Full Paper

Applied Organometallic Chemistry

Received: 7 December 2014 Revised: 26 December 2014 Accepted: 27 December 2014 Published online in Wiley Online Library: 17 February 2015

(wileyonlinelibrary.com) DOI 10.1002/aoc.3283

Cobalt manganese oxide nanoparticles as recyclable catalyst for efficient synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles under solvent-free conditions

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Cobalt manganese oxide nanocatalyst was synthesized and it was found that it is a highly efficient green catalyst for the synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles under solvent-free conditions. The marked advantages of this method are the simple experimental procedures, shorter reaction times, high yields of product, reusable and non-toxic catalyst and solvent-free conditions. Copyright © 2015 John Wiley & Sons, Ltd.

Keywords: cobalt manganese oxide; nanocatalyst; solvent-free; benzimidazoles

Introduction

Recently, supported nanoparticles have been extensively studied as catalysts for synthesis of organic compounds. As the particle size decreases, the relative number of surface atoms increases, and thus the activity increases.[1] Nanoparticle catalysts can also be easily separated and recycled with more retention of catalytic activity than their bulk counterparts.[2]

Benzimidazoles and their derivatives constitute an important class of heterocyclic compounds which possess a wide range of therapeutic and pharmacological properties. The derivatives possess various biological activities such as antioxidant,[3] antimicrobial,[4] 5-lipoxygenase inhibitory,[5] anticancer,[6] antihypertensive,[7] anti-inflammatory,[8] antihelmintic[9] and antiprotozoal activities.[10] The traditional synthesis of benzimidazoles involves the reaction between an *o*-phenylenediamine and a carboxylic acid or its derivatives (nitriles, amidates, orthoesters) under harsh dehydrating conditions.[11] Very recently, a literature survey revealed several methods for synthesis of benzimidazole and its derivatives using L-proline,[12] glyoxalic acid,[13] $SiO_2/ZnCl_2$,[14] $Fe(ClO_4)_3$,[15] trimethylsilyl chloride,[16] silica sulfuric acid,[17] oxalic acid,[18] mesoporous metal oxide nanocrystals,[19] Indion 190 resin,[20] sodium dodecylsulfate–water,[21] nano-In_2O_3,[22] and alumina–sulfuric acid.[23]

Generally, in the past we have used a new nano-zinc catalyst with Co and Mn in the synthesis of bis(indolyl)methanes.[24] In continuation of our works[25–28] and in the application of this catalyst, we showed that the zinc-supported nanocatalyst is usable, generalizable and also efficient for the synthesis of benzimidazole derivatives.

Experimental

Materials and Instrumentation

All reagents and solvents were commercially available and were used as such. Zinc oxide (ZnO, 99.5%, 20 nm) was purchased from Nanostructured & Amorphous Materials Inc. (http://www.nanoamor.com). Infrared spectra were obtained with a PerkinElmer GX FT-IR spectrometer. Melting points were determined using a Barnstead Electrothermal 9300 melting point apparatus. ^{1}H NMR spectra were recorded with Bruker 200 MHz NMR spectrometer.

Preparation of Catalyst

Aqueous solutions of $Co(NO_3)_2{\cdot}6H_2O$ (0.5 mol l^{-1}) and $Mn(NO_3)_2{\cdot}6H_2O$ (0.5 mol l^{-1}) with 1:6 molar ratios [Mn/Co] and nano-ZnO (15 wt%) were pre-mixed in a round-bottomed flask fitted with a condenser and the resulting solution heated. Aqueous Na_2CO_3 (0.5 mol l^{-1}) was added slowly to the mixed nitrate solution, which was continuously stirred whilst the temperature was maintained isothermally in the range 35–85°C. The final pH achieved was 10. This procedure took approximately 15 min to complete and was refluxed for 5–6 h. The precipitate was first filtered and then washed several times with warm distilled water until no further

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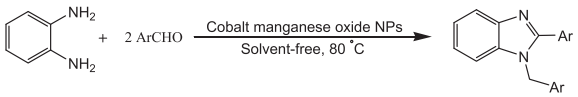


Scheme 1. Synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles (NPs, nanoparticles).

Na^+ was observed in the washings tested by flame atomic absorption. The precipitate was then dried at 150°C for 16 h.

General Procedure for Synthesis of 2-Aryl-1-arylmethyl-1H-1, 3-benzimidazoles

A mixture of *o*-phenylenediamine (1 mmol) and aryl aldehyde (2 mmol) was stirred with cobalt manganese oxide nanoparticles (0.1 g) at 80°C for the required period of time (Scheme 1). The reaction was monitored using TLC (*n*-hexane–acetone, 7:3). After completion of the reaction, H_2O (10 ml) was added. The mixture was extracted with CH_2Cl_2 (4 × 10 ml) and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure gave the crude products. Finally, the crude product was recrystallized from ethanol (90%).

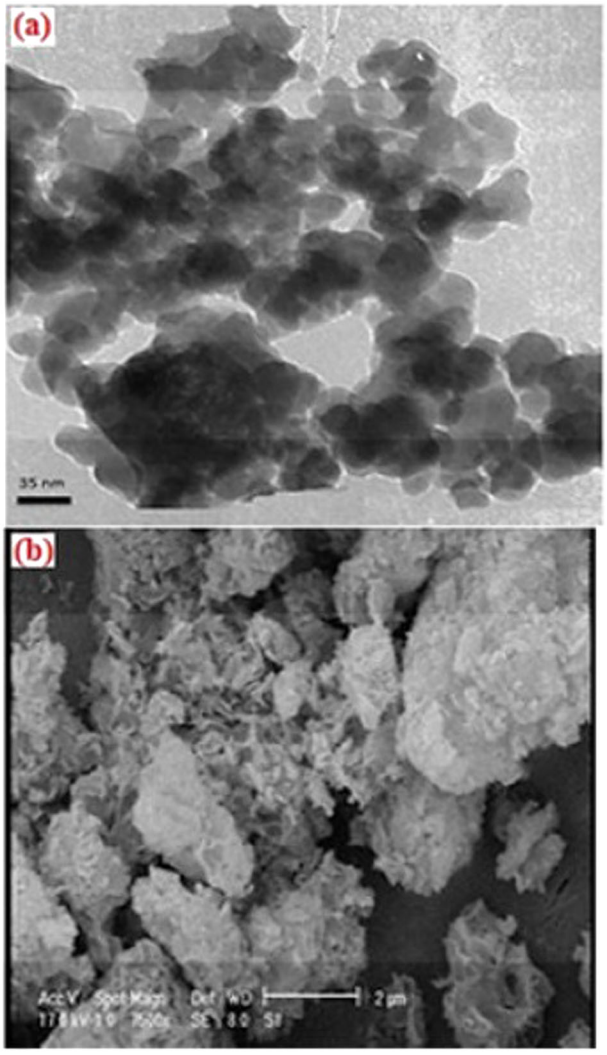


Figure 1. (a) TEM and (b) SEM images of the catalyst with optimum Co:Mn = 6:1 molar ratio.

Results and Discussion

Nanocrystals of cobalt manganese oxide nanocatalyst were characterized. The catalyst mainly consists of oxides Mn_2O_3 (cubic) and Co_3O_4 (cubic). Transmission electron microscopy (TEM) and scanning electronic microscopy (SEM) investigations were carried out to observe the morphology of the prepared catalyst. The TEM image in Fig. 1(a) reveals the product consists of spherical particles with an average size of 20–25 nm. SEM was used to obtain information on the microstructural and metal dispersion properties (Fig. 1(b)).

To choose optimum conditions, first we prepared 1-(4-chlorobenzyl)-2-(4-chlorophenyl)-1H-1,3-benzimidazole from the reaction of 4-chlorobenzaldehyde (2 mmol) and *o*-phenylenediamine (1 mmol) as a model reaction in the absence and presence of the cobalt manganese oxide nanocatalyst under thermal solvent-free conditions. As evident from Table 1, this transformation requires 0.1 g of cobalt manganese oxide nanocatalyst at 80°C for 10 min for the preparation of 2-aryl-1-arylmethyl-1H-1,3-benzimidazole derivatives.

The range of [Co]/[Mn] solution ratios varied from 100% Mn to 100% Co and the catalytic performance for the synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles was studied. Reaction time decreases with increasing concentration of cobalt. However, the shortest reaction time is related to the ratio [Co]/[Mn] = 6:1. To find

Table 1. Optimum conditions for the preparation of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles under solvent-free thermal conditions at 80°C[a]

Entry	Solvent	Catalyst weight (g)	Catalyst[b]	Temp. (°C)	Time (h)	Yield (%)[c]
Effect of solvent						
1	EtOH	0.1	Co/MnNPs	80	5	70
2	H_2O	0.1	Co/Mn NPs	80	5	50
3	*n*-Hexane	0.1	Co/Mn NPs	80	5	40
4	CH_3CN	0.1	Co/Mn NPs	80	5	50
5	Solvent-free	0.1	Co/Mn NPs	80	0.25	96
Effect of catalyst weight						
9	Solvent-free	0.04	Co/Mn NPs	80	0.25	27
10	Solvent-free	0.06	Co/Mn NPs	80	2	60
11	Solvent-free	0.08	Co/Mn NPs	80	4	80
12	Solvent-free	0.1	Co/Mn NPs	80	2	97
13	Solvent-free	0.12	Co/Mn NPs	80	5	97
Effect of temperature						
15	Solvent-free	0.1	Co/Mn NPs	80	0.25	96
16	Solvent-free	0.1	Co/Mn NPs	60	0.25	80
17	Solvent-free	0.1	Co/Mn NPs	40	0.25	30
Effect of catalyst						
18	Solvent-free	—	None	80	0.16	—
19	Solvent-free	0.1	ZnO	80	0.16	20
20	Solvent-free	0.1	$MnCl_2$	80	0.16	30
21	Solvent-free	0.1	$Co(NO_3)_2$	80	0.16	25
22	Solvent-free	0.1	Co/Mn NPs	80	0.16	97

[a]Reaction conditions: *o*-phenylenediamine (1 mmol) and aryl aldehyde (2 mmol) were stirred with cobalt manganese oxide nanoparticles (0.1g) at 80°C under solvent-free conditions.

[b]NP, nanoparticle.

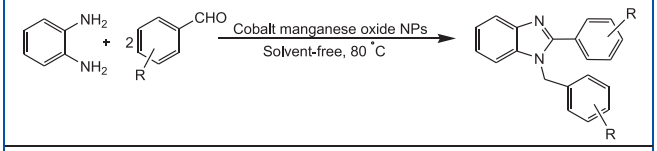
[c]Isolated yield.

the optimized amount of cobalt manganese oxide nanocatalyst as shown in Table 1, the reaction was carried out by varying the amount of the catalyst in the synthesis of 1-(4-chlorobenzyl)-2-(4-chlorophenyl)-1H-1,3-benzimidazole. The yield of product increases linearly with catalyst weight up to 100 mg and then becomes constant.

The effect of temperature on the rate of reaction was studied for the preparation of 1-(4-chlorobenzyl)-2-(4-chlorophenyl)-1H-1,3-benzimidazole (Table 1). It is observed that the reaction does not proceed at room temperature. Further increase in temperature to 40, 60 and 80°C increases the rate of reaction. Therefore, we kept the reaction temperature at 80°C (giving short reaction time and high yield).

We then studied various solvents to find the best one for the reaction of *o*-phenylenediamine (1 mmol) and 4-cholorobenzaldehyde (2 mmol) in the presence of 0.1 g of cobalt manganese oxide nanocatalyst (Table 1). Under solvent-free conditions, the reaction completes within 15 min and at 80°C to give 1-(4-chlorobenzyl)-2-(4-chlorophenyl)-1H-1,3-benzimidazole in 96% yield, because the solvent-free condition increases the effective collisions of molecules in the reaction. The reactions in other solvents require longer reaction times and lead to low yield.

Table 2. Synthesis of 1,2-disubstituted benzimidazoles



Product[a]	R	Time (min)	Yield (%)	M.p. (°C)	Reported (°C)
a	4-Me	10	97	123–125	126–128[29]
b	4-NO_2	20	85	184–186	192–194[29]
c	4-OMe	10	95	129–130	130–131[29]
d	4-Cl	15	96	135–137	137–139[29]
e	H	15	95	130–132	132–134[29]
f	2-OMe	5	97	152–154	151–153[29]
g	2-NO_2	15	91	170–172	169–170[11]
h	3-NO_2	20	89	204–206	205–207[29]

[a]Products were characterized from their physical properties, comparison with authentic samples.

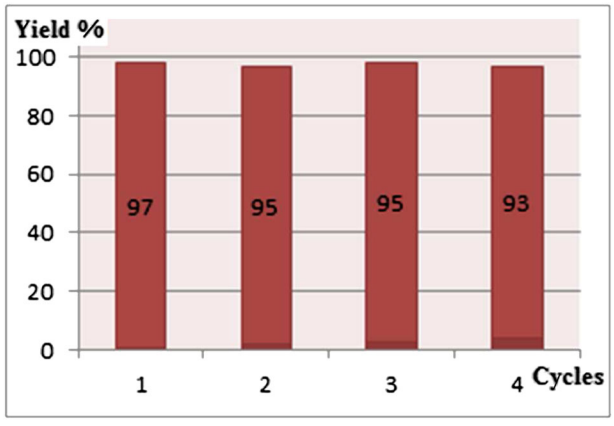
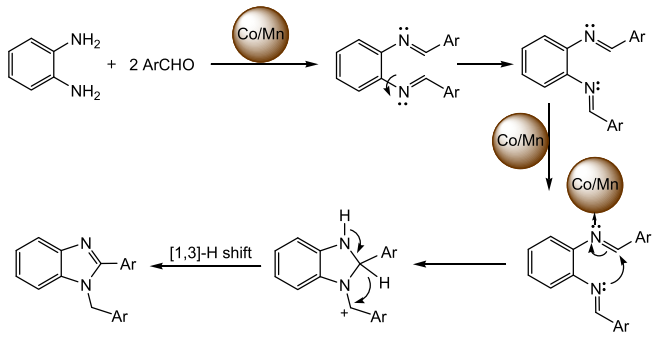


Figure 2. Reusability of the catalyst.



Scheme 2. Proposed mechanism for synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles.

The optimized conditions were further extended for the synthesis of substituted 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles (Table 2). As evident from Table 2, both electron-rich and electron-deficient aldehydes react without any significant difference to give the corresponding benzimidazoles in good yield.

There use of nano-zinc supported with cobalt and manganese was investigated in the reaction between 4-chlorobenzaldehyde and *o*-phenylenediamine. After the completion of the reaction, the products together with the catalyst precipitated out. The catalyst was separated from the precipitate by adding dichloromethane which dissolved the organic compound. The catalyst was dried at 110°C and subjected to fresh reaction. The catalyst was found to be reusable for four cycles without significant loss of activity (Fig. 2).

The proposed mechanism for the synthesis of the 1,2-disubstituted benzimidazoles may involve the iminium-catalysed formation of *N,N′*-dibenzylidene-*o*-phenylenediamine, activation by catalyst and ring closure giving a five-member ring either in a sequential or a concerted manner (Scheme 2).[30]

Conclusions

In summary, we have developed a new method for the synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles using nano-zinc supported with cobalt and manganese under solvent-free conditions. Our method has several advantages including short reaction times, mild conditions, excellent yields, inexpensive and non-toxic catalyst, and simple operation and work-up.

Acknowledgements

We are grateful to Payame Noor University (PNU) for partial support of this work.

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