Singh J. P., Wilson L. J.: *Biol. Chem.* **1997**, *272*, 7681.
4. O'Callaghan C. N., McMurry T. B. H., O'Brien J. E.: *J. Chem. Soc, Perkin Trans. 1* **1995**, 417.
5. Taylor E. C., McKillop A.: *The Chemistry of Cyclic Enaminonitriles and o-Aminonitriles*. Interscience Publishers, New York 1970.
6. Freeman F.: *Chem. Rev.* **1980**, *80*, 329.
7. Khafagy M. M., El-Wahas A. H. F. A., Eid F. A., El-Agrody A. M. I.: *Farmaco* **2002**, *57*, 715.
8. Smith W. P., Sollis L. S., Howes D. P., Cherry C. P., Starkey D. I., Cobley N. K.: *J. Med. Chem.* **1998**, *41*, 787.
9. Martinez A. G., Marco L. A.: *J. Bioorg. Med. Chem. Lett.* **1997**, *73*, 65.
10. Anderson D., Hegde D. R., Reinhard S., Gomez E., Vernier L., Lee W. F., Liu L., Sambandam S., Snider A., Masih P. A.: *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1587.
11. Skommer J., Wlodkowic D., Matto M., Eray M., Pelkonen J.: *Leukemia Res.* **2006**, *30*, 322; and references therein.
12. Wang J. L., Liu D., Zhang Z., Shan S., Han X., Srinvasula S. M., Croce C. M., Alnemeri E. S., Huang Z.: *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 7124.
13. Bianchi G., Tava A.: *Agric. Biol. Chem.* **1987**, *51*, 2001.
14. Hiramoto K., Nasuhara A., Michiloshi K., Kato T., Kikugawa K.: *Mutat. Res.* **1997**, *395*, 47.
15. Eiden F., Denk F.: *Arch. Pharm. (Weinheim, Ger.)* **1991**, *324*, 353.
16. Elagemey A. G. A., El-Taweel F. M. A. A.: *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1990**, *29*, 885.

17. Elagemey A. G. A., El-Taweel F. M. A. A., Khodeir M. N. M., Elnagdi M. H.: *Bull. Chem. Soc. Jpn.* **1993**, *66*, 464.
18. Bloxham J., Dell C. P., Smith C. W.: *Heterocycles* **1994**, *38*, 399.
19. Maggi R., Ballini R., Sartori G., Sartorio R.: *Tetrahedron Lett.* **2004**, *45*, 2297.
20. Ballini R., Bosica G., Conforti M. L., Maggi R., Mazzacani A., Righi P., Sartori G.: *Tetrahedron* **2001**, *57*, 1395.
21. Zhang A.-Q., Zhang M., Chen H., Chen H. J., Chen, H.-Y.: *Synth. Commun.* **2007**, *37*, 231.
22. Shanthi G., Perumal P. T.: *Tetrahedron Lett.* **2007**, *48*, 6785.
23. Ren Y., Cai C.: *Catal. Commun.* **2008**, *9*, 1017.
24. Kumar D., Reddy V. B., Mishra B. G., Rana R. K., Nadagaouda M. N., Verma R. S.: *Tetrahedron* **2007**, *63*, 3093.
25. Mandar P. S., Kshirsagar S., Samant S. D.: *Tetrahedron Lett.* **2009**, *50*, 719.
26. Hosseini-Sarvar M., Etemad S.: *Tetrahedron* **2003**, *64*, 5519.
27. Hosseini-Sarvari M., Sharghi H., Etemad S.: *Helv. Chem. Acta* **2008**, *91*, 715.
28. Kantam M. L., Kumar K. B. S., Sridhar Ch.: *Adv. Synth. Catal.* **2005**, *347*, 1212.
29. Mirjafary Z., Saeidian H., Sadeghi A., Matloubi Moghaddam F.: *Catal. Commun.* **2008**, *9*, 299.
30. Goswami P.: *Synth. Commun.* **2009**, *39*, 2271.
31. Wang M., Zhao N., Wei W., Sun Y.: *Indian Eng. Chem. Res.* **2005**, *44*, 7596.
32. Hosseini-Sarvari M.: *Catal. Lett.* **2011**, *141*, 347.
33. JCPDS diffraction database: Zincite [36-1451].
34. Cullity B. D., Stock S. R.: *Elements of X-ray Diffraction*, 3rd ed. Prentice-Hall, Englewood Cliffs (NJ) 2001.
35. Maensiri S., Laokul P., Promarak V.: *J. Cryst. Growth* **2006**, *289*, 102.
36. Sowellim S. Z. A.: *Proc. Pakistan Acad. Sci.* **1997**, *34*, 19.
37. Abdel-Latif F. F.: *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1990**, *29*, 664.
38. Shestopalov A. M., Emelianova Y. M., Nesterov V. N.: *Russ. Chem. Bull., Int. Ed.* **2002**, *51*, 2238.
39. Elagamey A. G. A., El-Taweel F. M. A.-A., Khodeir M. N. M., Elnagdi M. H.: *Bull. Chem. Soc. Jpn.* **1993**, *66*, 464.
40. Wang X. S., Shi D. Q., Yu H. Z., Wang G. F., Tu S. J.: *Synth. Commun.* **2004**, *34*, 509.
41. Zaki S., Sowellim A.: *Proc. Pakistan Acad. Sci.* **1997**, *34*, 19.
42. Kong X. Y., Wang Z. L.: *Nano Lett.* **2003**, *3*, 1625.
43. Ryland L. B., Tamele M. W., Wilson N.: *Catalysis* **1960**, *7*, 67.
44. Tanabe K., Yamaguch T.: *J. Res. Inst. Catal.* **1963**, 179.