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CdO nanoparticles as an efficient, mild and recyclable catalyst for the synthesis of 2-aryl benzoxazole derivatives by grinding method

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ABSTRACT

CdO nanoparticles efficiently catalyzes the condensation of aromatic aldehydes with 2-aminophenol at room temperature to afford 2-aryl benzoxazole derivatives by grinding method. The reactions proceed under heterogeneous and mild conditions to provide 2-aryl benzoxazoles in excellent yields (87-97 %) with high purity under solvent free condition. The reaction requires short time (5-23 minutes) under moderate conditions. The purification of products by non-chromatographic methods is additional feature of this method. A series of 2-aryl bezoxazole have been successfully synthesized by this method. Ease of recycled catalyst, cleaner process, solvent free and lower catalytic loading are the most advantages of the proposed method.

***Keywords**: Nano-catalyst, Benzoxazole derivatives, CdO nanoparticles, Grinding method, Solvent free.*

1. Introduction

2-Aryl benzoxazoles have received considerable attention in diverse areas of chemistry. The benzoxazole contains a phenyl ring fused to an oxazole ring. Benzoxazole have been reported to show a broad spectrum of biological activities and have wide range of therapeutical properties [1]. Various benzoxazole derivatives possess different pharmacological and biological activities of which the most potent is an antibiotic [2], antibacterial, antifungal, antitumor, anti-inflammatory, antiulcer, antitubercular activities, cathepsin S inhibitors, selective peroxisome proliferator-activated receptor antagonists, HIV reverse transcriptase inhibitors, anticancer agents, estrogen receptor agonists and orexin-1 receptor antagonists [3-8]. Benzoxazole derivatives have also found application as herbicides and as fluorescent whitening agent dyes [9].

There are two general methods for synthesizing substituted benzoxazoles. One is the coupling of 2-aminophenols with carboxylic acid derivatives, which is either catalyzed by strong acids [10] or microwave conditions [11].

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The other is the oxidative cyclization of phenolic Schiff bases derived from the condensation of 2-aminophenols and aldehydes. In the latter reactions, various oxidants such as DDQ [12], pyridinium chlorochromate [13], $Mn(OAc)_3$ [14], $PhI(OAc)_2$ [15], $BaMnO_4$ [16], NiO2 [17], nickel supported silica [18], hydrogen tetrachloroaurate [19], heteropolyacids [20], zinc triflate [21], PFG400 [22], SBA-Pr-SO_3H [23], potassium cyanide [24], $ZrOCl_2$ $8H_2O$ [25], ($[Hbim]BF_4$) [26], silica sulfuric acid [27], $Cu(OTf)_2$ [28], $In(OTf)_3$ [29], copper(II) oxide nanoparticles [30], nano SnO_2 [31], $Pb(OAc)_4$ [32], nano CeO_2 [33], zinc acetate [34], glycerol [35] and ZnO nanoparticles [36] have been used. However, all of these oxidants are required in stoichiometric or excess amounts relative to their respective substrates and some of these methods suffer from certain disadvantages such as long reaction time, organic solvents and tedious work-up procedures. Solvent-free organic synthesis decreases both the cost of the synthesis and the amount of waste flow. As a part of our research interest towards development of efficient and safe for organic synthesis [37-40], herein we report the synthesis of benzoxazole derivatives using CdO nanoparticles as a recyclable catalyst at room temperature under solvent free condition by grinding method.

2. Experimental

2.1. General

CdO nanoparticles was synthesized by the hydrothermal method and characterized by different analytical techniques [39]. Melting points of organic compounds were determined in an open capillary and are uncorrected. IR spectrum was recorded on Schimadzu 8400S spectrometer using KBr pellets. ^{1}HNMR spectra were recorded with a Bruker Advance II 400-MHz spectrometer in DMSO as solvent and with TMS as internal standard. ^{13}CNMR spectra were recorded with a Bruker Advance II 100 MH spectrometer in DMSO. Mass spectra were recorded with a Varian-Saturn GC-MS instrument.

2.2. General procedure for the synthesis of 2-aryl benzoxazole

A mixture of 2-aminophenol (1.0 mmol), benzaldehydes (1.0 mmol) and cadmium oxide nanoparticles catalyst (0.05 mmol) was grinded in a mortar pestle at room temperature. The progress of the reaction was monitored by thin layer chromatographic technique. After completion of the reaction, the product was isolated using dichloromethane and the catalyst was filtered off. The dichloromethane was evaporated to get crude product. The crude product was further purified by recrystallization with ethanol to afford pure product. All products were identified by comparison of their physical and spectroscopic data with those reported for authentic samples. The products were obtained in high yields (87-97%). Spectral data (FT-IR, ^{1}HNMR, ^{13}CNMR and MS) for all synthesized compounds are reported. The characterization data of some representative synthesized compounds are shown below.

Selected spectral data

*2-Phenylbenzoxazole **(3a)**:*

FT-IR (KBr): $\bar{\nu}$= 2972, 1612, 1244, 1037, 805 cm^{-1}. ^{1}HNMR (DMSO-d_6, 400 MHz): δ = 8.21-8.18 (m, 2H, Ar-H), 7.75 (t, 1H, *J* = 7.7 Hz, Ar-H), 7.55-7.47 (m, 4H, Ar-H), 7.31-7.26 (m, 2H, Ar-H) ppm. ^{13}CNMR (DMSO-d_6, 100 MHz): δ = 160.9, 149.7, 140.5, 130.7, 126.9, 125.2, 124.0, 123.5, 123.1, 117.2, 108.6 ppm. MS: m/z= 196 (M+1).

*2-(4-Nitorophenyl) benzoxazole. **(3c)**:*

FT-IR (KBr): $\bar{\nu}$= 1636, 1528, 1340, 1236, 1052 cm^{-1}. ^{1}HNMR (DMSO-d_6, 400 MHz): δ= 8.33 (d, 2H, *J*= 8.7Hz), 8.09 (d, 2H, *J* =8.6Hz), 7.37 (d, 1H, *J* =7.8Hz), 7.30 (t, 1H, *J* =7.8Hz), 7.06 (d, 1H, *J* =7.9Hz), 6.92 (t, 1H, *J* =7.7Hz) ppm. ^{13}CNMR (DMSO-d_6, 100 MHz): δ = 152.9, 151.7, 148.7, 140.1, 133.4, 129.4, 128.5, 123.4, 119.2, 114.4, 113.2 ppm. MS: m/z= 241 (M+1).

*2-(4-Chlorophenyl) benzoxazole **(3f)**:*

FT-IR (KBr): $\bar{\nu}$= 3304, 2992, 1618, 1572, 1485, 1371, 1232, 1190, 741 cm^{-1}. ^{1}HNMR (DMSO-d_6, 400 MHz): δ = 7.88 (d, 2H, *J* =8.7Hz), 7.49 (d, 2H, *J* =8.6Hz), 7.31 (d, 1H, *J* =7.8Hz), 7.24 (t, 1H, *J* =7.7Hz), 7.04 (d, 1H, *J* =7.9Hz), 6.95 (t, 1H, *J* =7.8Hz) ppm. ^{13}CNMR (DMSO-d_6, 100 MHz): δ = 154.2, 151.3, 136.2, 134.2, 133.4, 128.7, 128.0, 127.5, 119.2, 114.7, 113.6 ppm. MS: m/z= 230 (M+1).

*2-(4-Methylphenyl) benzoxazole **(3h)**:*

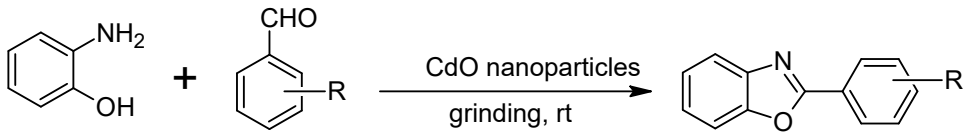
FT-IR (KBr): $\bar{\nu}$= 3081, 1633, 1241, 1059 cm^{-1}. ^{1}HNMR (DMSO-d_6, 400 MHz): δ = 8.16 (d, 2H, *J* = 8.0 Hz), 7.77 (d, 1H, *J* = 4.0 Hz), 7.58 (d, 1H, *J* = 4.5 Hz), 7.35-7.32 (m, 4H), 2.42 (s, 3H) ppm. ^{13}CNMR (DMSO-d_6, 100 MHz): δ = 161.3, 149.7, 140.9, 139.9, 128.6, 125.9, 123.1, 122.8, 121.9, 118.4, 109.7, 20.8 ppm. MS: m/z= 210 (M+1).

*2-(4-Methoxyphenyl) benzoxazole. **(3k)**:*

FT-IR (KBr): $\bar{\nu}$= 3058, 1611, 1262, 1241, 1031, 1028, 800 cm^{-1}. ^{1}HNMR (DMSO-d_6, 400 MHz): δ = 8.18 (d, 2H, *J* = 9.2 Hz, Ar-H), 7.74 (t, 1H, *J* = 7.8 Hz, Ar-H), 7.54 (t, 1H, *J* = 7.5 Hz, Ar-H), 7.33-7.26 (m, 2H, Ar-H), 7.01 (d, 2H, *J* = 8.8 Hz, Ar-H), 3.81 (s, 3H, OCH_3) ppm. ^{13}CNMR (DMSO-d_6, 100 MHz): δ = 162.0, 160.4, 149.2, 140.1, 127.8, 122.2, 121.2, 118.4, 117.4, 112.3, 109.4, 54.3 ppm. MS: m/z= 226 (M+1).

*2-(Thiophen-3-yl) benzoxazole **(3l)**:*

FT-IR (KBr): $\bar{\nu}$= 2937, 1630, 1256, 1131, 1040, 742 cm^{-1}. ^{1}HNMR (DMSO-d_6, 400 MHz): δ = 8.18 (dd, 1H, *J* = 2.8, 1.0 Hz), 7.78 (dd, 1H, *J* = 4.8, 1.0 Hz), 7.76 (t, 1H, *J* = 7.8 Hz, Ar-H), 7.56 (t, 1H, *J* = 7.4 Hz, Ar-H), 7.42 (s, 1H, Ar-H), 7.35-7.30 (m, 2H, Ar-H) ppm. ^{13}CNMR (DMSO-d_6, 100 MHz): δ = 158.2, 149.1, 140.3, 128.1, 127.2, 125.2, 125.4, 123.5, 123.2, 118.1, 109.8 ppm. MS: m/z= 202 (M+1).



Scheme 1. Synthesis of 2-aryl benzoxazole derivatives

3. Results and Discussion

A model reaction between 2-aminophenol and benzaldehyde was used to optimize the reaction condition. The amount of catalyst required for completion of model reaction is shown in Table 1. It was found that the yields of model reactions varies with amounts of catalyst, the optimum amount of catalyst required was completion of reaction 0.05 mmol. No significant increase in yield was observed beyond 0.05 mmol of CdO nanoparticles catalyst. All other reactions were performed with 0.05 mmol amount of catalyst.

In order to study the effect of solvent on the reaction between benzaldehyde and 2-aminophenol was carried out with different solvent (Table 2). For each solvent the substrates were taken in the solvent with 0.05 mmol of CdO nanoparticles catalyst and stirred at room temperature. The solvents like methanol, ethanol, dichloromethane, chloroform, water and solvent free system was used to demonstrate the solvent effect. The formation of product was found to be more facile and proceeded to give the highest yield only under solvent free reaction conditions (Table 2). The environment of the reaction system in the absence of a solvent is different from that in solution resulting in higher concentration of local reaction sites and an improved efficiency.

To show the general applicability of the method, various aromatic aldehydes were efficiently reacted with one equivalent of 2-aminophenol under same conditions. These results encouraged us to investigate the scope and the generality of this new protocol for various aromatic aldehydes under optimized conditions. A series of aromatic aldehydes having different substituents underwent electrophilic substitution reaction with 2-aminophenol to afford a wide range of 2-arylbenzoxazole derivatives in good to excellent yields without any side products. The nature and electronic properties of the substituents on the aromatic ring, affects the conversion rate. The aromatic aldehydes having electron-withdrawing groups on the aromatic ring react faster than aldehyde having electron-donating groups. It was observed that meta- and para-substituted aromatic aldehydes gave good results while ortho-substituted aromatic aldehydes gave lower yields due to the steric effects (Table 3).

Table 1. Effect of amount of CdO nanoparticles catalyst in the reaction between benzaldehyde and 2-aminophenol.

Entry	Amount of catalyst (mmol)	Time (min)	Yield (%)[a]
1	0.01	45	67
2	0.02	39	74
3	0.03	33	80
4	0.04	28	88
5	0.05	23	91
6	0.06	23	91
7	0.07	23	91
8	0.08	23	91
9	0.09	23	91
10	0.10	23	91

[a]Isolated yields.

Table 2. Effect of solvent in the reaction between benzaldehyde and 2-aminophenol in presence of CdO nanoparticles.

Entry	Solvent	Time (min)	Yield (%)[a]
1	MeOH	34	85
2	EtOH	32	86
3	CH_2Cl_2	36	81
4	$CHCl_3$	35	82
5	Water	37	80
6	Solvent-free	23	91

[a]Isolated yields.

Table 3. Synthesis of 2-aryl benzoxazole derivatives.

Entry	Product (R group)	Time (min)	Yield (%)[a]	m.p. (°C)
3a	H	23	91	102-103
3b	3-NO_2	5	97	212
3c	4-NO_2	8	87	266-267
3d	2-Cl	17	90	71-72
3e	3-Cl	14	93	134-135
3f	4-Cl	12	96	144-145
3g	2-CH_3	16	90	65
3h	4-CH_3	14	94	113-114
3i	2-OCH_3	20	90	55-56
3j	3-OCH_3	16	91	73-74
3k	4-OCH_3	14	93	98-99
3l	2-Thiophenyl	19	96	106

[a]Isolated yields.

The reusability of the catalyst is an important feature from economical and environmental point of view and has attracted much attention in recent years. Therefore, we have examined the recovery and reuse of the catalyst in the reaction. The recovered catalyst was further used in several successive runs under identical reaction condition. It was found that the catalyst showed good activity and stable even after five runs. The yield of the product in the second, third, fourth and fifth runs was 90, 89, 88 and 88% respectively almost the same as that in the first run (91%). The efficiency of catalytic activity of the CdO nanoparticles in comparison with other catalyst by different workers is presented in Table 4. It is observed that the present method is better as compared to earlier reported methods in terms of catalyst amount, yield of products and reaction time. Results obtained reveals that very small amount of CdO nanoparticles was sufficient to synthesize 2-aryl benzoxazole derivatives by grinding method under solvent free condition.

Table 4. Screening of catalytic activity of several catalysts in the reaction between benzaldehyde and 2-aminophenol.

Entry	Catalyst	Reaction conditions	Time	Yield (%)[a]	Ref.
1	Nickel supported silica	Ethanol/stirring	1.5 h	93	[18]
2	Hydrogen tetrachloroaurate	O_2/THF/solvent free-66°C	6 h	96	[19]
3	Heteropolyacids	THF/reflux	5 h	94.8	[20]
4	Zinc triflate	Ethanol/reflux	5 h	90	[21]
5	PEG_{400}	Reflux/80-85°C	4 h	90	[22]
6	SBA-Pr-SO_3H	Acetic acid/reflux	8 h	91	[23]
7	Nano SnO_2	Ethanol/stirring	21 min	90	[31]
8	Nano CeO_2	H_2O/r. t	20 min	95	[33]
9	$Zn(OAC)_2.2H_2O$ (0.5 mmol)	Grinding/Solvent free/ r.t.	4 min	92	[34]
10	Glycerol	Microwave heating/110°C	3 min	92	[35]
11	ZnO nanoparticles	Ball mill, 600 rpm, r.t.	30 min	90	[36]
12	CdO nanoparticles (0.05 mmol)	Grinding/Solvent free/r.t.	23 min	91	This work

[a]Isolated yields.

4. Conclusion

The present method offers use of CdO nanoparticles as an efficient catalyst for the synthesis of 2-aryl benzoxazole derivatives at room temperature. The mild reaction condition, cleaner process, easy work up, good yield with high purity, solvent free, lower catalytic loading and reusability of catalyst are important features of this method.

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