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ORIGINAL PAPER

Nano-ZnO: an efficient and reusable catalyst for one-pot synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones and pyrazolo[1,2-a][1,2,4]triazole-1,3-diones

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Abstract The catalytic activity of nano-structured ZnO has been explored in the synthesis of 1*H*-pyrazolo[1,2-b]phthalazine-5,10-dione and pyrazolo[1,2-a][1,2,4]triazole-1,3-dione derivatives via a three-component coupling reaction between aromatic aldehydes, malononitrile, and phthalhydrazides or 4-arylurazoles, respectively. High yield, low reaction times, non-toxicity and recyclability of the catalyst, and easy work-up are the main merits of this protocol.

Keywords ZnO nanoparticles · Nano-catalyst · Pyrazolo[1,2-b]phthalazine-5 · 10-Dione · Pyrazolo[1,2-a][1,2,4]triazole-1 · 3-Dione · 4-Arylurazoles

Introduction

Heterogeneous catalysts have emerged as economically viable because of their high potent of recyclability [1–4]. In particular, nano-particles as heterogeneous catalysts have received considerable attraction in recent years owing to their interesting structures and outstanding catalytic activities [5–10]. Currently, use of nano-metal oxides has appeared as interesting challenge in synthetic organic chemistry due to their extraordinary physical and chemical properties [11–15]. The advantages allocated to these nano-metal oxides are high activity, strong oxidizing power, recyclability, and long-term stability [16–20]. Nano-crystalline metal oxides such as nano zinc oxide exhibit versatile applications as active adsorbents for gases or destruction of hazardous chemicals [21–23], and also as catalysts in various organic transformations [8, 24–29].

On the other hand, one-pot multi-component reactions (MCRs) are known to be superior to conventional linear-type processes that usually suffer from complex isolation procedures and produce significant amounts of waste materials [30–32]. In addition, multi-component processes provide rapid and efficient approach to organic transformations including diverse synthesis of polyfunctionalized heterocycles [33–35]. Such heterocycles are of significant biological and pharmaceutical importance and play vital roles in drug discovery process. Among these, the multi-component synthesis of polyfunctionalized heterocyclic compounds has become more challenging in organic and medicinal chemistry [33–35]. Pyrazolo-fused 1,2,4-triazolidine-3,5-dione derivatives exhibit a wide range of biological activities as anti-convulsant and fungicidal agents, [36, 37]. Also, pyrazolo-fused phthalazine derivatives constituting a bridgehead hydrazine are reported to possess multiple biological and pharmacological properties including anti-convulsant [38], vasorelaxant [39], cardiotonic [40], anti-pyretic, anti-inflammatory and anti-bacterial activities [41–43]. Raghuvanshi and co-worker have recently reported a highly efficient green synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones of photophysical importance [44].

Experimental

Chemicals

Chemicals used in this work were purchased from Fluka and Merk chemical companies and used without

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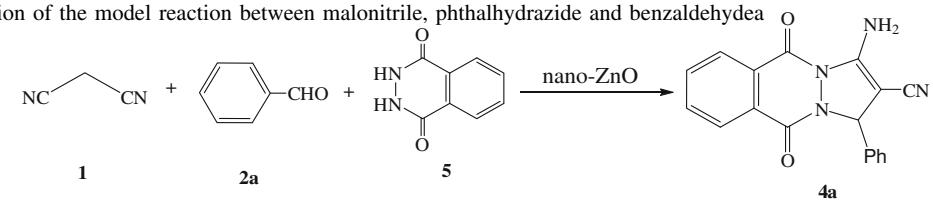
Table 1 Optimization of the model reaction between malonitrile, phthalhydrazide and benzaldehydea



1 2a 5 4a

Entry	Temperature (°C)	Solvent	Catalyst (mol %)	Time (min)	Yield (%)[b]
1	rt	EtOH	Nano-ZnO (15)	120	Trace
2	rt	MeCN	Nano-ZnO (15)	120	Trace
3	rt	H_2O	Nano-ZnO (15)	120	Trace
4	100	Solvent free	None	120	Trace
5	100	Solvent free	Nano-ZnO (5)	14	53
6	100	Solvent free	Nano-ZnO (10)	14	72
7	100	Solvent free	Nano-ZnO (15)	14	90
8	100	Solvent free	Nano-ZnO (20)	14	91
9	100	H_2O/reflux	Nano-ZnO (15)	40	48
10	80	EtOH/reflux	Nano-ZnO (15)	40	61
11	80	CH_3CN/reflux	Nano-ZnO (15)	40	53

[a] Conditions: malononitrile (1 mmol), phthalhydrazide (1 mmol), benzaldehyde (1 mmol)

[b] Isolated yield

purification. IR spectra were recorded on a Shimadzu 435-U-04 FT spectrophotometer from KBr pellets. ^{1}H and ^{13}C NMR spectra were measured for samples in DMSO-d_6 using a BRUKER DRX-300 AVANCE instrument at 300.13 and 75.47 MHz, respectively, using Me_4Si as internal standard. Mass spectra were recorded with a spectrometer FINNIGAN-MAT 8430 operating at an ionization potential of 70 eV. Melting points were measured on a SMPI apparatus. Elemental analysis for C, H and N atoms were performed using a Perkin–Elmer 2400 series analyzer. Urazoles were synthesized according to the reported procedures [45–48].

Synthesis of ZnO nanoparticles

ZnO Nanorods are prepared according to the literature method developed by Pacholski and co-workers with some modification [49]. In a flask containing methanol (50 mL) was added $Zn(OAc)_2$ (2.195 g). The solution was heated to 60 °C under magnetic stirring. Then, in a separate flask, 85 % pure potassium hydroxide (0.953 g) was dissolved in methanol (50 mL) and the solution was added dropwise to the stirring solution of zinc acetate during 10–15 min. At the constant temperature of 60 °C, it takes 135 min until ZnO nanospheres with 6 nm diameter is obtained.

General procedure for the synthesis of 1H-pyrazolo[1,2-b] phthalazine-5,10-diones 4a–n and pyrazolo[1,2-a] [1,2,4]triazole-1,3-diones 6a–o A mixture of malononitrile **1** (1.0 mmol), aldehyde **2** (1.0 mmol), phthalhydrazide **3** (1.0 mmol), or 4-arylurazole **5** (1.0 mmol), and nano-ZnO (15 mol %) are placed in a mortar. The reaction mixture was then heated at 80–100 °C for an appropriate time (Table 2) until the completion of the reaction was achieved as monitored by TLC. Then, the reaction mixture was cooled, washed with ethanol (2 × 3 mL) and evaporated under vacuum to give the products **5** and **6**. The structures of the products were fully established on the basis of their ^{1}H NMR, ^{13}C NMR and IR spectra as well as the elemental and MS spectral analysis for the new compounds as given below.

Physical and spectroscopic data

3-Amino-1-(2-bromophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4 g) Yellow powder. M.p. 248–250 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.30 (s, 1H, CH), 7.63–8.37 (m, 10H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 60.7, 62.6, 116.4, 122.3, 123.9, 127.1, 127.7, 128.7, 129.3, 130.7, 134.2, 134.3, 135.1, 141.0, 148.4, 151.5, 154.4, 157.2. IR (KBr, cm^{-1}): 3363, 3259, 2193, 1681, 1655 ppm. MS (70 eV) *m/z:* 394 [M^+]. Anal. Calcd. for $C_{18}H_{11}BrN_4O_2$: C 54.69, H 2.78, N 14.18; Found: C 54.56, H 2.73, N 14.12.

3-Amino-5,10-dihydro-1-(3-methoxyphenyl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4 h) Yellow powder. M.p. 232–234 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 3.72 (s, 3H, OCH_3), 6.04 (s, 1H, CH), 6.84–8.19 (m, 10H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 55.5, 61.7, 63.3, 113.1, 113.7, 116.5, 119.1,

Table 2 Synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones 4a–n catalyzed by nano-ZnOa

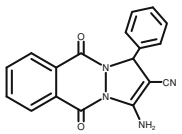
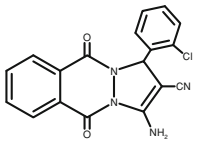
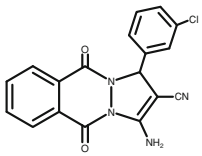
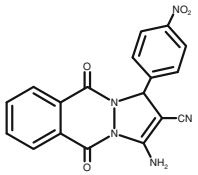
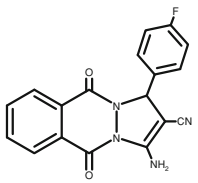
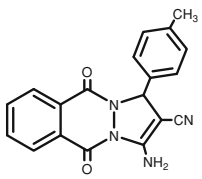
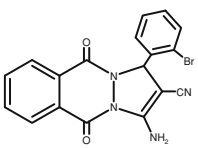
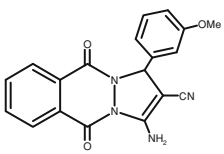
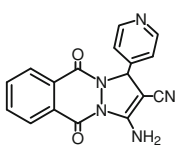
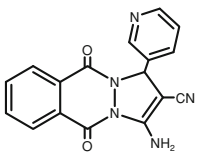
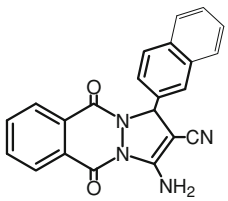
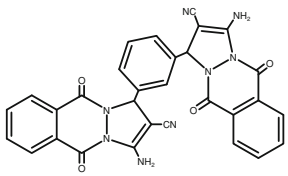
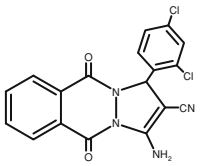
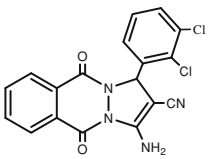
Entry	Ar[1]	Product 4	Time (min)	Yield (%)[b]	M.p. (°C)	
					Found	Reported
a	C_6H_5		14	90	249–251	251–253
b	2-ClC_6H_4		11	89	256–258	257–259
c	3-ClC_6H_4		8	91	265–267	265–267
d	4-$NO_2C_6H_4$		9	87	264–266	266–267
e	4-FC_6H_4		8	93	265–267	264–265
f	4-MeC_6H_4		20	86	253–255	255–256
g	2-BrC_6H_4		10	90	248–250	–
h	3-$MeOC_6H_4$		18	87	232–234	–
i	4-Pyridyl		15	86	260–262	–

Table 2 continued

Entry	Ar[1]	Product 4	Time (min)	Yield (%)[b]	M.p. (°C)	
					Found	Reported
j	3-Pyridyl		12	90	267–270	–
k	2-Naphthyl		18	91	267–269	–
l	3-$CHOC_6H_4$		45	88	271–273	–
m	2,4-$Cl_2C_6H_3$		11	92	231–232	–
n	2,3-$Cl_2C_6H_3$		14	91	261–263	–

[a] Conditions: aldehyde (1 mmol), malononitrile (1 mmol), phthalhydrazide (1 mmol), nano-ZnO catalyst (15 mol %), solvent free at 100 °C

[b] Isolated yield

127.1, 127.7, 128.8, 129.1, 130.3, 134.3, 135.2, 140.3, 151.0, 154.1, 157.1, 159.8 ppm. IR (KBr, cm^{-1}): 3373, 3267, 2192, 1665, 1603. MS (70 eV) *m/z:* 346 [M^+]. Anal. Calcd. for $C_{19}H_{14}N_4O_3$: C 65.89, H 4.04, N 16.18; Found: C 65.76, H 3.98, N 16.13.

3-Amino-5,10-dihydro-5,10-dioxo-1-(pyridin-4-yl)-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4i) Yellow powder. M.p. 260–262 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.19 (s, 1H, CH), 7.40–8.72 (m, 10H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 60.0, 61.8, 116.1, 128.3, 128.9, 134.5, 135.4, 150.5, 151.6, 154.0, 157.1 ppm. IR (KBr, cm^{-1}): 3367, 3246, 2201, 1684, 1667. MS (70 eV) *m/z:* 317 [M^+]. Anal. Calcd. for $C_{17}H_{11}N_5O_2$: C 64.35, H 3.47, N 22.08; Found: C 64.28, H 3.45, N 22.04.

3-Amino-5,10-dihydro-5,10-dioxo-1-(pyridin-3-yl)-1*H*-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4j) Yellow powder. M.p. 268–270 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.21 (s, 1H, CH), 7.37–8.72 (m, 10H, Ar–H and NH_2) ppm. ^{13}C-NMR (75 MHz, DMSO-d_6): δ 60.7, 62.1, 116.5, 128.9, 129.4, 133.5, 134.4, 149.0, 149.1, 150.0, 151.3, 151.4, 154.2, 157.1 ppm. IR (KBr, cm^{-1}): 3368, 3265, 2193, 1681, 1654. MS (70 eV) *m/z:* 317 [M^+]. Anal. Calcd. for $C_{17}H_{11}N_5O_2$: C 64.35, H 3.47, N 22.08; Found: C 64.23, H 3.37, N 21.96.

3-Amino-5,10-dihydro-1-(naphthalen-2-yl)-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4k) Yellow powder. M.p. 267–269 °C. ^{1}H-NMR (DMSO-d_6, 300 MH,): δ 6.28 (s, 1H, CH), 7.50–8.26 (m, 13H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 61.8, 63.7, 116.6, 124.8, 126.5,126.8, 126.9, 127.1, 127.7, 128.3, 128.9, 129.1, 129.3, 133.2, 133.3, 134.2, 135.1, 136.4, 151.1, 154.2, 157.1 ppm. IR (KBr, cm^{-1}): 3368, 3265, 2192, 1681, 1658. MS (70 eV) *m/z:*

Table 3 Synthesis of pyrazolo[1,2-a][1,2,4]triazole-1,3-diones 6**a–o** catalyzed by nano-ZnOa

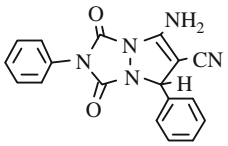
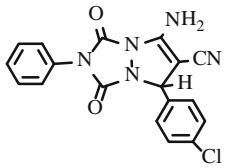
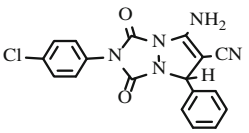
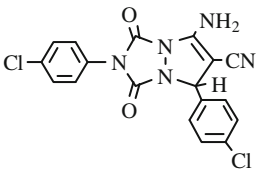
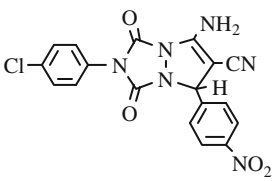
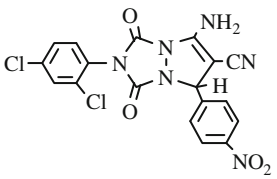
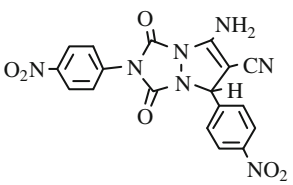
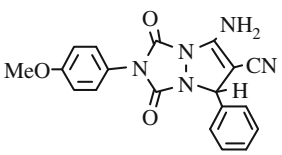
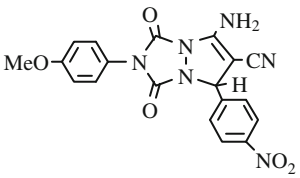
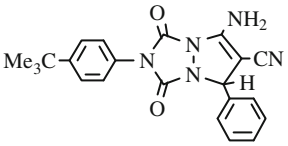
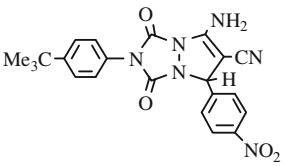
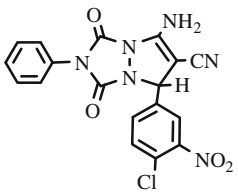
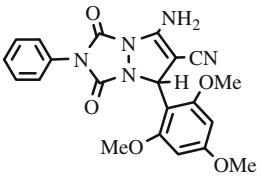
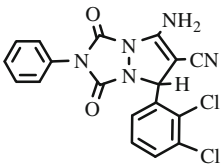
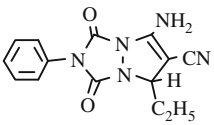
Entry[b]	Ar^1	Ar^2	Product **6**	Time (min)	Yield (%)[c]
a	C_6H_5	C_6H_5		25	90
b	4-ClC_6H_4	C_6H_5		25	88
c	C_6H_5	4-ClC_6H_4		18	91
d	4-ClC_6H_4	4-ClC_6H_4		20	91
e	4-$NO_2C_6H_4$	4-ClC_6H_4		30	90
f	4-$NO_2C_6H_4$	2,4-$Cl_2C_6H_3$		20	86
g	4-$NO_2C_6H_4$	4-$NO_2C_6H_4$		25	71
h	C_6H_5	4-$MeOC_6H_4$		30	84

Table 3 continued

Entry[b]	Ar^1	Ar^2	Product **6**	Time (min)	Yield (%)[c]
i	$4\text{-}NO_2C_6H_4$	$4\text{-}MeOC_6H_4$		25	81
j	C_6H_5	$4\text{-}Me_3CC_6H_4$		25	80
k	$4\text{-}NO_2C_6H_4$	$4\text{-}Me_3CC_6H_4$		30	75
l	$(4\text{-}Cl\text{-}3\text{-}NO_2)C_6H_3$	C_6H_5		25	86
m	$2,4,6\text{-}(OMe)_3C_6H_2$	C_6H_5		30	78
n	$2,3\text{-}Cl_2C_6H_3$	C_6H_5		15	91
o	C_2H_5	C_6H_5		120	–

[a] Conditions: aldehyde (1 mmol), malononitrile (1 mmol), 4-arylurazole (1 mmol), nano-ZnO catalyst (15 mol %), solvent-free at 80 °C

[b] All the products decompose (>300 °C) prior to melting as reported [53, 54]

[c] Isolated yield

366 [M^+]. Anal. Calcd. for $C_{22}H_{14}N_4O_2$: C 72.13, H 3.82, N 15.30; Found: C 72.05, H 3.78, N 15.26.

1,3-Bis{3-amino-2-cyano-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazin-2- yl}benzene (4l) Yellow powder. M.p. 271–273 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.20 (s, 1H, CH), 7.63–8.46 (m, 16H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 61.2, 82.6, 113.6, 114.5, 116.3,128.9,129.2, 132.2, 151.2, 154.1, 157.1 ppm. IR (KBr, cm^{-1}): 3363, 3262, 2228, 2190, 1651, 1604. MS (70 eV) *m/z:* 554 [M^+]. Anal. Calcd. for $C_{30}H_{18}N_8O_4$: C 64.98, H 3.25, N 20.21; Found: C 64.84, H 3.22, N 20.16.

3-Amino-1-(2,4-dichlorophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4m) Yellow powder. M.p. 231–232 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.43 (s, 1H, CH), 7.39–8.25 (m, 9H, Ar–H and NH_2) ppm. ^{13}C-NMR (75 MHz, DMSO-d_6): δ 61.2, 62.5, 116.5, 127.1, 127.9, 128.6, 128.9, 129.2, 130.3, 130.5, 131.5, 134.4, 138.2, 138.9, 151.6, 154.1, 157.0 ppm. IR (KBr, cm^{-1}): 3364, 3262, 2197, 1681, 1660. MS (70 eV) *m/z:* 384 [M^+]. Anal. Calcd. for $C_{18}H_{10}Cl_2N_4O_2$: C 56.10, H 2.59, N 14.54; Found: C 56.03, H 2.54, N 14.43.

3-Amino-1-(2,3-dichlorophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (4n) Yellow powder. M.p. 261–263 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.51 (s, 1H, CH), 7.33–8.27 (m, 9H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 60.7, 61.8, 116.6, 124.9, 125.9, 126.2, 126.5, 127.1, 127.8, 128.1, 128.3, 129.0, 129.2, 138.8, 138.9, 151.1, 154.0, 157.1 ppm. IR (KBr, cm^{-1}): 3372, 3236, 2211, 1686, 1661. MS (70 eV) *m/z:* 384 [M^+]. Anal. Calcd. for $C_{18}H_{10}Cl_2N_4O_2$: C 56.10, H 2.59, N 14.54; Found: C 55.97, H 2.53, N 14.58.

7-Amino-5-(4-chloro-3-nitrophenyl)-1,3-dihydro-1,3-dioxo-2-phenyl-2*H*,5*H*-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (6l) White powder. M.p. >300 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.03 (s, 1H, CH), 7.45–8.27 (m, 10H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 61.1, 62.9, 116.8, 124.4, 125.5, 127.3, 129.2, 129.9, 131.4, 140.9, 145.9, 148.4, 150.7, 150.9, 154.1 ppm. IR (KBr, cm^{-1}): 3422, 3302, 2179, 1781, 1721. MS (70 eV) *m/z:* 410 [M^+]. Anal. Calcd. for $C_{18}H_{11}ClN_6O_4$: C 52.61, H 2.67, N 20.46; Found: C 52.56, H 2.64, N 20.38.

7-Amino-1,3-dihydro-1,3-dioxo-2-phenyl-5-(2,4,6-trimethoxyphenyl)-2*H*,5*H*-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (6m) White powder. M.p. >300 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 3.69 (s, 3H, OCH_3), 3.81(s, 6H, $2OCH_3$), 5.82 (s, 1H, CH), 6.76–7.63 (m, 9H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 56.4, 60.5, 60.8, 104.5, 127.3, 129.1, 129.5, 129.9, 130.1, 130.39, 131.5, 145.9, 153.6, 154.1 ppm. IR (KBr, cm^{-1}): 3361, 3283, 2186, 1756, 1716. MS (70 eV) *m/z:* 421 [M^+]. Anal. Calcd. for $C_{21}H_{19}N_5O_5$: C 59.85, H 4.51, N 16.62; Found: C 59.82, H 4.48, N 16.56.

7-Amino-5-(2,3-dichlorophenyl)-1,3-dihydro-1,3-dioxo-2-phenyl-2*H*,5*H*-pyrazolo[1,2-a][1,2,4]triazole-6-carbonitrile (6n) White powder. M.p. >300 °C. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 6.30 (s, 1H, CH), 7.45–7.75 (m, 10H, Ar–H and NH_2) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ 60.9, 62.5, 116.6, 127.3, 128.7, 129.5, 129.9, 130.1, 130.4, 131.3, 131.4, 132.7, 139.2, 145.9, 150.7, 151.1, 154.2 ppm. IR (KBr, cm^{-1}): 3417, 3298, 2167, 1782, 1689. MS (70 eV) *m/z:* 400 [M^+]. Anal. Calcd. for $C_{18}H_{11}Cl_2N_5O_2$: C 54.00, H 2.75, N 17.50; Found: C 53.92, H 2.70, N 17.56.

Results and discussion

In continuation of our ongoing efforts to develop newer and more benign approaches to the synthesis of various heterocyclic compounds [50–54], and also owing to the numerous advantages associated with participation of nano-catalysts in organic transformations, we were encouraged to examine the use of hitherto unexplored ZnO nanoparticles as efficient and reusable catalyst in the one-pot synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones **4a–n** and pyrazolo[1,2-a][1,2,4]triazole-1,3-diones **6a–n** (Scheme 1).

In order to establish the conditions of the titled reactions, we preliminary examined the model condensation reaction between malononitrile 1 (1 mmol), benzaldehyde 2a (1 mmol) and phthalhydrazide 3 (1 mmol) as test compounds. Screening of the reaction parameters was studied by using different solvents such as EtOH, MeCN, and H2O. The results are summarized in Table 1. As seen in this Table, it was noticed that, the reaction worked out best at 100 °C under solvent-free conditions with 15 mol % nano-ZnO catalyst loading (entry 7). To substantiate the important role of the catalyst, the reaction was carried out at 100 °C in the absence of the catalyst under solvent-free conditions. As a result, only trace amounts of the product was formed and the starting materials remained almost intact (entry 4). Also the reaction was conducted under conventional heating at reflux point using various solvents such as EtOH, MeCN, and H2O that resulted in the formation of only trace amounts of the product (entries 9–11).

To develop the scope of these reactions, various other aromatic aldehydes **2a–n** were subjected to condensation with malononitrile **1** under the optimized conditions (solvent-free/100 °C, 15 mol % nano-ZnO catalyst). Almost all the reactions proceeded smoothly in relatively short reaction times (8–20 min) to afford the respective 1H-pyrazolo[1,2-b]phthalazine-5,10-diones **4a–n** in high yields (86–93 %). The experimental results are summarized in Table 2.

Also, the reaction between malononitrile **1**, benzaldehyde **2a** and 4-phenylurazole **5a** as test compounds for the synthesis of pyrazolo[1,2-a][1,2,4]triazole-1,3-diones worked out best at 80 °C under solvent-free conditions catalyzed with nano-crystalline ZnO catalyst (15 mol %) as shown in Table 3 (entry **a**). Similarly, this reaction was successfully extended to various other 4-arylurazoles to furnish the corresponding products **6a–n** in high yields as

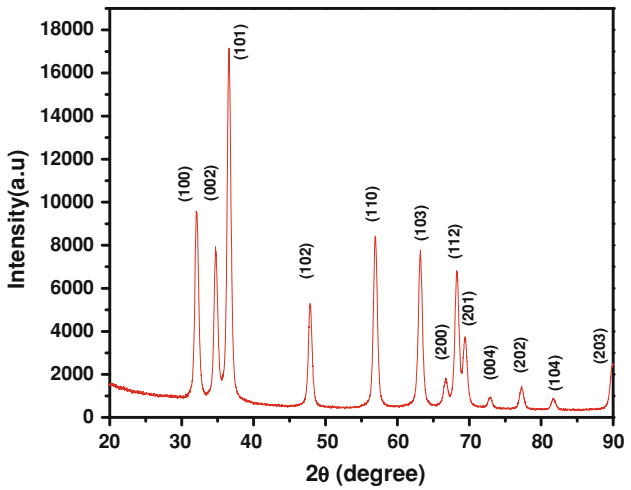


Fig. 1 X-ray diffraction (XRD) patterns of the prepared ZnO nanoparticles

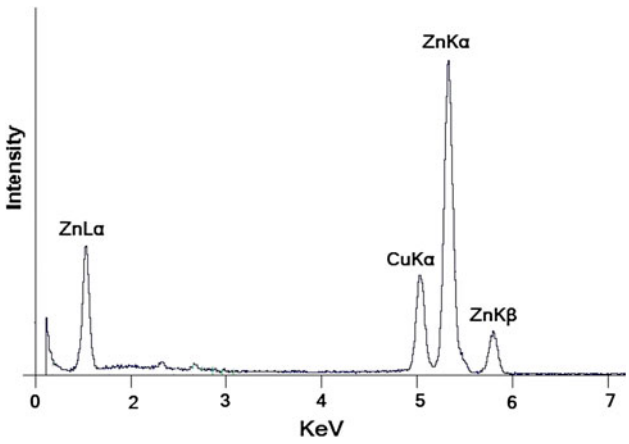


Fig. 3 EDAX spectrum of the prepared ZnO nanoparticles

given in Table 3. However, this method appears to be unsuitable for aliphatic aldehydes (entry **o**). The known products **4a–f** [43] and **6a–k** [53, 54] were characterized based on their physical and spectral (IR, ^{1}H NMR, ^{13}C NMR, MS) data which were in accord with the reported data. The new products **4g–n** and **6l–n** were characterized by their elemental and spectral (IR, ^{1}H NMR, ^{13}C NMR, MS) analysis as reported below.

Structural analysis of ZnO nanoparticles

The X-ray diffraction (XRD) spectrum of ZnO nanoparticles is shown in Fig. 1. Single phase formation has been observed and hardly appearance of any significant extra diffraction peaks other than ZnO crystal in the synthesized sample suggests that the nanocrystals have preferential orientation. All the XRD peaks are indexed by hexagonal Wurtzite phase of ZnO (JCPDS Card No. 80-0075). Powder XRD patterns were recorded on a Burker D4 ENDEAVOR X-ray diffractometer with Cu Kα radiation.

The specific surface area (SSA_{BET}) of ZnO samples has been measured using Brunauer–Emmett–Teller (BET) analysis. The average BET equivalent particle diameter (d_{BET}) were calculated using the average of the density of ZnO nanoparticles. The BET specific surface areas of the ZnO nanoparticles were determined using an accelerated surface area and porosimetry system (ASAP 2010) Micrometrics Instrument Corporation. Sample was degassed overnight at 373 K and surface area was measured by N_2 adsorption/desorption at 77 K. The measured BET

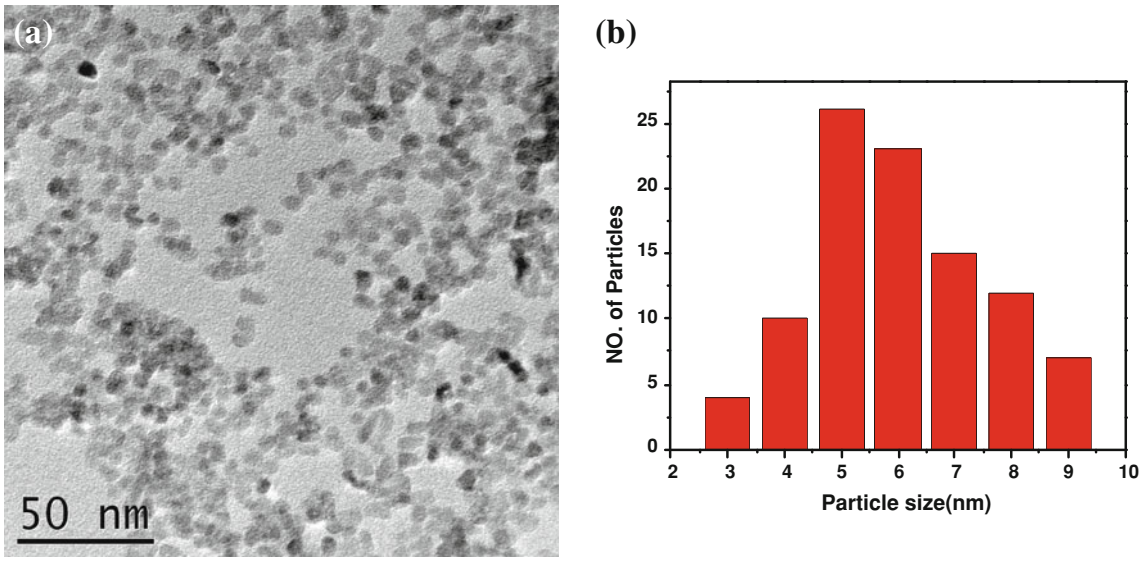
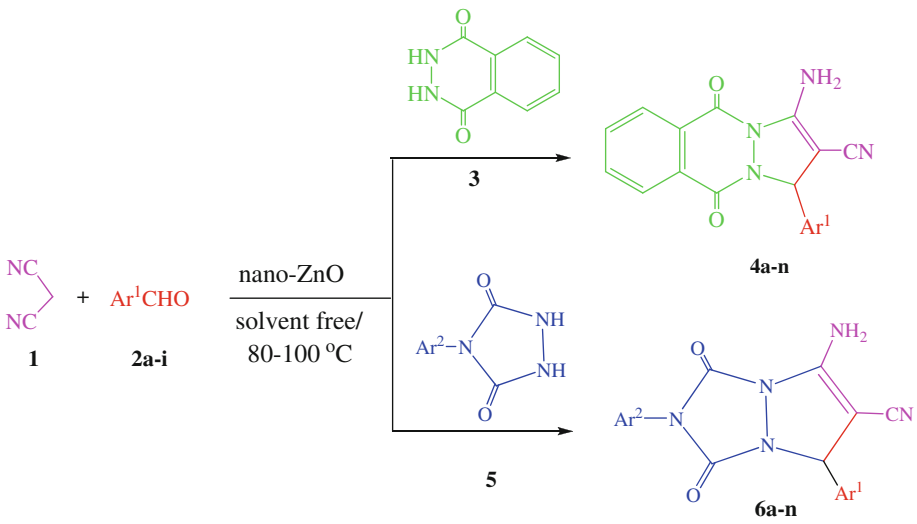
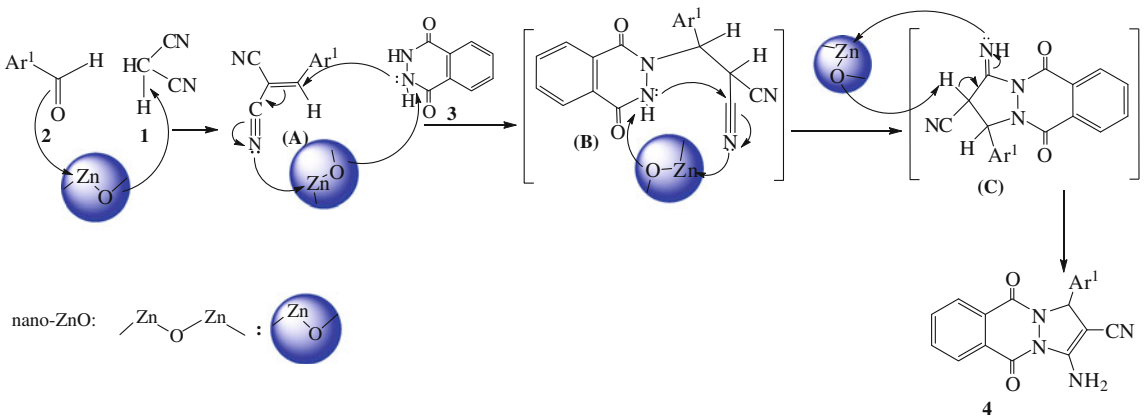


Fig. 2 Transmission electron micrographs (TEM) picture of ZnO is shown in (**a**) and the particle size distribution as obtained from TEM micrograph is shown in (**b**)



Scheme 1 Nano-ZnO-catalyzed synthesis of 1H-pyrazole[1,2-b]phthalazine-5,10-diones **4a–n** and pyrazolo[1,2-a]triazole-1,3-diones 6**a–n**



Scheme 2 A putative mechanism for the formation of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones **4**

surface area of the ZnO nanoparticles catalyst was found to be 29.06 m^2/g. Also using the same instrument almost no surface porosity was found on the surface of the nanopraticles.

TEM and EDX

The transmission electron microscopy (TEM) image determined for the pure ZnO nanoparticles is given in Fig. 2a. It is indicated that, the average size is ca 8 nm which approximately matches with the particle size calculated using Sherrer's formula. Figure 2b shows the particle size (diameter) distribution which is in the range of 3–9 nm.

The corresponding energy-dispersive X-ray (EDAX) spectrum of ZnO in Fig. 3 indicates the high purity of ZnO nanoparticles. In addition to the Zn peaks, the cupper peaks are also detected which are due to the used copper grid. The TEM image and EDAX spectrum were obtained on a Jeol 2010 microscope operated at 200 kV with Link Si(Li) X-ray detector. Sample powders were suspended in methanol and then directly deposited on a copper grid coated with a carbon film.

ZnO Nanoparticles possess an amphoteric structure creating both Lewis acid and base properties. Accordingly, a possible mechanism to explain the formation of 1*H*-pyrazolo[1,2-b]phthalazine-5,10-diones **4a–n** is depicted in Scheme 2. As shown in this Scheme, the reaction is likely initiated by a Knoevenagel-type condensation reaction between malononitrile **1** and aromatic aldehyde **2** under the catalytic effect of nano-ZnO followed by dehydration to provide the malononitrile derivative (**A**). This occurs through the activation of C–H bond in malononitrile by basic oxygen in the catalyst from the one hand, and the activation of the carbonyl group in aldehyde by the acidic part (Zn) of the catalyst on the other hand. Subsequently, a Michael-type addition of intermediate (**A**) to phthalhydrazide **3** under the catalytic effect of nano-ZnO occurs to yield a second intermediate (**B**) which successively undergoes cyclization to (**C**) and nano-ZnO-promoted tautomerization to afford the expected product **4**.

In conclusion, we have developed a convenient one-pot three component cyclocondensation reaction between aromatic aldehydes, malononitrile and phthalhydrazide or 4-arylurazoles for the synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones and pyrazolo[1,2-a][1,2,4]triazole-1,3-diones, respectively. High surface area and recyclability of the nano-crystalline ZnO catalyst, solvent-free conditions, easy preparation of the catalyst, low reaction times and high yields products are the main advantages of this method.

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References

1. S. Ikegami, H. Hamamoto, Chem. Rev. **109**, 583 (2009)
2. J. Lu, P.H. Toy, Chem. Rev. **109**, 815 (2009)
3. G.M. Scheuermann, L. Rumi, P. Steure, W. Bannwarth, R. Mulhaupt, J. Am. Chem. Soc. **131**, 8262 (2009)
4. L.D. Pachon, G. Rothenberg, Appl. Organomet. Chem. **22**, 288 (2008)
5. N.R. Shiju, V.V. Guliants, Appl. Catal. A Gen. **356**, 1 (2009)
6. H. Itoh, S. Utamapanya, J.V. Stark, K.J. Klabunde, J.R. Schlup, Chem. Mater. **5**, 71 (1993)
7. J. Guzman, B.C. Gates, Nano Lett. **1**, 689 (2001)
8. B.M. Choudary, M.L. Kantam, K.V.S. Ranganath, K. Mahender, B. Sreedhar, J. Am. Chem. Soc. **126**, 3396 (2004)
9. M.R. Hoffman, S.T. Martin, W. Choi, D.W. Bahnemann, Chem. Rev. **95**, 69 (1995)
10. S. Anadan, A. Vinu, N. VenkataChalam, B. Arabindoo, V. Murugesan, J. Mol. Catal. A Chem. **256**, 312 (2006)
11. B.M. Choudary, R.S. Mulukutla, K.J. Klabunde, J. Am. Chem. Soc. **125**, 2020 (2003)
12. M.J. Aliaga, D.J. Ramon, M. Yus, Org. Biomol. Chem. **8**, 43 (2010)
13. S. Shylesh, V. Schünemann, W.R. Thiel, Angew. Chem. Int. Ed. **49**, 3428 (2010)
14. T.Q. Zeng, W.W. Chen, C.M. Cirtiu, A. Moores, G.H. Song, C.-J. Li, Green Chem. **12**, 570 (2010)
15. B. Sreedhar, A.S. Kumar, P.S. Reddy, Tetrahedron Lett. **51**, 1891 (2010)
16. K.J. Klabunde, R. Mulukutla, *Nanoscale materials in chemistry* (Wiley Interscience, New York, 2001)
17. A.J. Amali, R.K. Rana, Green Chem. **11**, 1781 (2009)
18. V. Polshettiwar, R.S. Varma, Org. Biomol. Chem. **7**, 37 (2009)
19. A.G. Hu, G.T. Yee, W.B. Lin, J. Am. Chem. Soc. **127**, 12486 (2005)
20. K. Tanabe, *Solid acids and bases* (Academic Press, New York, 1970)
21. R. Schlogl, S.B. Abd Hamid, Angew. Chem. Int. Ed. **43**, 1628 (2004)
22. A.T. Bell, Science **299**, 1688 (2003)
23. C.L. Carnes, K.J. Klabunde, Langmuir **16**, 3764 (2000)
24. B.M. Choudary, K. Mahendar, K.V.S. Ranganath, J. Mol. Catal. A Chem. **234**, 25 (2005)
25. M.L. Kantam, K.V.S. Ranganath, K. Mahendar, L. Chakrapani, B.M. Choudary, Tetrahedron Lett. **48**, 7646 (2007)
26. M.H. Sarvari, H. Sharghi, J. Org. Chem. **69**, 2573 (2004)
27. E.K. Goharshadi, Y. Ding, P. Nancarrow, J. Phys. Chem. Solids **69**, 2057 (2008)
28. F. Matloubi Moghaddam, H. Saeidian, Mater. Sci. Eng. B **139**, 265 (2007)
29. F. Tamaddon, M.A. Amrollahi, L. Sharafat, Tetrahedron Lett. **46**, 7841 (2005)
30. I. Ugi, A. Dömling, Angew. Chem. Int. Ed. Engl. **39**, 3168 (2000)
31. I. Ugi, A. Dömling, Endeavor **18**, 115 (1994)
32. A. Dömling, Chem. Rev. **106**, 17 (2006)
33. E.C. Franklin, Chem. Rev. **16**, 305 (1935)
34. F.W. Bergstrom, Chem. Rev. **35**, 77 (1944)
35. F.W. Lichtenthaler, Acc. Chem. Res. **35**, 728 (2002)
36. A. Kiriazis, T. Ruffer, S. Jantti, H. Lang, J. Yli-Kauhaluama, J. Comb. Chem. **9**, 263 (2007)
37. V.M. Kolb, J.P. Dworkin, S.L. Miller, J. Mol. Evol. **38**, 549 (1994)
38. S. Grasso, G. DeSarro, N. Micale, M. Zappala, G. Puia, M. Baraldi, C. Demicheli, J. Med. Chem. **43**, 2851 (2000)
39. N. Watanabe, Y. Kabasawa, Y. Takase, M. Matsukura, K. Miyazaki, H. Ishihara, K. Kodama, H. Adachi, J. Med. Chem. **41**, 3367 (1998)
40. Y. Nomoto, H. Obase, H. Takai, M. Teranishi, J. Nakamura, K. Kubo, Chem. Pharm. Bull. **38**, 2179 (1990)
41. A.A. Bekhit, H.T.Y. Fahmy, S.A.F. Rostom, A.M. Baraka, Eur. J. Med. Chem. **38**, 27 (2003)
42. A.I. Eid, M.A. Kira, H.H. Fahmy, J. Pharm. Belg. **33**, 303 (1978)
43. H.A. Park, K. Lee, S.J. Park, B. Ahn, J.C. Lee, H.Y. Cho, K.I. Lee, Bioorg. Med. Chem. Lett. **15**, 3307 (2005)
44. D.S. Raghuvanshi, K.N. Singh, Tetrahedron Lett. **52**, 5702 (2011)
45. M.R. Nabid, S.J. Tabatabaei Rezaei, R. Ghahremanzadeh, A. Bazgir Ultrason, Sonochem. **17**, 159 (2010)
46. S. Mallakpour, Z. Rafiee, Synth. Commun. **37**, 1927 (2007)
47. S. Mallakpour, J. Chem. Educ. **69**, 238 (1992)
48. M.A. Zolfigol, G. Chehardoli, E. Ghaemi, E. Madrakian, R. Zare, T. Azadbakht, K. Niknam, S. Mallakpour, Monatsh. Chem. **139**, 261 (2008)
49. C. Pacholski, A. Kornowski, H. Weller, Angew. Chem. Int. Ed. **41**, 1188 (2002)
50. D. Azarifar, D. Sheikh, Heteroatom Chem. **22**, 106 (2011)
51. D. Azarifar, K. Khosravi, Z. Najminejad, K. Soleimani, Heterocycles **81**, 2855 (2010)
52. D. Azarifar, E. Nadimi, M.M. Ghanbari, Chin. Chem. Lett. **22**, 447 (2011)
53. D. Azarifar, R. Nejat-Yami, Heterocycles **81**, 2063 (2010)
54. D. Azarifar, R. Nejat-Yami, M.A. Zolfigol, J. Heterocycl. Chem. 2012 (in press).