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REVIEW

Recent developments on nano-ZnO catalyzed synthesis of bioactive heterocycles

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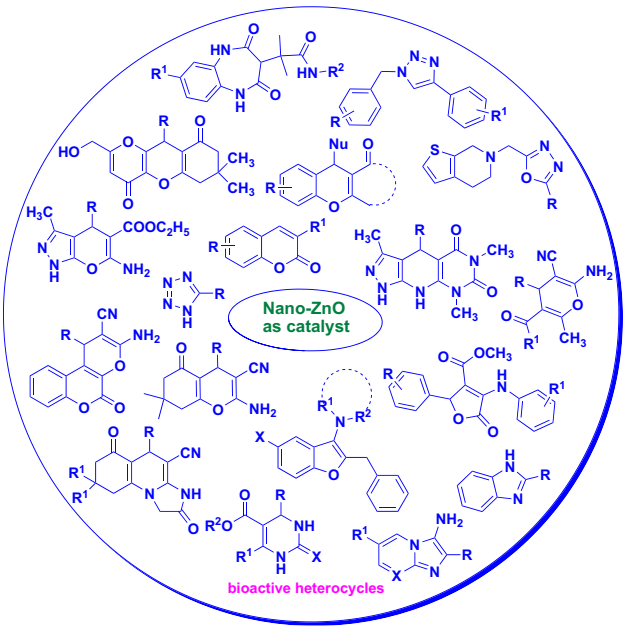
Abstract

Last decade has seen tremendous applications of nano-ZnO as a mild, cheap, efficient, commercially available, environmentally benign, non-toxic, reusable, heterogeneous catalyst for the various organic transformations. The present review summarizes the applications of nano-ZnO as an efficient heterogeneous catalyst for the synthesis of diverse biologically relevant heterocycles reported so far.

Graphical abstract



Keywords Bioactive heterocycles · Environmetally benign, Heterogeneous catalysts · Nano-ZnO · Organic synthesis

Introduction

Heterocycles are the core structural motif in the majority of organic compounds, known so far [1, 2]. Heterocyclic moieties are very common in naturally occurring compounds and are important because of their significant biological efficacies that include anticancer [3], cytotoxic [4], anti-malarial [5], anti-microbial [6], anti-inflammatory [7], anti-oxidant

In the memory of my heavenly grandfather, Amritapada Bandopadhyay.

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[8] and many more [9, 10]. Figure 1 represents a glimpse of marketed drugs containing heterocycles as the core structural unit [11–16].

It is well-established that along with other favorable conditions catalyst plays a crucial role for synthesis of heterocycles [17, 18]. Worldwide scientists are always trying to modify the catalyst to increase the efficiency of the reaction and to reduce their toxicity level as well. Screening of suitable catalyst is the key to success among the other significant parameters during chemical synthesis. Recently, various nano catalysts have gained much attention due to their greater surface area per unit mass [19]. In recent past, among the other nano catalysts, metal oxides such as ZnO, CuO, SiO_2, CeO_2, Fe_3O_4, CaO, In_2O_3 ZrO_2, etc. in nano form, have drawn considerable attention as efficient, environmentally sustainable, heterogeneous catalysts and have found immense applications in various organic transformations that include C-H funtionalizaion [20], synthesis of 2-aminobenzimidazoles,

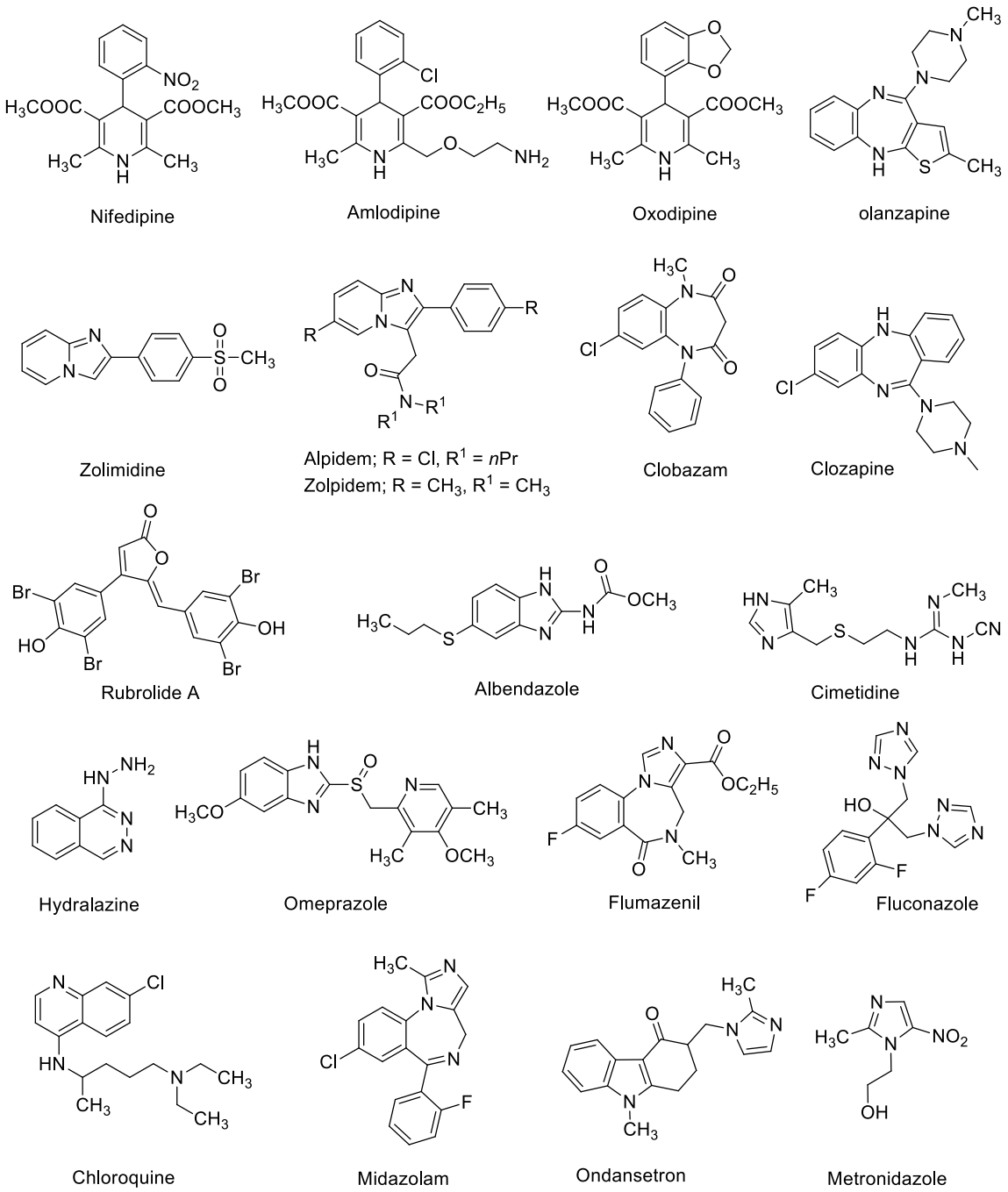


Fig. 1 Some of the marketed drugs containing heterocycles

2-aminobenzothiazoles, benzoxazoles [21], tetrahydrobenzofurans [22], α-aminophosphonate [23], *bis*-2,3-dihydroquinazolin-4(1*H*)-ones [24], 1,4-substituted 1,2,3-triazoles [25], xanthenes [26], pyrano[2,3-*d*]pyrimidines, 4*H*-chromenes, and dihydropyrano[3,2-*c*]chromenes [27], substituted pyridines [28], quinoxalin-2-amine [29] and many more [30, 31].

Among these, ZnO-nanoparticles were used in various areas, such as optoelectronics [32, 33], ferromagnetism [34], piezoelectric transducers [35], solar cell [36], gas sensors [37], etc. [38]. They also possess antibacterial [39] and antioxidant efficacies [40]. Various ZnO nanostructures, such as nanoparticles, nanorods, nanowires, nanobelts, nanotubes, nanobridges and nanonails, nanowalls, nanohelixes and polyhedral cages, have been synthesized and well characterized in recent years [41–43]. ZnO-nanoparticles can easily be synthesized from zinc acetate using either sol–gel [44] or precipitation method [45]. In many occasions, it was also synthesized in biogenic pathway using various plant extracts [46]. Thereby, past decade has seen tremendous applications of various morphologies of nano-ZnO as catalysts in different organic name reactions that include Mannich reaction [47], knoevenagel condensation [48, 49] and in various organic transformations, such as the synthesis of antiplatelet drug (Clopidogrel) [50], phosphonomalonates [51], ferrocenylphosphonates [52], 3-indolyl-3-hydroxy oxindoles [53], β-acetamido ketones/esters [54], *O*-acylation of alcohol [55], enamination of 1,3-dicarbonyls [56] and β-amino carbonyl compounds [57], etc.

The favorable physical and chemical properties like mild, low toxicity, low corrosion, large surface area, high pores volume, reusability, low cost, environmental sustainability and commercial availability make this Lewis acidic heterogeneous nano catalyst superior than others.

The present review focuses on the nano-ZnO catalyzed synthesis of diverse biologically relevant heterocycles and when possible to compare its catalytic efficiency with the rest of the congeners reported so far. The research groups working with this fascinating nano catalyst will surely be attracted by this review.

The following sections describe the catalytic applicability of nano-ZnO for the synthesis of biologically relevant heterocycles.

Nano-ZnO catalyzed synthesis of *N*-heterocycles

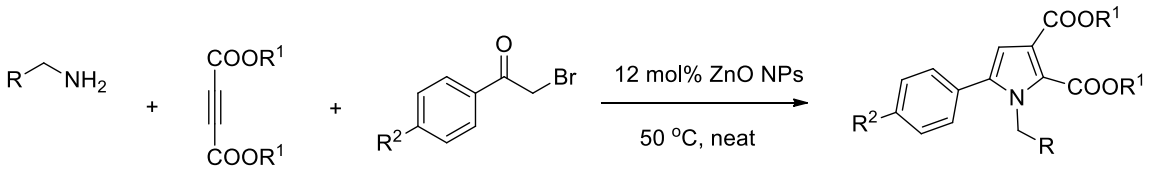
Synthesis of polysubstituted pyrroles

Pyrroles are very common in naturally occurring porphyrins, alkaloids and co-enzymes possessing various pharmacological efficacies [58–61]. Some marketed drugs like tallimustine, atorvastatin (Lipitor) contains pyrrol skeleton [62, 63]. Sabbaghan et al. (Table 1) [64] employed ZnO-nanorod as an efficient, reusable catalyst for the synthesis of polysubstituted pyrroles (**4**) via a one-pot three-component reaction between primary amines (**1**), dialkyl acetylenedicarboxylates (**2,2a**) and phenacyl bromide (**3**) under solvent free conditions at 50 °C. The catalyst was reused for the successive runs without significant loss of its activity. ZnO nanorod was found to be much more efficient than the commercial ZnO and even better that the ZnO-nanoparticles or sheets.

Synthesis of imidazoles

Imidazole and its derivatives possess a wide-range of biological activities that include anti-inflammatory [65], anti-tumor [66], anti-fungal [67] efficacies. Some marketed drugs like omeprazole consist of modified

Table 1 ZnO nanoparticles catalyzed synthesis of polysubstituted pyrroles



1 **2**; $R^1 = C_2H_5$ **2a**; $R^1 = CH_3$ **3** **4**

Entry	R	R^1	R^2	Time (min)	Yield (%)	Entry	R	R^1	R^2	Time (min)	Yield (%)
1	CH_3	CH_3	H	45	90	6	$4\text{-}CH_3C_6H_4$	H	C_2H_5	60	86
2	CH_3	C_2H_5	H	45	88	7	$4\text{-}ClC_6H_4$	H	C_2H_5	60	82
3	C_6H_5	CH_3	H	50	90	8	C_5H_{11}	H	C_2H_5	45	86
4	C_6H_5	C_2H_5	H	50	94	9	CH_3	OCH_3	C_2H_5	60	75
5	CH_3	CH_3	Cl	60	78	10	C_5H_{11}	H	CH_3	45	92

imidazole as a core unit [68]. Nikoofar et al. [69] synthesized ZnO-nanorods. After characterized it by X-ray diffraction (XRD), IR, and scanning electron microscopy (SEM) techniques, they successfully employed this ZnO-nanorods as an efficient, mild, reusable catalyst for the synthesis of 2,4,5-triaryl-1*H*-imidazolesin (**8**) via one-pot, three-component reactions of various aldehydes (**5**), benzils (**6**) and ammonium acetate (**7**) in water under reflux conditions (Table 2).

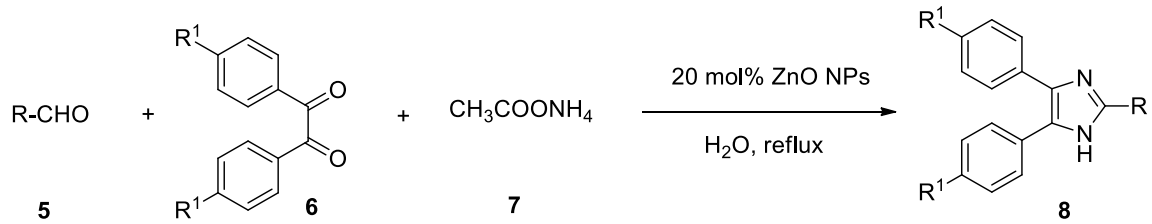
Synthesis of benzimidazoles

In 2012, Alinezhad et al. (Table 3) [70] reported the synthesis of benzimidazoles (**11**) from the reaction of *o*-phenylenediamines (**9**) and formic acid (**10**) in the presence of nano-ZnO as catalyst under solvent-free conditions at 70 °C. Very recently, in 2017, Paul et al. [71] have synthesized ZnO-nanoparticles under biogenic pathway from the seeds extract of *Parkia roxburghii.* Using these ZnO-nanoparticles as catalyst they have synthesized a series of 2-substituted-benzimidazoles (**11a**) from the reaction of *o*-phenylenediamine (**9**) and various aldehydes (**5**) under ultrasonic irradiation in ethanol at room temperature (Table 4).

Synthesis of imidazo-fused polyheterocycles

Nano-crystalline ZnO catalyzed simple, efficient, environmentally benign protocol was developed by Swami et al.

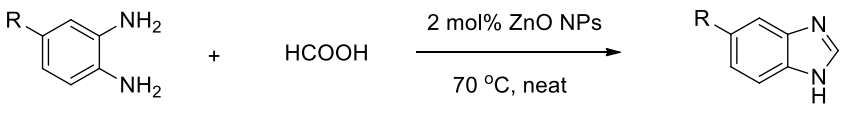
Table 2 ZnO nanoparticles catalyzed synthesis of 2,4,5-triaryl-1*H*-imidazoles



5 **6** **7** **8**

Entry	R	R^1	Time (h)	Yield (%)	Entry	R	R^1	Time (h)	Yield (%)
1	C_6H_5	H	2.5	80	14	1-Naphthyl	H	3.45	78
2	4-ClC_6H_4	H	1.45	83	15	2-furyl	H	3.45	79
3	4-BrC_6H_4	H	1.45	86	16	Cinnamyl	H	3.5	80
4	4-$N(CH_3)_2C_6H_4$	H	3.5	75	17	C_6H_5	Cl	2.5	82
5	4-$CH_3C_6H_4$	H	3.45	81	18	4-ClC_6H_4	Cl	2.25	87
6	4-$NO_2C_6H_4$	H	1.15	90	19	4-$OCH_3C_6H_4$	Cl	3	85
7	3-ClC_6H_4	H	2	90	20	4-$CH_3C_6H_4$	Cl	3	84
8	3-$OCH_3C_6H_4$	H	2.25	81	21	4-$N(CH_3)_2C_6H_4$	Cl	3.25	86
9	2-$NO_2C_6H_4$	H	1.45	78	22	C_6H_5	CH_3	3.5	87
10	2-OHC_6H_4	H	3.25	78	23	4-ClC_6H_4	CH_3	2.45	83
11	2-$OCH_3C_6H_4$	H	3.45	70	24	4-$OCH_3C_6H_4$	CH_3	4	82
12	3,5-$(OCH_3)_2C_6H_3$	H	4	78	25	4-$OCH_3C_6H_4$	OCH_3	4	80
13	2-OH-6-NO_2-C_6H_3	H	3.15	80					

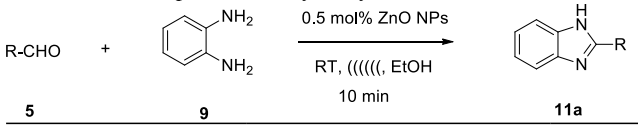
Table 3 ZnO nanoparticles catalyzed synthesis of benzimidazoles



9; 1 mmol **10**; 2 mmol **11**

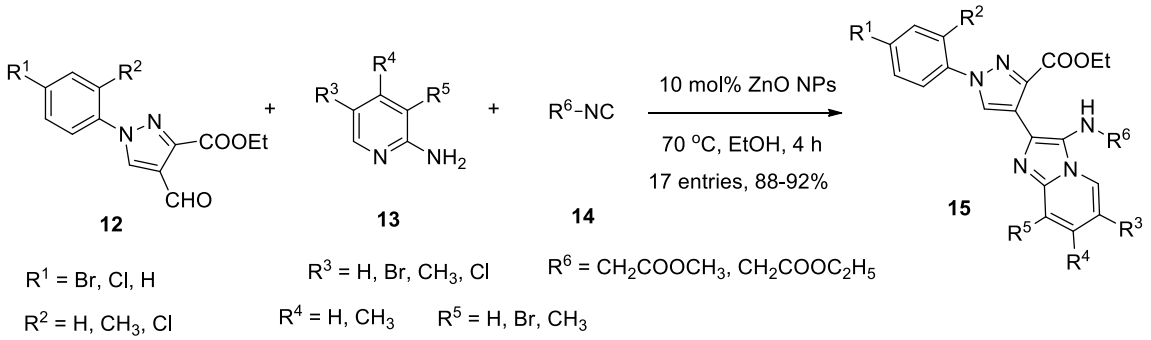
Entry	R	Time (min)	Yield (%)	Entry	R	Time (min)	Yield (%)
1	H	6	97	4	COOH	120	90
2	CH_3	30	94	5	COC_6H_5	150	92
3	OCH_3	240	98				

Table 4 ZnO nanoparticles catalyzed synthesis of 2-substituted-benzimidazoles



5 9 11a

Entry	R	Yield (%)	Entry	R	Yield (%)
1	H	93	6	3-OH-C_6H_4	93
2	C_6H_5	97	7	4-OCH_3-C_6H_4	92
3	4-OH-C_6H_4	95	8	4-Cl-C_6H_4	92
4	2-OH-C_6H_4	91	9	4-NO_2-C_6H_4	94
5	4-CH_3-C_6H_4	96			

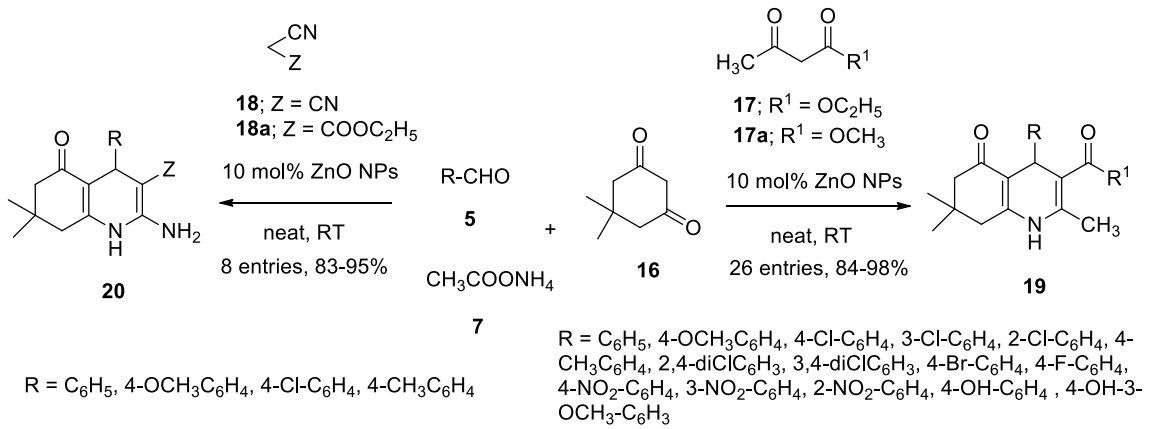


Scheme 1 ZnO nanoparticles catalyzed synthesis of imidazo-fused polyheterocycles

(Scheme 1) [72] for the synthesis of biologically promising pyrazole coupled imidazo[1,2-*a*]pyridine derivatives (**15**) via a one-pot three component reaction between various alkyl-4-formyl-1-phenyl-1*H*-pyrazole-3-carboxylates (**12**), 2-aminopyridines (**13**) and isocyanides (**14**) in ethanol at 70 °C.

Synthesis of polyhydroquinoline

A simple, efficient one-pot, four-component condensation of aldehydes (**5**), dimedone (**16**), alkyl acetoacetate (**17/17a**) and ammonium acetate (**7**) was achieved by Kassaee et al. (Scheme 2) [73] to synthesize 2-methyl-hexahydroquinoline derivatives (**19**) using ZnO nano-particles as catalyst under solvent-free conditions at room temperature. Changing alkyl acetoacetate (**17/17a**) by malononitrile (**18**) of the four component reaction they also synthesized a series of 2-amino-hexahydroquinolines (**20**) under the same optimized reaction conditions. After completion of the reaction, the catalyst was recovered and reused four times without any significant loss in catalytic activity.



Scheme 2 ZnO nanoparticles catalyzed synthesis of polyhydroquinoline

Synthesis of 1,4-diaryl dihydropyridine derivatives

ZnO-nanoparticles were found to be an efficient, reusable catalyst for the synthesis of 1,4-diaryl dihydropyridines (**21**) from the reaction between aldehydes (**5**), alkyl acetoacetate (**17/17a**) and substituted anilines (**20**) (Table 5) [74].

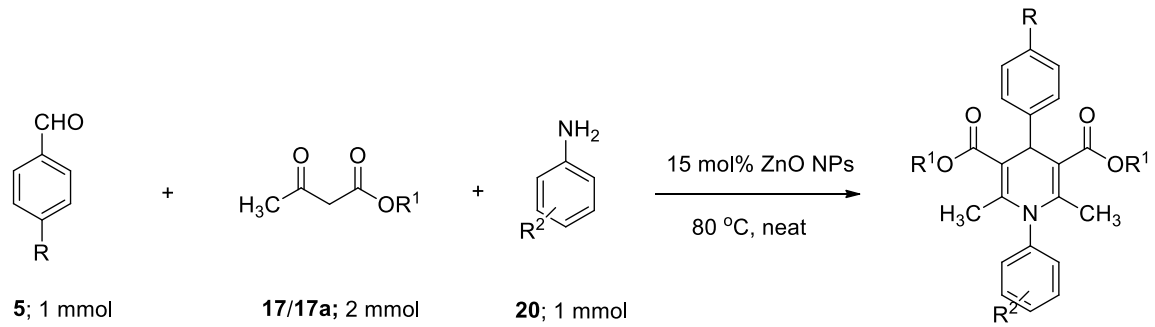
Synthesis of substituted 2,4,6-triaryl pyridines

Shafiee et al. (Table 6) [75] demonstrated a simple, convenient, ZnO nanopowder catalyzed condensation between benzaldehydes (**5**), acetophenones (**22**) and ammonium acetate (**7**) for the synthesis of substituted 2,4,6-triaryl pyridines (**23**) in good yields under solvent-free condition at 120 °C.

Synthesis of quinoxalines

Sadeghi et al. [76] described ZnO nanoparticles as an efficient and reusable catalyst for the synthesis of a series of quinoxaline derivatives (**24**) via the condensation between various 1,2-diketones (**6**) and 1,2-diamines (**9**) under solvent-free condition at room temperature (Scheme 3).

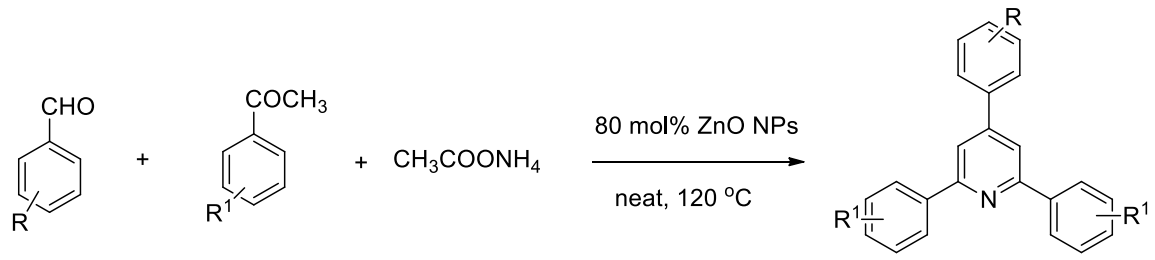
Table 5 ZnO nanoparticles catalyzed synthesis of 1,4-diaryl dihydropyridine derivatives



5; 1 mmol **17/17a;** 2 mmol **20**; 1 mmol **21**

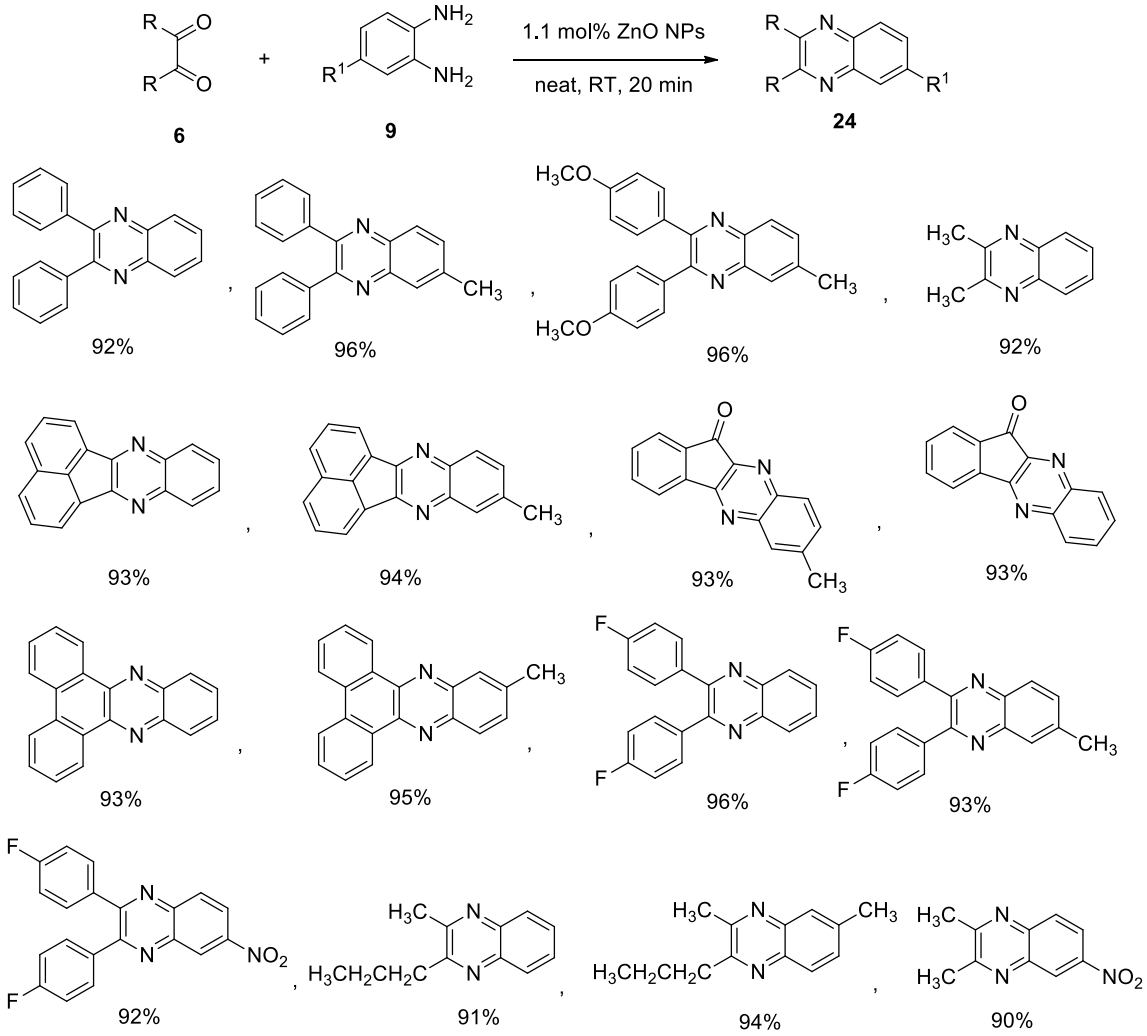
Entry	R	R^1	R^2	Time (min)	Yield (%)	Entry	R	R^1	R^2	Time (min)	Yield (%)
1	H	C_2H_5	H	120	82	6	H	C_2H_5	3-CH_3	135	85
2	H	C_2H_5	4-Br	90	92	7	H	C_2H_5	4-OCH_3	100	87
3	H	C_2H_5	4-Cl	80	90	8	Cl	C_2H_5	4-OCH_3	120	89
4	H	C_2H_5	4-CH_3	110	88	9	Cl	CH_3	4-CH_3	105	88
5	H	C_2H_5	3-Cl	120	86	10	Cl	CH_3	3-Br	109	87

Table 6 ZnO nanoparticles catalyzed synthesis of substituted 2,4,6-triaryl pyridines



5; 1 mmol **22**; 2 mmol 7; 1.3 mmol **23**

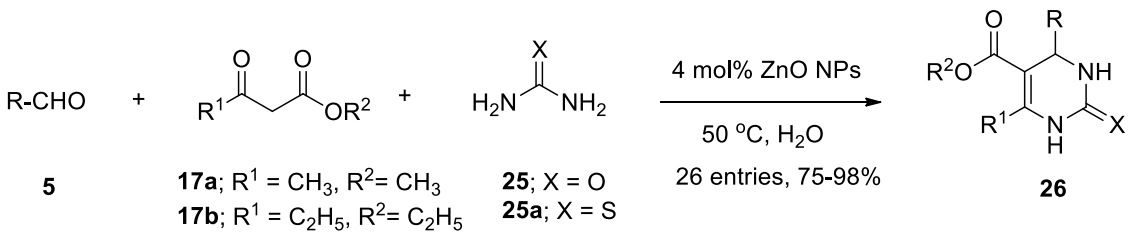
Entry	R	R^1	Time (min)	Yield (%)	Entry	R	R^1	Time (min)	Yield (%)
1	H	4-Br	135	86	7	4-Cl	4-Cl	135	83
2	4-Cl	4-Br	120	88	8	H	4-OCH_3	45	75
3	4-F	4-Br	100	91	9	4-CH_3	4-OCH_3	30	82
4	4-OCH_3	4-Br	90	95	10	4-Cl	4-OCH_3	45	78
5	H	4-Cl	105	87	11	4-NO_2	4-OCH_3	20	83
6	4-CH_3	4-Cl	150	85	12	H	4-OH	30	86



Scheme 3 ZnO nanoparticles catalyzed synthesis of quinoxalinein

Synthesis of dihydropyrimidinones

Dihydropyrimidinones (**26**) possess significant biological efficacies that include antiviral, antibacterial, antihypertensive and antitumor activity [77]. In 1893, Biginelli [78] first reported the synthesis of dihydropyrimidinones (**26**) with only 20–50% yields. In 2015, Hassanpour et al. [79] successfully employed ZnO nanoparticles as an efficient catalyst for the synthesis of dihydropyrimidinones (**26**) in good yields via a one-pot three component reaction between various aldehydes (**5**), alkyl acetoacetate (**17a**/**17b**) and urea (**25**) or thiourea (**25a**) in water at



Scheme 4 ZnO nanoparticles catalyzed synthesis of dihydropyrimidinones

50 °C. ZnO nanoparicles was found to be much more efficient than the commercial ZnO (Scheme 4). After completion of the reaction, the catalyst was recovered and reused successfully without any significant loss in catalytic activity.

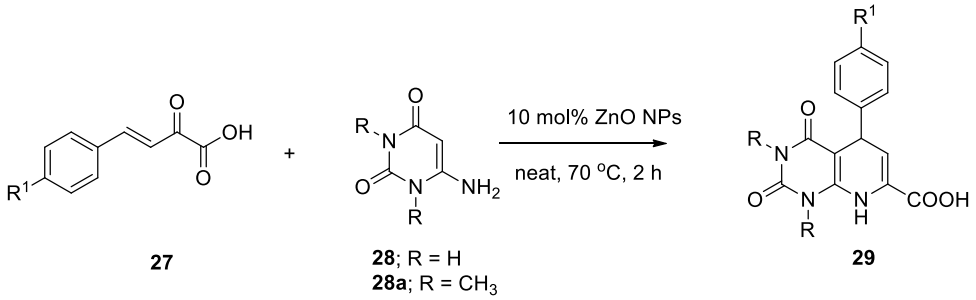
Synthesis of hexahydropyrido[2,3-d]pyrimidines

Abdolmohammadi [80] synthesized a series of hexahydropyrido[2,3-*d*]pyrimidine derivatives (**29**) via the cyclocondensation reaction between arylmethylidenepyruvic acids (**27**) and 6-aminouracils (**28**,**28a**) in the presence of catalytic amount of ZnO nanoparticles under solvent-free condition at 70 °C. After completion of the reaction, ZnO nanoparticles were recovered and recycled three times without any apparent loss in catalytic activity (Table 7).

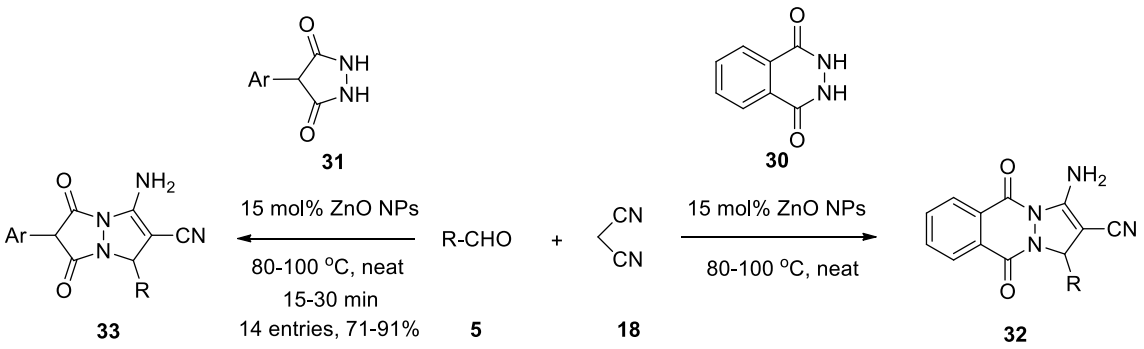
Synthesis of 1H-pyrazolo[1,2-b] phthalazine-5,10-diones and pyrazolo[1,2-a] [1, 2, 4] triazole-1,3-diones

Azarifar et al. [81] explored the catalytic activity of ZnO nano-particles for the synthesis of 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-diones (**32**) and pyrazolo[1,2-*a*] [1, 2, 4] triazole-1,3-dione derivatives (**33**) via a three-component coupling reaction between aromatic aldehydes (**5**), malononitrile (**18**), and phthalhydrazides (**30**) or 4-arylurazoles (**31**), respectively, under solvent-free condition at 80–110 °C. High product yields, short reaction times, non-toxicity, easy work-up and reusability of the catalyst are some of the merits of this developed protocol (Scheme 5).

Table 7 ZnO nanoparticles catalyzed synthesis of hexahydropyrido[2,3-*d*]pyrimidines



Entry	R	R^1	Yield (%)	Entry	R	R^1	Yield (%)
1	Cl	H	93	4	Cl	CH_3	98
2	OCH_3	H	94	5	OCH_3	CH_3	93
3	CH_3	H	91	6	CH_3	CH_3	96

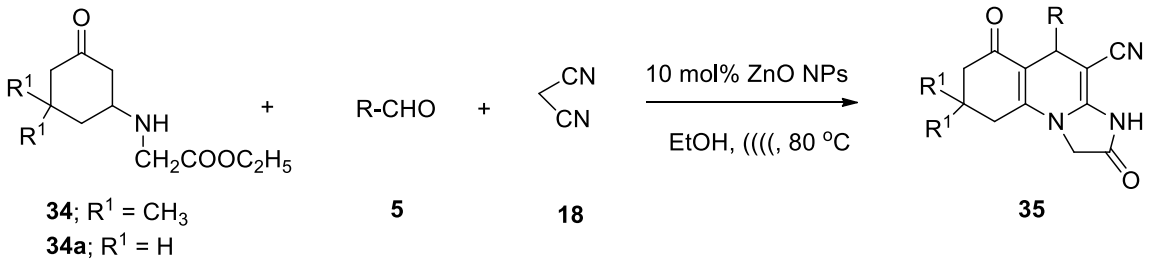


Ar = C_6H_5, 4-ClC_6H_4, 2,4-diClC_6H_3, 4-$NO_2C_6H_4$, 4-$OCH_3C_6H_4$

R = C_2H_5, C_6H_5, 4-ClC_6H_4, 3-ClC_6H_4, 3-$CHOC_6H_4$, 2,3-diClC_6H_3, 2,4-diClC_6H_3, 2,4,6-$(OCH_3)_3C_6H_2$, 4-Cl-3-NO_2-C_6H_3, 4-$NO_2C_6H_4$, 3-pyridyl, 4-pyridyl, 2-naphthyl, 3-$OCH_3C_6H_4$, 2-BrC_6H_4, 4-$CH_3C_6H_4$, 4-FC_6H_4

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

Table 8 ZnO nanoparticles catalyzed synthesis of imidazo[1,2-*a*]quinoline



34; $R^1 = CH_3$
34a; $R^1 = H$

5

18

35

Entry	R	R^1	Time (min)	Yield (%)	Entry	R	R^1	Time (min)	Yield (%)
1	C_6H_5	CH_3	45	90	4	C_6H_5	H	48	89
2	4-$CH_3C_6H_4$	CH_3	48	88	5	4-$CH_3C_6H_4$	H	55	88
3	4-ClC_6H_4	CH_3	42	92	6	4-ClC_6H_4	H	45	90

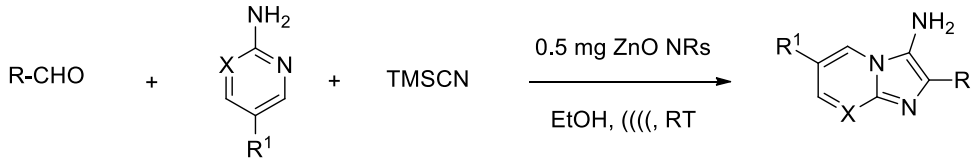
Synthesis of imidazo[1,2-a]quinoline

Imidazo[1,2-*a*]quinolines possess immense biological efficacies that include antiallergic [82], anxiolytic [83] activity. Recently, in 2014, a simple, efficient and ultrasound-assisted convenient protocol was developed by Abaszadeh et al. [84] for the synthesis of a series of imidazo[1,2-*a*]quinoline derivatives (**35**) via a one-pot three-component reaction between cyclic enaminoketones (**34**), aromatic aldehydes (**5**) and malononitrile (**18**) in the presence of catalytic amount of ZnO nanoparticles in EtOH at 80 °C (Table 8).

Synthesis of imidazo[1,2-a]pyridine/pyrimidine derivatives

Imidazo[1,2-*a*]pyridine/pyrimidines have gained significant attention from the pharmaceutical industry because of their promising biological efficacies that include antibacterial, antifungal, antiviral and anti-inflammatory activities [85, 86]. Many marketed drugs such as alpidem (anxiolytic), zolpidem (hypnotic), and zolimidine (antiulcer) contains imidazo[1,2-*a*]pyridine as the core structural unit [87, 88]. Sadjadi et al. [89] successfully employed ZnO-nanorods as an efficient, cost effective catalyst for the rapid synthesis of imidazo[1,2-*a*]pyrimidines (**38**) and imidazo[1,2-*a*]pyridines (**39**) via the one-pot three-component condensation between benzaldehydes (**5**), trimethylsilylcyanide (**37**) and pyrimidin-2-amines (**36**) or pyridin-2-amines **(36a)**, respectively, in ethanol under the influence of ultrasonic irradiation at room temperature. After completion of reaction they were able to recover ZnO nanoparticles and reused it up to third run without any significant loss in its catalytic activity (Table 9).

Table 9 ZnO nanoparticles catalyzed synthesis of imidazo[1,2-*a*]pyridine/pyrimidines



5

36; X = N
36a; X = CH

37

38; X = N
39; X = CH

Entry	R	R^1	Time (min)	Yield (%) of **38**	Entry	R	R^1	Time (min)	Yield (%) of **39**
1	4-$NO_2C_6H_4$	H	7	90	1	C_6H_5	Br	10	85
2	4-$OCH_3C_6H_4$	H	12	83	2	3-$NO_2C_6H_4$	CH_3	8	88
					3	4-ClC_6H_4	CH_3	7	90
					4	4-$CH_3C_6H_4$	CH_3	12	85

Synthesis of 5-substituted 1H-tetrazoles

A simple, mild and eco-friendly method was developed for the synthesis of 5-substituted 1*H*-tetrazoles (**42**) via the cycloaddition reaction of various nitriles (**40**) and sodium azide (**41**) using ZnO nanoparticles as a heterogeneous, reusable catalyst in DMF as solvent at 120–130 °C (Table 10) [90].

Synthesis of benzo[b][1,5]diazepines

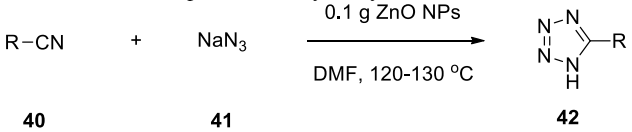
Benzodiazepine represents core structural motif in many marketed drugs such as olanzapine and clozapine (schizophrenia treatment) [91], clobazam (anxiolytic agents) [92], etc. Ghasemzadeh et al. (Table 11) [93] reported a mild, simple and convenient approach for the efficient synthesis of a series of biologically promising benzo[*b*][1,5]diazepines (**44**) via one-pot three-component reactions of aromatic diamines (**9**), various isocyanides (**14**) and Meldrum's acid (**43**) in the presence of a catalytic amount of ZnO nanoparticles in dichloromethane at room temperature. For this transformation, ZnO nanoparicles were found to be much more efficient than the commercial ZnO. After completion of the reaction, they were able to recover ZnO nanoparticles and reused six times without apparent loss in catalytic activity.

Nano-ZnO catalyzed synthesis of *O*-heterocycles

Synthesis of furan derivatives

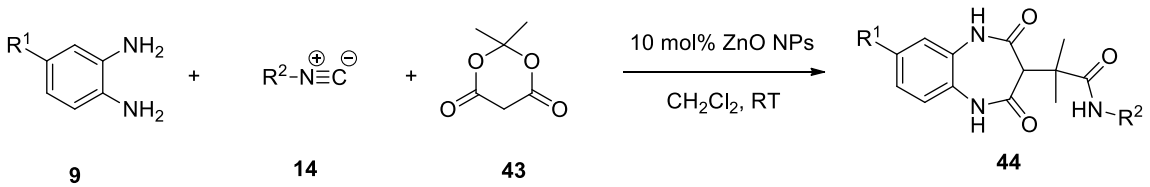
Furans are very common in naturally occurring bioactive heterocycles. This important structural motif has gained considerable attention because of its significant biological efficacies. Many marketed drugs such as rubrolide, sarcophine, benfurodil hemisuccinate [94, 95] contain furan skeleton. 5*H*-Furan-2-one derivatives exhibit many pharmacological and biological activities including antifungal, antibacterial, anti-oxidants, anti-inflammatory, anti-microbial and anticancer agents [96–100]. Benzo[*b*]furan containing heterocycles possesses immense pharmaceutical efficacies that include antifungal [101], antitumor [102] activity. Tekale et al. [103] synthesized a series of biologically promising 3,4,5-trisubstituted furan-2(5*H*)-one derivatives (**45**) by the one-pot three-component condensation between various

Table 10 ZnO nanoparticles catalyzed synthesis of 5-substituted 1*H*-tetrazoles



Entry	R	Time (min)	Yield (%)	Entry	R	Time (min)	Yield (%)
1	C_6H_5	14	72	5	4-$CHOC_6H_4$	14	69
2	4-ClC_6H_4	14	74	6	4-$ClC_6H_4CH_2$	24	71
3	2-ClC_6H_4	14	70	7	2-pyridyl	6	79
4	2-CNC_6H_4	24	81	8	pyrazine-2-yl	5	82

Table 11 ZnO nanoparticles catalyzed synthesis of benzo[*b*][1,5]diazepines



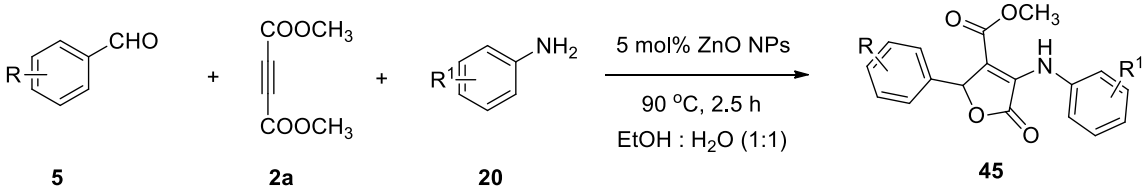
Entry	R^1	R^2	Time (h)	Yield (%)	Entry	R^1	R^2	Time (h)	Yield (%)
1	H	cyclohexyl	3.5	93	6	CH_3	cyclohexyl	3	95
2	H	$C(CH_3)_3$	3	95	7	CH_3	$C(CH_3)_3$	3	96
3	H	$CH_2C_6H_5$	3.5	91	8	CH_3	$CH_2C_6H_5$	3.5	94
4	H	$CH_2(CH_2)_3CH_3$	3.5	92	9	CH_3	$CH_2(CH_2)_3CH_3$	3.5	95
5	H	4-$OCH_3C_6H_4$	4	91	10	CH_3	4-$OCH_3C_6H_4$	3.5	93

aromatic aldehydes (**5**), dimethylacetylenedicarboxylate (**2a**) and substituted anilines (**20**) using nano-ZnO as an efficient, reusable, heterogeneous catalyst in aqueous ethanol at 90 °C (Table 12). After completion of the reaction, ZnO nanoparticles were recovered and reused several times without apparent loss in its catalytic efficacy. Safaei-Ghomi et al. [104] demonstrated a ZnO-nanoparticles catalyzed simple and efficient method for the convenient synthesis of 2,3-disubstituted benzo[*b*]furans (**49**) via a one-pot three-component coupling reaction between substituted salisaldehydes (**46**), secondary amines (**47**) and phenylacetylene (**48**) in aqueous ethanol under reflux conditions. ZnO nanoparicles was found to be more efficient than the other bulk metal oxides such as MgO, CuO, Fe_2O_3 etc (Table 13).

Synthesis of pyran derivatives

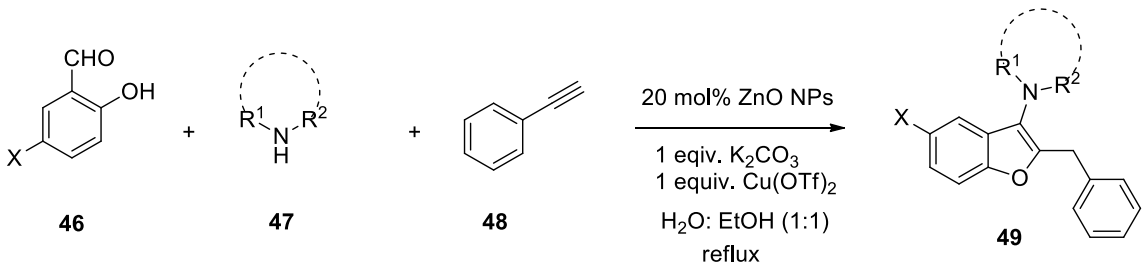
Pyrans and pyran-annulated heterocyclic scaffolds possess a broad spectrum of significant biological activities that include anticancer, cytotoxic, anti-HIV, anti-inflammatory, antimalarial, antimicrobial activity [105–107]. Das and his group reported a simple, efficient, environmentally benign protocol for the synthesis of 2-amino-3-cyano-4*H*-pyran derivatives via a one-pot three-component coupling reaction between a series of aromatic aldehydes (**5**), malononitrile (**18**) and 1,3-dicarbonyl compounds (**17**,**50**) using nano-ZnO as the catalyst in water at room temperature [108] (Scheme 6). Under the same optimized condition they also synthesized 2-amino-3-cyano-4*H*-chromenes (**52**) in good

Table 12 ZnO nanoparticles catalyzed synthesis of 3,4,5-trisubstituted furan-2(5*H*)-ones



Entry	R	R^1	Yield (%)	Entry	Q	R^1	Yield (%)
1	H	H	94	7	3-OCH_3	H	85
2	H	4-CH_3	95	8	4-CH_3	H	84
3	4-OCH_3	H	88	9	H	4-$CH(CH_3)_2$	88
4	H	4-F	84	10	H	2-F	84
5	4-Cl	H	89	11	2,4-diCl	2-F	85
6	2-Cl	H	87	12	2,4-$(OCH_3)_2$	H	83

Table 13 ZnO nanoparticles catalyzed synthesis of benzo[*b*]furans



Entry	X	R^1 and R^2	Time (min)	Yield (%)	Entry	X	R^1 and R^2	Time (min)	Yield (%)
1	H	Morpholine	90	92	7	Cl	Morpholine	60	92
2	H	Piperidine	90	90	8	Cl	Piperidine	65	94
3	H	Dibenzyl	110	80	9	Cl	Dibenzyl	80	85
4	Br	Morpholine	70	94	10	NO_2	Morpholine	55	96
5	Br	Piperidine	75	94	11	NO_2	Piperidine	55	94
6	Br	Dibenzyl	90	85	12	NO_2	Dibenzyl	65	88

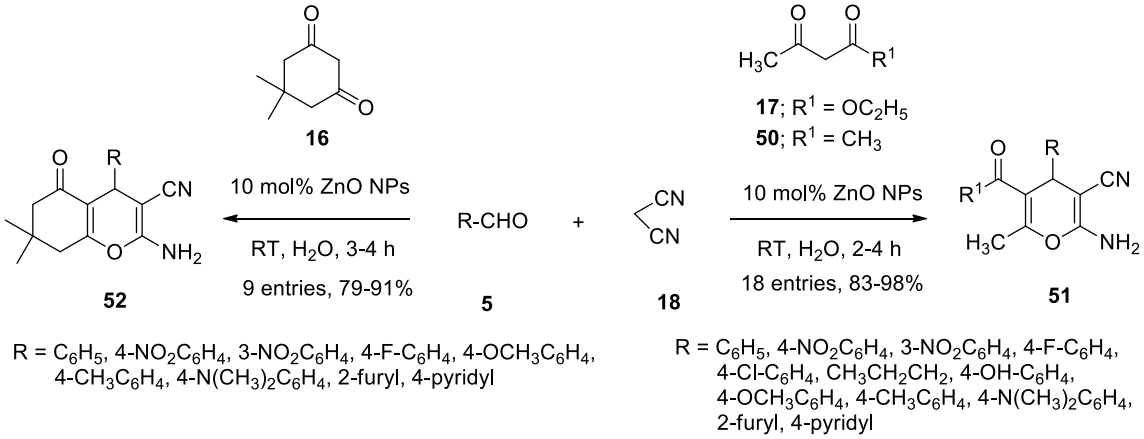
yields from the three-component reaction between aldehydes (**5**), malononitrile (**18**) and dimedone (**16**) (Scheme 6).

Very recently, in 2017, Zavar [109] has also synthesized a series of 2-amino-3-cyano-4*H*-chromenes (**52**) within just 10 min using nano-ZnO as catalyst in ethanol under reflux conditions (Table 14).

Synthesis of xanthenes

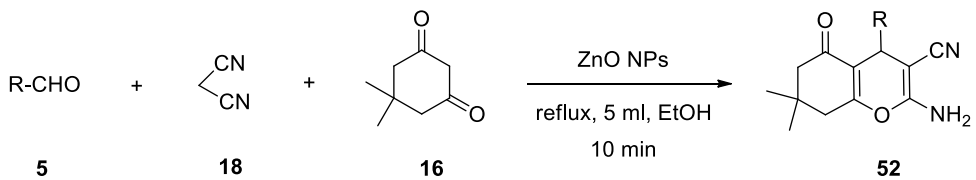
Xanthenes, in particular, 1,8-dioxo-octahydroxanthene moieties, have received significant attention due to their potent pharmacological efficacies such as antimicrobial, anticancer and enzyme inhibitory activity [110–112]. Recently, Safaei-Ghomi et al. have synthesized a variety of structurally diverse xanthene derivatives using ZnO-nanoparticles as catalyst. In 2013, they developed a simple protocol for the efficient synthesis of 1,8-dioxooctahydroxanthene derivatives (**53**) via a one-pot pseudo three-component condensation between various aldehydes (**5**) and dimedone (**16**) in the presence of catalytic amount of ZnO-nanoparticles at 90 °C under solvent-free conditions [113] (Scheme 7). The optimized reaction conditions also worked satisfactorily in synthesizing a variety of *N*-aryl-1,8-dioxodecahydroacridine derivatives (**54**) in one-pot when the reaction was carried out in presence of aromatic amines (**20**) with excellent yield of 70–91% within just 5–25 min (Scheme 7). After completion of reaction, nano-ZnO was successfully recovered and recycled for five successive runs with little loss in the catalytic activity.

To explore the catalytic efficiency of this fascinating catalyst, the same group has also employed nano-ZnO as catalyst for the synthesis of tetrahydrobenzo[*a*]xanthen-11-ones (**56**) via one-pot three-component reactions of aldehydes (**5**), 2-naphthol (**55**) and dimedone (**16**) under solvent-free condition at 120 °C [114] (Table 15). By changing 4-hydroxycoumarin (**57**) instead of dimedone (**16**) in the above-mentioned reaction they were also able to synthesize a range of 7-alkyl-6*H*,7*H*-naphtho[1′,2′:5,6]pyrano[3,2-*c*]chromen-6-one

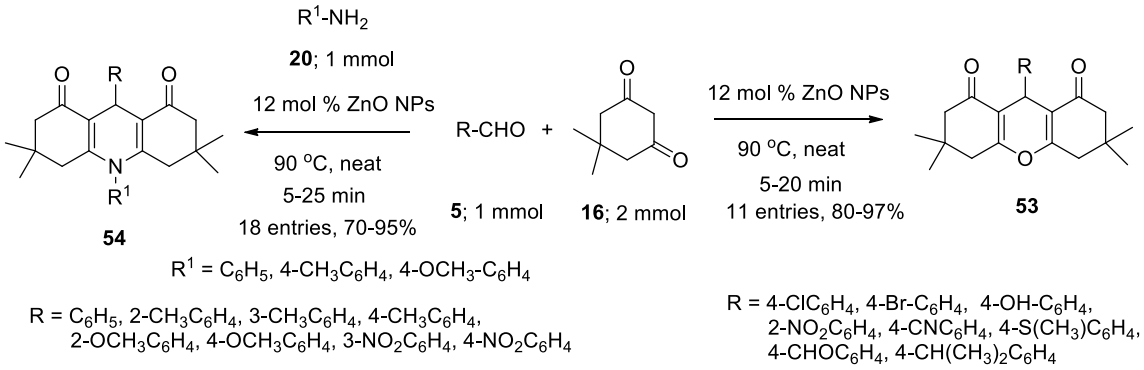


Scheme 6 ZnO nanoparticles catalyzed synthesis of 4*H*-pyran derivatives

Table 14 Nano-ZnO catalyzed synthesis of 2-amino-3-cyano-4*H*-chromenes

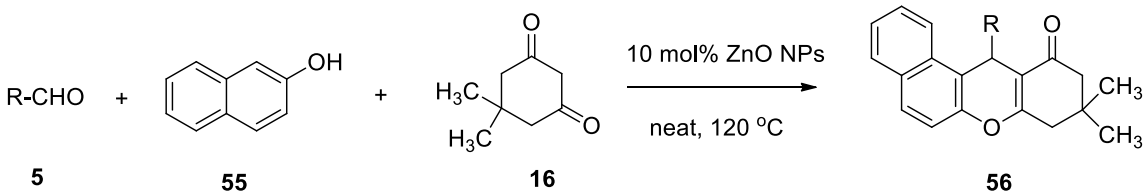


Entry	R	Yield (%)	Entry	R	Yield (%)
1	C_6H_5	90	6	2-$NO_2C_6H_4$	85
2	4-$N(CH_3)_2C_6H_4$	80	7	3-$NO_2C_6H_4$	92
3	4-$OCH_3C_6H_4$	78	8	2,4-diClC_6H_4	80
4	2-$OCH_3C_6H_4$	75	9	4-ClC_6H_4	80
5	3,4-$(OCH_3)_2C_6H_3$	80	10	4-BrC_6H_4	95



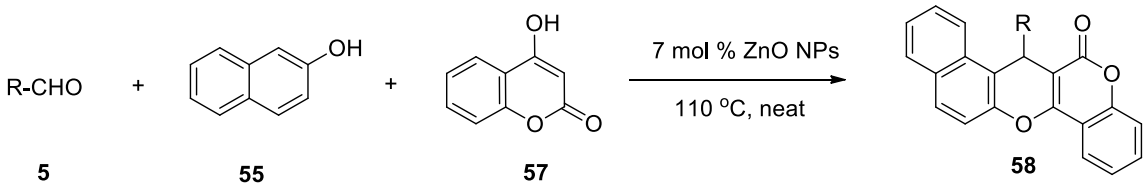
Scheme 7 ZnO nanoparticles catalyzed synthesis of 1,8-dioxo-decahydroacridines and 1,8-dioxooctahydro-xanthenes

Table 15 ZnO nanoparticles catalyzed synthesis of tetrahydrobenzo[*a*]xanthen-11-ones



Entry	R	Time (min)	Yield (%)	Entry	R	Time (min)	Yield (%)
1	C_6H_5	16	88	9	4-$CHOC_6H_4$	18	91
2	3-$NO_2C_6H_4$	15	90	10	2-$S(CH_3)C_6H_4$	22	87
3	4-$NO_2C_6H_4$	10	95	11	4-$CH(CH_3)_2C_6H_4$	20	86
4	4-ClC_6H_4	12	93	12	4-$OCH_3C_6H_4$	22	88
5	2,4-diClC_6H_3	20	92	13	2-$OCH_3C_6H_4$	30	85
6	4-BrC_6H_4	15	90	14	4-OHC_6H_4	25	90
7	4-FC_6H_4	15	92	15	3-$CH_3C_6H_4$	22	85
8	4-CNC_6H_4	15	90	16	4-$CH_3C_6H_4$	18	90

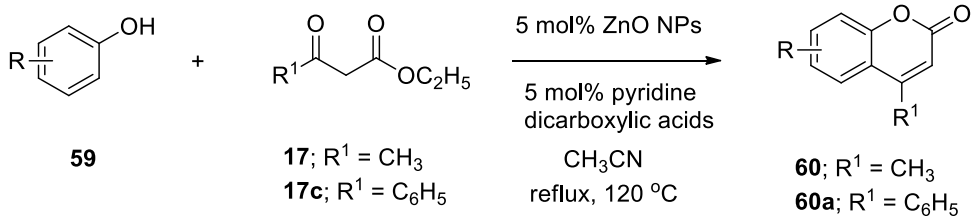
Table 16 ZnO nanoparticles catalyzed synthesis of pyrano[3,2-*c*]chromen derivatives



Entry	R	Time (min)	Yield (%)	Entry	R	Time (min)	Yield (%)
1	C_6H_5	50	70	7	2,4-diClC_6H_3	45	85
2	4-ClC_6H_4	40	91	8	4-BrC_6H_4	40	89
3	4-FC_6H_4	40	92	9	4-$OCH_3C_6H_4$	50	89
4	4-$CH_3C_6H_4$	60	85	10	4-OHC_6H_4	50	90
5	4-$NO_2C_6H_4$	40	93	11	3,4-diClC_6H_3	60	86
6	3-$NO_2C_6H_4$	60	70	12	2,5-$(OCH_3)_2C_6H_3$	60	81

derivatives (**58**) using the same nano-ZnO as catalyst under solvent-free condition at 110 °C [115] (Table 16). Short reaction times, high yields, easy workup procedure, wide substrate tolerance, small catalyst loading, reusability of the catalyst and solvent-free conditions are some of the salient features of these developed protocols.

Table 17 ZnO nanoparticles catalyzed synthesis of coumarins



59

17; $R^1 = CH_3$
17c; $R^1 = C_6H_5$

60; $R^1 = CH_3$
60a; $R^1 = C_6H_5$

Entry	R	Time (h)	Yield (%) of **60**	Entry	R	Time (h)	Yield (%) of **60a**
1	H	3	90	1	3-OH	4	88
2	3-OH	3	93	2	3,5-diOH	4	85
3	3,5-diOH	3	89	3	$3\text{-}OCH_3$	4	87
4	$3\text{-}OCH_3$	3	93	4	$3,5\text{-}diCH_3$	4	85
5	$2\text{-}CH_3\text{-}3\text{-}OH$	3.5	86				
6	$3\text{-}NH_2$	4	89				
7	$4\text{-}NO_2$	4	92				
8	4-Cl	4	73				

Synthesis of coumarins

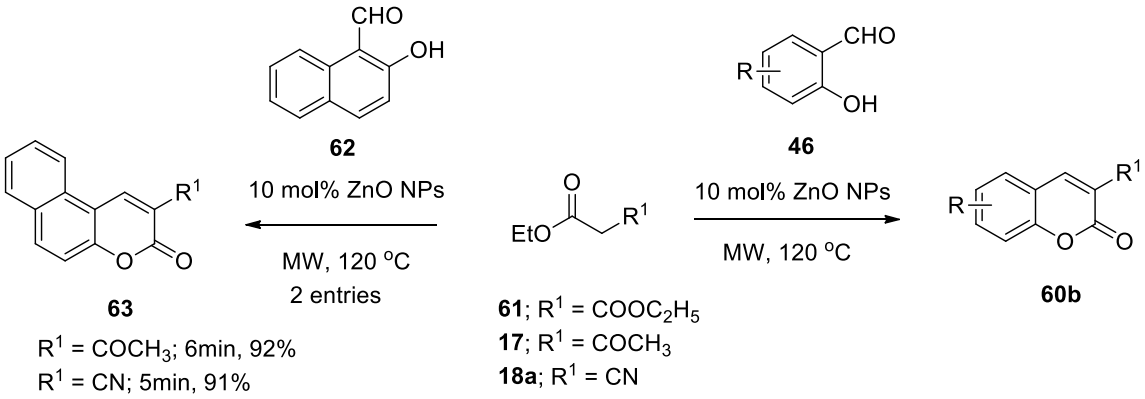
Coumarins are very common in the naturally occurring heterocycles like warfarin, phenprocoumon, coumatetralyl, carbochromen, bromadialone, etc. Heterocycles containing this important structural motif exhibit a wide range of pharmaceutical activities that include antibacterial, anti-HIV, antiviral, anticoagulant, antioxidant and anticancer activities [116–120]. Goswami [121] synthesized a wide range of 4-substituted coumarins (**60**) by the reaction of a wide range of structurally diverse phenols (**59**) and ethyl acetoacetate (**17**) or ethyl benzoyl acetate (**17c**) in the presence of nanocrystalline ZnO as catalyst and pyridine dicarboxylic acid as co-catalyst in acetonitrile under reflux conditions (Table 17).

Kumar et al. [122] achieved the synthesis of various 3-substituted coumarins (**60b**) by the nano-ZnO catalyzed reactions between salisaldehydes (**46**) and various 1,3-dicarbonyl compounds (**17**,**18a**,**61**) under microwave irradiation at 120 °C (Table 18). Under the same optimized reaction conditions they also synthesized benzo[*f*] chromen-3-ones (**63**) by using 2-hydroxy naphthaldehyde (**62**) instead of salisaldehyde (**46**) (Table 18). After completion of reaction, nano-ZnO was successfully recovered and recycled for several runs with consistent catalytic activity. During optimization, ZnO nanoparicles were found to be much more efficient than the commercially available bulk ZnO. Das and his group employed nanocrystalline ZnO as an efficient, reusable catalyst for the one-pot green synthesis of a series of benzylamino coumarin derivatives (**64**) from the reactions of various aromatic aldehydes (**5**), 4-hydroxycoumarin (**57**) and cyclic secondary amines (**47**) in water at room temperature [123] (Scheme 8).

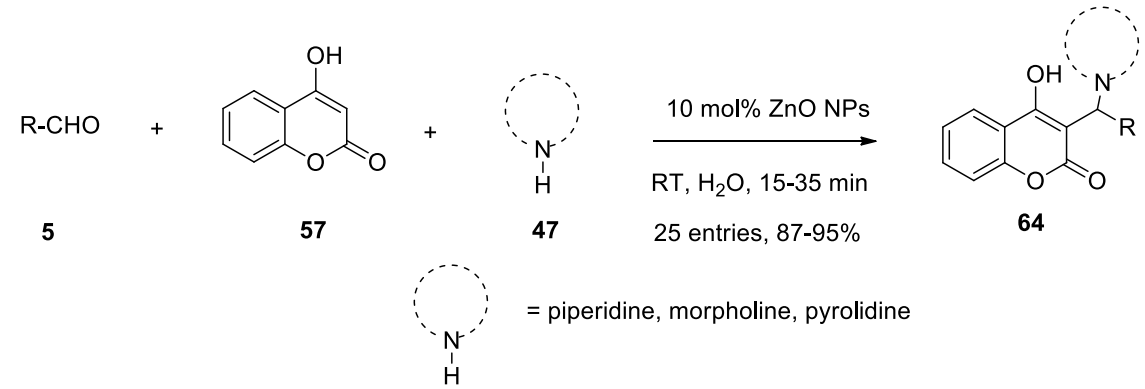
Synthesis of highly functionalized 4H-chromenes

Das and his group developed another nano-ZnO catalyzed protocol for the efficient synthesis of dihydropyrano[2,3-*c*]chromenes (**66**) via a one-pot, three-component coupling reaction between aromatic aldehydes (**5**), malononitrile (**18**) and 3-hydroxycoumarin (**65**) in water at 70 °C [124] (Table 19). Later on, the same group also synthesized a series of structurally diverse 4*H*-chromene derivatives (**69**) by the reactions of salisaldehydes (**46**), active methylene compounds (**16**,**16a**,**18**,**67a**) and C-H activated nucleophiles (**28**,**55**,**57**,**68a**,**68b**,**68c**,**68d**) employing the same nano-ZnO as catalyst in aqueous medium at 55 °C [125] (Scheme 9). During optimization it was found that the catalytic activity of nano-ZnO is superior to the other nano metal oxides such as nano-Al_2O_3, nano-MgO tested for these reactions. Nano-ZnO was recovered easily and recycled six times without significant loss in catalytic activity.

Table 18 ZnO nanoparticles catalyzed synthesis of coumarins

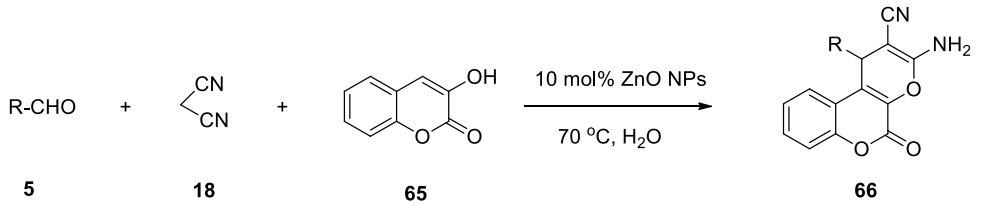


Entry	R	R^1	Time (min)	Yield (%) of **60b**
1	H	$COOC_2H_5$	5	92
2	H	$COCH_3$	6	90
3	3,4-$(OH)_2$	$COOC_2H_5$	4	86
4	3-OCH_3	$COOC_2H_5$	5	92
5	3-OCH_3	$COCH_3$	5	90
6	4-OCH_3	$COOC_2H_5$	6	92
7	4-OCH_3	$COCH_3$	5	93
8	3-$N(C_2H_5)_2$	$COOC_2H_5$	5	87
9	3-$N(C_2H_5)_2$	$COCH_3$	7	88
10	3-$N(C_2H_5)_2$	CN	7	90
11	3-OH	$COOC_2H_5$	5	62
12	4-OH	$COOC_2H_5$	7	85
13	5-Cl	$COCH_3$	9	92
14	5-Br	$COCH_3$	6	95
15	5-NO_2	$COCH_3$	8	93
16	5-OH	$COCH_3$	6	93



Scheme 8 ZnO nanoparticles catalyzed synthesis of benzylamino coumarin derivatives

Table 19 ZnO nanoparticles catalyzed synthesis of dihydropyrano[2,3-*c*]chromenes



5 18 65 66

Entry	R	Time (h)	Yield (%)	Entry	R	Time (h)	Yield (%)
1	C_6H_5	3	87	6	2-naphthyl	2.5	89
2	4-$NO_2C_6H_4$	2.5	91	7	4-FC_6H_4	2	90
3	4-$OCH_3C_6H_4$	3	78	8	4-CNC_6H_4	2.5	90
4	4-BrC_6H_4	2.5	89	9	2-thienyl	3	75
5	4-$CH_3C_6H_3$	3	83	10	4-$CHOC_6H_4$	4	65

Nano-ZnO catalyzed synthesis of *N*- as well as *O*-heterocycles

Synthesis of 6-amino-5-cyano-pyrano[2,3-c] pyrazoles

Pyrano[2,3-*c*]pyrazole and its derivatives possess significant biological efficacies that include anti-inflammatory, molluscicidal, insecticidal, antitumor and anticancer activity [126, 127]. Tekale et al. [128] developed a simple, convenient and practical method for the efficient synthesis of 6-amino-5-cyano-pyrano[2,3-*c*]pyrazoles (**71**) via a four-component reaction of ethyl acetoacetate (**17**), hydrazine hydrate (**70**), malononitrile (**18**) and various aromatic aldehydes (**5**) using nano-ZnO as a recyclable heterogeneous catalyst in aqueous medium at 70 °C (Table 20). In the same year, from the same batch of reactions, Sachdeva et al. [129] replaced malononirile (**18**) by ethylcyano acetate (**18a**) and synthesized ethyl 6-amino-pyrano[2,3-*c*]pyrazoles-5-carboxylate derivatives (**71a**) in good yields using the same nano-ZnO as a reusable catalyst in aqueous medium at room temperature (Table 21).

Synthesis of pyrazole based pyrido[2,3-d] pyrimidine-diones

Heravi et al. [130] reported the efficient synthesis of a series of pyrazolo-[4′,3′:5,6]pyrido[2,3-*d*]pyrimidine-dione derivatives (**72**) via a one-pot five-component condensation between hydrazine hydrate (**70**), ethyl acetoacetate (**17**), 1,3-dimethyl barbituric acid (**67a**), aromatic aldehydes (**5**) and ammonium acetate (**7**) in the presence of nano-ZnO in water under reflux conditions (Table 22). Use of nano-ZnO as catalyst offers several advantages such as operational simplicity, wide range of substrate tolerance, easy work-up and high yields of products.

Synthesis of structurally diverse pyridine derivatives

Siddiqui et al. [131] demonstrated the catalytic efficiency of ZnO-nanoparticles for the efficient synthesis of a series of novel pyridine derivatives (**76**,**77**,**78**,**79**,**80**) via a sequential three-component reaction of β-enaminones (**73**), ammonium acetate (**7**) and various active methylene compounds (**16**,**17**,**17a**,**43**,**57**,**67a**,**67aa**,**74**) under solvent-free conditions at 70 °C. Nano-ZnO was recovered easily and recycled six times without significant loss in catalytic activity (Scheme 10).

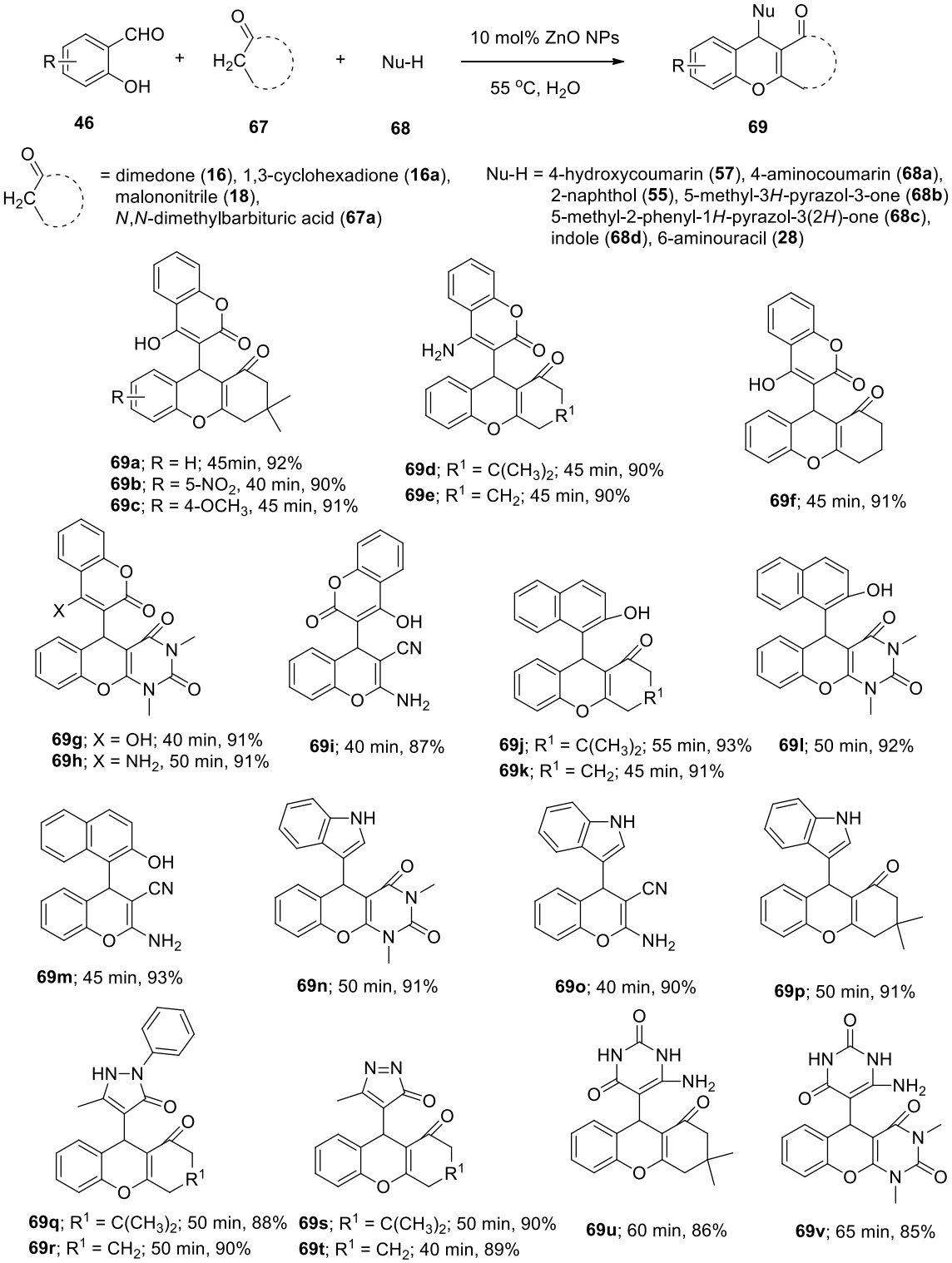
Synthesis of 1,3-oxazoline-2-thione derivatives

Haerizade et al. [132] synthesized a series of functionalized 2-thioxo-2,3-dihydro-1,3-oxazoles (**83**) from one-pot three-component reactions of ammonium thiocyanate (**81**), various acid chlorides (**82**) and phenacyl bromides (**3**) in the presence of a catalytic amount of nano-ZnO and *N*-methylimidazole as co-catalyst under solvent-free conditions at room temperature (Table 23).

Supported nano-ZnO catalyzed heterocycles synthesis

Synthesis of thieno[2,3-c]pyridine derivatives

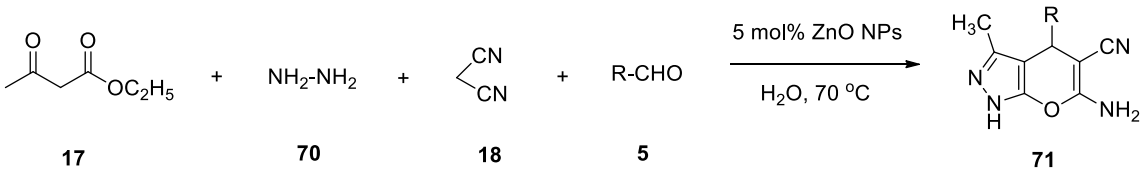
Sangshetti et al. [133] employed combined nano zinc oxide and titanium dioxide [nano (ZnO–TiO_2)] as an efficient catalytic system for the synthesis of a series of novel 4,5,6,7-tetrahydro-6-((5-substituted-1,3,4-oxadiazol-2-yl) methyl)thieno[2,3-*c*]pyridines (**85**) from the reactions of 2-(4,5-dihydrothieno[2,3-*c*]pyridin-6(7*H*)-yl)acetohydrazide



Scheme 9 ZnO nanoparticles catalyzed synthesis of densely functionalized 4*H*-chromenes

(**84**) and various substituted aldehydes (**5**) in ethanol under reflux conditions (Table 24). Catalytic activity of nano ($ZnO–TiO_2$) was found to be superior to the individual effect of nano ZnO or nano TiO_2. All the synthesized compounds were screened for their antimicrobial activities. Among them compounds **85f**, **85k**, **85l** have promising antibacterial as well as antifungal efficacies whereas compound **85j** possess promising antibacterial activity.

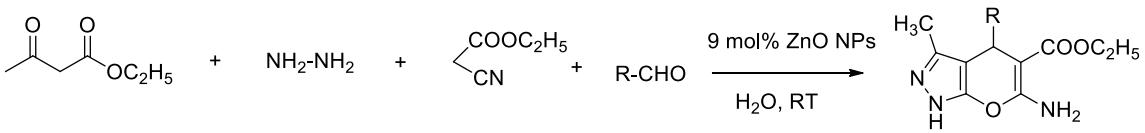
Table 20 ZnO nanoparticles catalyzed synthesis of 6-amino-5-cyano-pyrano[2,3-c]pyrazoles



17 **70** **18** **5** **71**

Entry	R	Time (min)	Yield (%)	Entry	R	Time (min)	Yield (%)
1	C_6H_5	60	94	8	4-BrC_6H_4	65	85
2	4-ClC_6H_4	60	90	9	4-$NO_2C_6H_4$	90	87
3	4-$N(CH_3)_2C_6H_4$	70	86	10	4-$OCH_3C_6H_4$	70	90
4	4-$S(CH_3)C_6H_4$	70	88	11	4-$NO_2C_6H_4$	90	87
5	4-OH-C_6H_4	90	82	12	2-furyl	80	86
6	2-ClC_6H_4	80	89	13	4-OH-3-$OCH_3C_6H_3$	80	91
7	4-$CH_3C_6H_4$	70	90				

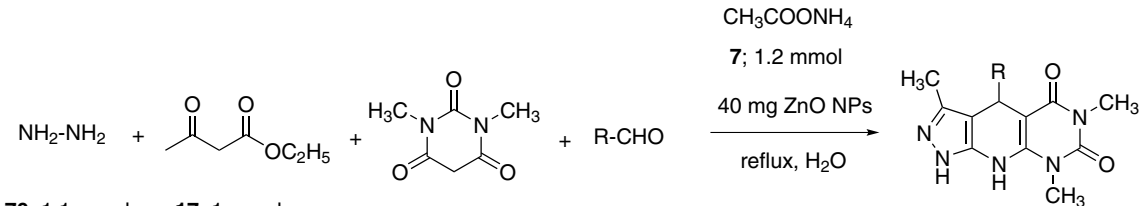
Table 21 ZnO nanoparticles catalyzed synthesis of ethyl 6-amino-pyrano[2,3-*c*]pyrazoles-5-carboxylate derivatives



17 **70** **18a** **5** **71a**

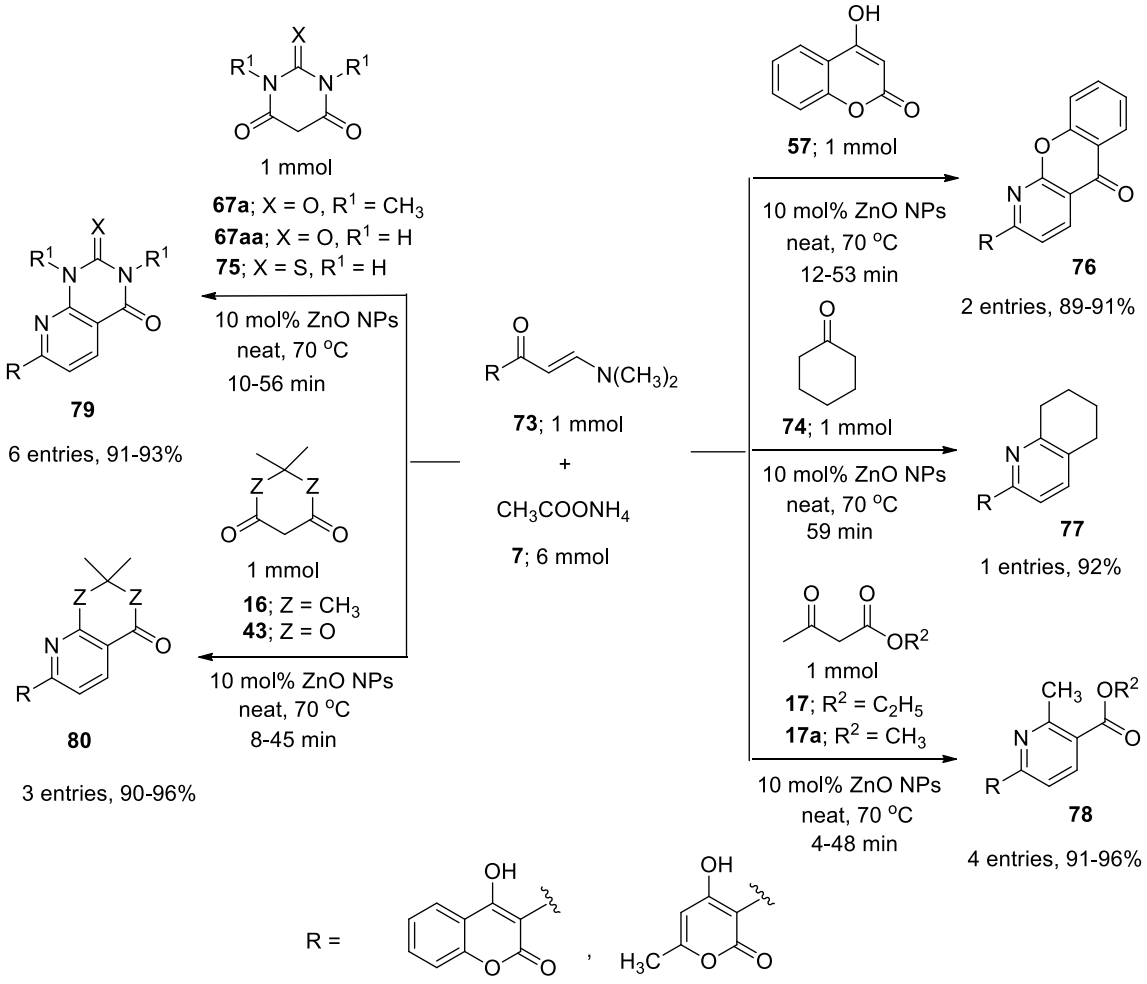
Entry	R	Time (min)	Yield (%)	Entry	R	Time (min)	Yield (%)
1	3,4-$(OCH_3)_2C_6H_3$	60	90	6	3-CH_3-2-furyl	60	86
2	3-$OCH_3C_6H_4$	55	85	7	2-thienyl	55	87
3	3,4,5-$(OCH_3)_3C_6H_2$	55	86	8	3-pyridyl	60	85
4	4-ClC_6H_4	60	87	9	2-OH-C_6H_4	60	87
5	4-$OCH_3C_6H_4$	55	89	10	3-OH-4-OCH_3-C_6H_3	60	85

Table 22 ZnO nanoparticles catalyzed synthesis of pyrido[2,3-*d*]pyrimidine-diones



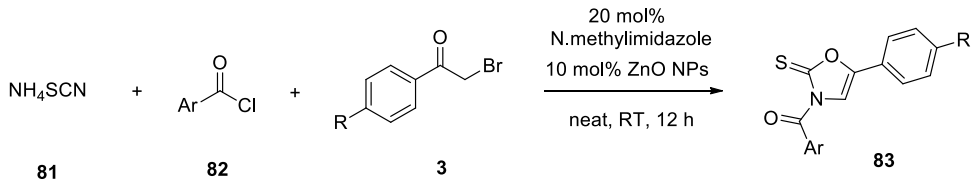
70; 1.1 mmol **17**; 1 mmol **67a**; 1 mmol **5**; 1 mmol **72**

Entry	R	Time (h)	Yield (%)	Entry	R	Time (h)	Yield (%)
1	C_6H_5	4	91	6	4-$NO_2C_6H_4$	4	91
2	4-FC_6H_4	3.5	90	7	3-$NO_2C_6H_4$	4.2	89
3	4-ClC_6H_4	3.5	91	8	4-OHC_6H_4	4.5	85
4	4-BrC_6H_4	3.8	90	9	4-$N(CH_3)_2C_6H_4$	4.5	85
5	2,4-diClC_6H_3	4	90				



Scheme 10 ZnO nanoparticles catalyzed synthesis of structurally diverse pyridine derivatives

Table 23 ZnO nanoparticles catalyzed synthesis of 1,3-oxazoline-2-thione derivatives

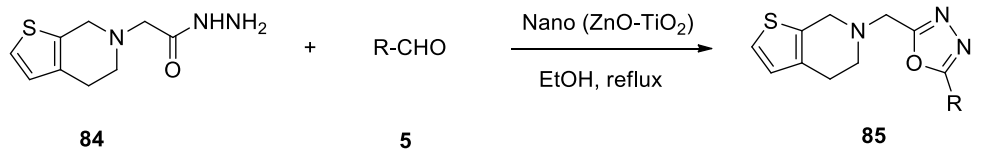


Entry	Ar	R	Yield (%)	Entry	Ar	R	Yield (%)
1	$4\text{-}BrC_6H_4$	$4\text{-}NO_2$	95	4	$4\text{-}OCH_3C_6H_4$	4-Br	85
2	$4\text{-}NO_2C_6H_4$	4-Br	75	5	$4\text{-}BrC_6H_4$	$4\text{-}OCH_3$	83
3	$4\text{-}NO_2C_6H_4$	$4\text{-}CH_3$	70				

Synthesis of pyrano[3,2-b]chromene

Ziraka et al. [134] prepared bismuth oxide supported nano zinc dioxide [nano Bi_2O_3-ZnO] by sol–gel method and characterized it by FT-IR, XRD, SEM, TEM and energy-dispersive X-ray analysis (EDX) analysis. They employed this newly synthesize catalytic system for the synthesis of pyrano[3,2-*b*]chromenes (**87**) via one-pot three-component reactions of various aromatic aldehydes (**5**), kojic acid (**86**) and dimethone (**16**) under solvent-free

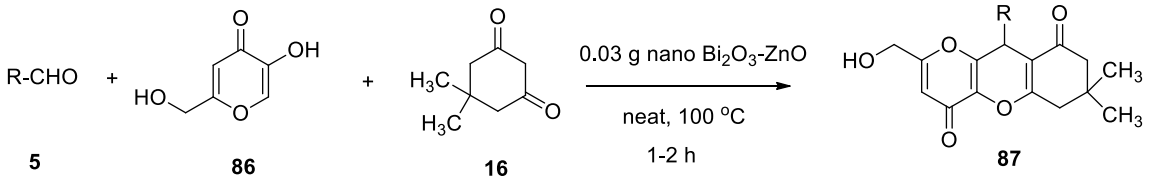
Table 24 ZnO nanoparticles catalyzed synthesis of thieno[2,3-*c*]pyridine derivatives



84 **5** **85**

Entry	R	Product	Time (min)	Yield (%)
1	4-ClC_6H_4	**85a**	12	96
2	C_6H_5	**85b**	12	91
3	4-$OCH_3C_6H_4$	**85c**	13	95
4	3,4-$(OH)_2C_6H_3$	**85d**	14	91
5	2-ClC_6H_4	**85e**	12	95
6	2,6-$(Cl)_2C_6H_3$	**85f**	12	91
7	2,4-$(OCH_3)_2C_6H_3$	**85g**	14	94
8	4-OH-C_6H_4	**85h**	13	94
9	C_4H_4N	**85i**	15	95
10	C_4H_3S	**85j**	14	94
11	4-FC_6H_4	**85k**	13	94
12	2,4-diClC_6H_3	**85l**	12	92
13	C_5H_4N	**85m**	15	95

Table 25 ZnO nanoparticles catalyzed synthesis of pyrano[3,2-*b*]chromene



5 **86** **16** **87**

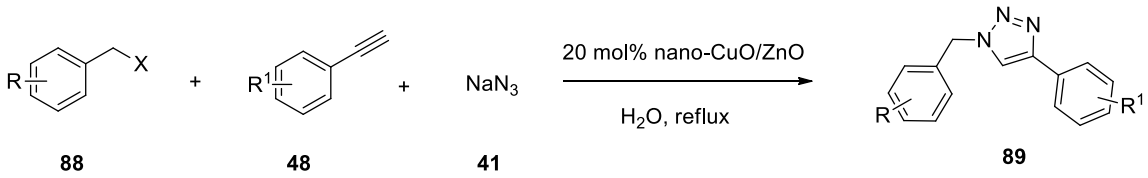
Entry	R	Yield (%)	Entry	R	Yield (%)
1	C_6H_5	80	6	4-$NO_2C_6H_4$	81
2	4-ClC_6H_4	82	7	2,4-diClC_6H_3	78
3	2-ClC_6H_4	79	8	4-$OCH_3C_6H_4$	75
4	3-$NO_2C_6H_4$	84	9	4-$CH_3C_6H_4$	77

condition at 100 °C (Table 25). During optimization it was found that the catalytic activity of combined nano ($ZnO–TiO_2$) is superior to the individual effect of nano ZnO or nano Bi_2O_3.

Synthesis of 1,2,3-triazoles

Albadi et al. [135] synthesized CuO supported nano-ZnO [nano-CuO–ZnO] by a co-precipitation method and well characterized it by XRD, SEM, TEM and EDS analysis. Using this newly prepared efficient catalytic system they synthesized a series of 1,2,3-triazoles (**89**) via one-pot three-component reactions of various benzyl halides (**88**) phenylacetylenes (**48**) and sodium azide (**41**) in water under reflux condition (Table 26). During optimization combined nano (CuO–ZnO) showed better catalytic efficacy than the individual nano-ZnO or nano-CuO. After completion of reaction, the catalyst was recovered easily and recycled for several runs without loss in catalytic activity.

Table 26 ZnO nanoparticles catalyzed synthesis of 1,2,3-triazoles



88 48 41 89

Entry	R	X	R^1	Time (min)	Yield (%)
1	H	Br	H	20	92
2	3-CH_3	Br	H	20	91
3	4-OCH_3	Br	H	15	92
4	2,4-diCl	Br	H	35	90
5	4-NO_2	Br	H	35	91
6	H	Br	3-NH_2	30	89
7	4-OCH_3	Br	3-NH_2	20	90
8	H	Cl	H	30	92
9	2,4-diCl	Cl	H	18	89

Conclusions

The present review describes the recent developments on the synthesis of biologically promising heterocycles using nano zinc oxide as a mild, cheap, non-toxic, efficient, reusable, Lewis acidic heterogeneous catalyst. For many organic transformations, catalytic efficacy of nano ZnO was found to be superior to the commercially available bulk ZnO. After completion of reaction, in many occasions nano-ZnO was successfully recovered and reused further for the several runs without significant loss in catalytic activity. This review will enrich the readers about the developments of ZnO nanoparticles catalyzed synthesis of various heterocycles reported so far. Therefore, the present review will surely attract attention of the organic methodologists working with this fascinating catalyst worldwide.

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