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$ZrOCl_2.8H_2O$@nano SiO_2: a green and recyclable catalyst for the synthesis of benzimidazoles

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Abstract

$ZrOCl_2.8H_2O$@nano SiO_2 has been synthesized for the first time *via* a simple procedure and characterized by SEM (scanning electron microscopy), FT-IR, and EDX (energy-dispersive X-ray) techniques. The efficiency of the prepared nanostructure has been explored for the synthesis of benzimidazoles *via* the condensation reaction of orthoesters and diamines at 60 °C under solvent-free conditions. The successful synthesis of benzoxazole has also been explored through the condensation of orthoesters with 2-aminophenol in water media at room temperature. The recovery and reusability of the nanocatalyst has also been examined *via* 4 runs without activity loss. Partial short reaction times, high yields of products, mild reaction conditions in the absence of any hazardous solvent, and reusability of the nanocatalyst are noteworthy advantages of this method.

Keywords: Benzimidazoles; benzoxazole; green chemistry; $ZrOCl_2.8H_2O$; $ZrOCl_2.8H_2O$@nano SiO_2; orthoester.

Introduction

Nanotechnology in the last decade have turned into an admired field for research. Today, nanotechnology plays an important role in industry and business [1]. Due to the particular chemical and physical properties of nanoscale materials in comparison to the macro and micro systems, they attend in application fields including optoelectronics, sensing, medicine and catalysis [2,3]. Based on their large surface area, the nano compounds could be utilized in catalysis zone as both heterogeneous [4] and homogeneous catalysts [5-8]. Heterogeneous catalysis have shown some advantages such as easy removal form the media and possible use at high temperatures.

In recent years, attempts for the research on benzimidazoles, benzoxazoles, and oxazole[4,5-b]pyridines syntheses have been expanded because of their occurrence in a number of natural products [9-11] and their potential use as cytotoxic agents [12,13]. They also exhibit properties in selective, and noncovalent inhibitors of Cathepsin S (as a proliferator-activated receptor) [14], estrogen receptor-β agonists of rheumatoid arthritis and endometriosis [15], antitumor agents [16], HIV reverse transcriptase inhibitors [17], and fluorescent whitening agents [18]. The reported methods to provide benzimidazoles and benzoxazoles include conventional, thermal- or microwave-accelerated

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condensation of diamine/or 2-aminophenols with carboxylic acid derivatives in the presence of different catalysts such as refluxing HCl [19], and SiO_2/H_2SO_4 [20]. Another general route for the benzimidazoles and benzoxazoles preparation is *via* the oxidative condensation of diamine/or 2-aminophenols with aldehydic precursors in the presence of activated carbon [21], L-proline [22], nano ceria (CeO_2) [23], sulfonated ordered nanoporous carbon (CMK-5-SO_3H) [24], NH_4Cl [25], and $CdCl_2$ [26]. Orthoesters are another carbonylic substrates which have also been utilized for the condensation with diamines/or 2-aminophenols in the presence of sulfonated rice husk ash (RHA-SO_3H) [27], $ZrOCl_2.8H_2O$ [28], sulfamic acid [29], and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) [30]. In addition, some unique protocols have also been utilized for the preparation of benzimidazole and benzoxazole heterocycles such as ligand-accelerated copper-catalyzed cyclization of *o*-halobenzanilides [31], intramolecular cyclization of *o*-bromoaryl derivatives using copper(II) oxide nanoparticles [32], and oxidative cyclization of structurally diverse thiophenolic and phenolic Schiff's bases in the presence of pyridinium chlorochromate (PCC) supported on silica gel [33].

In recent years, many heterogeneous organic reactions have been performed using various reagents supported on solid materials [34-36]. The silica-based catalysts have many advantages over unsupported analogues such as cleaner reactions medium which make them environmentally benign, easier work-up, less reaction time, high yields of products, and its reusability over some runs without activity loss. In continuation of our studies on developing safe and environmentally benign nano-based methodologies for organic syntheses [37-45], herein, we report the preparation of $ZrOCl_2.8H_2O$@nano SiO_2 as a new green heterogeneous nanocatalyst for the preparation of benzimidazole and benzoxazole derivatives *via* the condensation reaction of trialkylorthoformates and diamines/2-aminophenol at 60 °C under solvent-free conditions or in water media at room temperature.

Experimental

General

Chemicals and solvents were purchased from Merck, Aldrich, and Alfa Aesar and used without further purifications. The amorphous nano silica (average particle size 20-30 nm and specific surface area of 180-270 m^2/g) was purchased from Tecnan Company. IR spectra were recorded from KBr disk using FT-IR Bruker Tensor 27 instrument. Melting points were determined on a shimadzu DSC-50 thermal analyzer and are uncorrected. ^1H NMR spectra were recorded in DMSO (d_6) solvent on a Bruker drx (400 MHz) machine. Preparative layer chromatography (PLC) was carried out on 20×20 cm^2 plates, coated with a 1 mm layer of Merck silica gel PF_{254}, and prepared by applying the silica as slurry and drying in air. The scanning electron microscope (SEM, model ∑-IJMA) was used to characterize the nano structures.

Preparation of $ZrOCl_2.8H_2O$@nano SiO_2

In a round bottom flask, a mixture of commercial nano SiO_2 (0.2 g) in a H_2O/HCl (1:1, 10 mL) was magnetically stirred at 100 °C for 4 h. The resulting solid was cooled up to room temperature and filtered. The filtrate washed with distilled water until the pH became neutral. The solid

residue was dried at room temperature and pressure, added to a mixture of $ZrOCl_2.8H_2O$ (0.01 g) in $(CH_3CH_2)_2O$ (5 mL), and magnetically stirred at room temperature for 60 min. Then $(CH_3CH_2)_2O$ was evaporated at room pressure. The solid heated in oven at 100 °C for 4 h. The obtained white solid is $ZrOCl_2.8H_2O$@nano SiO_2 which containing 5% of $ZrOCl_2.8H_2O$. It was also characterized by FT-IR spectra (Figure 1), SEM image (Figure 2), and EDX analysis (Figure 3).

General procedure for the synthesis of benzimidazole and benzoxazole derivatives

A mixture of diamine derivatives (*1a-c*, 1 mmol), orthoesters (*2a-b*, 7 mmmol), and $ZrOCl_2.8H_2O$@nano SiO_2 (0.01 g) was stirred at 60 ˚C under solvent-free conditions for the appropriate time monitored by TLC. After completion, methanol (10 mL) was added and filtered. The solid residue washed with methanol (2×5 mL). The solvent was evaporated and the crude product was purified by PLC (eluent: hexane/EtOAc, 7:3) to afford the pure products *3a-c* (69-88%, Table 2, Entries 1-6). In the case of benzoxazole *3d*, a mixture of *o*-amino phenol (***1d,*** 1 mmol), *2a-b* (7 mmol), and $\underline{ZrOCl_2.8H_2O@nano}$ SiO_2 (0.01 g) in water (5 mL) was stirred at room temperature until the reaction completion. The work-up procedure is as the same as benzimidazoles. All the products were characterized by comparison of their melting points and spectroscopic data (FT-IR and ^1H NMR) with those of the authentic samples in the literature.

Results and discussion

Characterization of the nanocatalyst

First, the synthesized $ZrOCl_2.8H_2O$@nano SiO_2 has been characterized by FT-IR, SEM, and EDX techniques. According to the FT-IR spectra (Figure 1), the broad band at 3412 and 971 cm^{-1} was assigned to the stretching vibrations of Si-OH, which are related to the silanol groups in the structure of amorphous nano SiO_2, respectively. The strong and broad band at 1093 cm^{-1} with a shoulder at 1118 cm^{-1} is assigned to the TO and LO modes of the Si-O-Si asymmetric stretching vibrations [46]. The peak at 875 cm^{-1} can be assigned to Si-O-Si symmetric stretching vibrations, whereas the band at 471 cm^{-1} is due to O-Si-O bending vibrations. The stretching band at 1633 cm^{-1} is the features spectrum of $ZrOCl_2.8H_2O$. The SEM image of $ZrOCl_2.8H_2O$@nano SiO_2 (Figure 2) revealed that the average particle size of the prepared nanostructure is 30-40 nm where the average diameters of the grains in commercial nano SiO_2 is 20-30 nm.

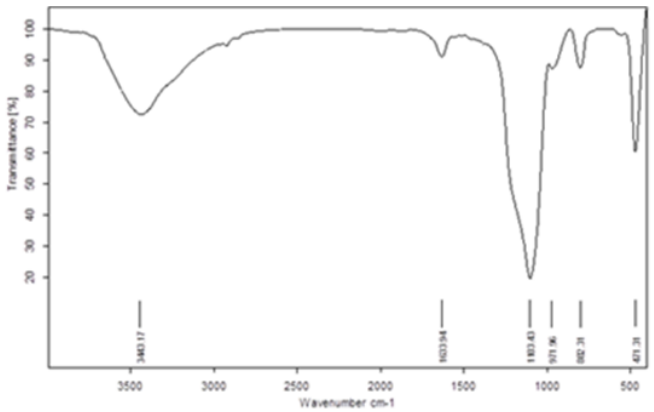


Figure 1. FT-IR spectrum of $ZrOCl_2.8H_2O$@nano SiO_2

The EDX analysis confirms the existence of Zr, Cl, Si and O in $ZrOCl_2.8H_2O$@nano SiO_2 structure. The percentages are in agreement with the utilizing amount of each precursor, which means no mass loss or dgradation has been occurred.

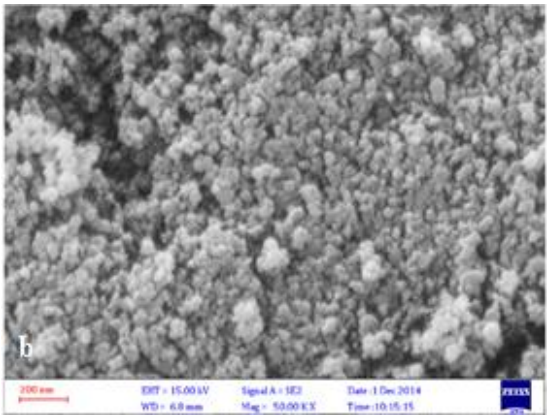


Figure 2. SEM image of $ZrOCl_2.8H_2O$@nano SiO_2

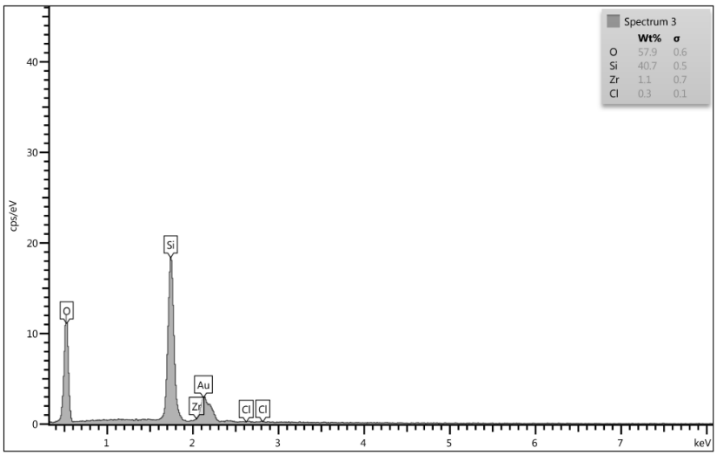


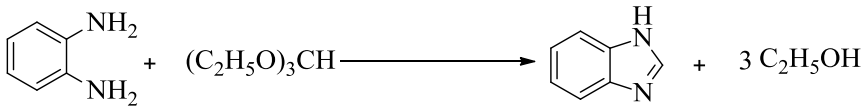
Figure 3. EDX analysis of $ZrOCl_2.8H_2O$@nano SiO_2

Investigation of catalyst activity

In order to determine the catalyst activity of $ZrOCl_2.8H_2O$@nano *SiO_2 in the synthesis of ben*zimidazoles, the optimized reaction condition has been obtained using *o*-phenylenediamine ***1a*** (1 mmol) and tiethylorthoformate ***2a*** (7 mmol) as the model reaction. The results are shown in Table 1. As could be seen, examining the solvent effect (Entries 1-5) confirmed that the solvent-free condition is the best choice (Entry 5). The suitable heat for the model reaction was 60 °C (Entries 5-7). The nanocatalyst amount survey on the model reaction (Entries 8-11) demonstrated that the best results obtained in 0.01 g usage of $ZrOCl_2.8H_2O$@nano SiO_2 (Entry 10) and using more amount did not promote the reaction more. The ***2a*** amount was another variable parameter which has been studied (Entries 12 and 13). The optimized results were obtained with 7 mmol of the catalyst. At the final step, in order to detonate the efficiency of

$ZrOCl_2.8H_2O$@nano SiO_2, the model reaction has been performed in the presence of sole nano SiO_2 (Entry 14). The observation confirmed the notability of the synthesized nano structure to promote the reaction.

Table 1. Optimization the conditions in the synthesis of benzimidazoles in the presence of $ZrOCl_2.8H_2O$@nano SiO_2

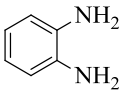
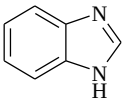
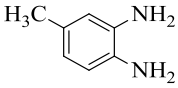
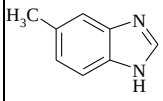
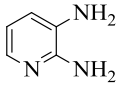
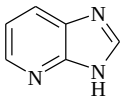
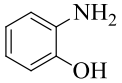
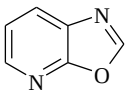


1a ***2a*** ***3a***

Entry	Conditions Solvent/ $ZrOCl_2.8H_2O$@nano SiO_2 (g)/ temperature (°C)/ ethyl orthoformate (mmol)	Yield (%)	Time (h)
1	H_2O/ 0.005/ reflux/ 7	65	12
2	EtOH/ 0.005/ reflux/ 7	_	24
3	CH_3CN/ 0.005/ reflux/ 7	_	24
4	H_2O:C_2H_5OH (1:1)/ 0.005/ reflux/ 7	_	24
5	-/ 0.005/ rt/ 7	60	9
6	-/ 0.005/ 60/ 7	75	4.30
7	-/ 0.005/ 70/ 7	75	4.30
8	-/ 0.007/ 60/ 7	75	3.45
9	-/ 0.009/ 60/ 7	83	2.20
10	-/ 0.01/ 60/ 7	90	1.30
11	-/ 0.015/ 60/ 7	90	1.30
12	-/ 0.01/ 60/ 5	82	2.10
13	-/ 0.01/ 60/ 10	90	1.30
14	-/ nano SiO_2(0.01g)/ 60	54	4.35

As shown in Table 2, under the optimized reaction conditions, diamines ***1a-1c*** reacted with orthoesters ***2a-b*** to obtain the benzimidazole derivatives ***3a-c*** successfully (Table 2, Entries 1-6). As could be seen, triethylorthoformate ***2a*** performed the reaction a bit faster than its methyl analogous. Under the same conditions, the reaction of 2-aminophenol ***1d*** with ***2a-b*** did not produce the corresponding benzoxazoles, but the condensation was accomplished at room temperature in H_2O in high yields (Entries 7 and 8). The reusability of the catalyst is an important factor from economical and environmental point of views and has attracted much attention in recent years. Therefore, the reusability of $ZrOCl_2.8H_2O$@nano SiO_2 was examined *via* the reaction of triethylorthoformate ***2a*** with *o*-phenylenediamine ***1a***. After reaction completion (1.30'), the catalyst was simply separated by diluting the reaction with methanol and subsequent filtration. The solid residue was heated in oven at 100 °C for 1 h and cooled up to room temperature. The recycled nanocatalyst was used for another run. The recovery and reusability has been done within four runs without any activity loss (Figure 4).

Table 2. Synthesis of benzimidazoles, benzoxazoles, and oxazole[4,5-b]pyridine in the presence of $ZrOCl_2.8H_2O$@nano SiO_2

Entry	Amine		Orthoester		product		Yield (%)	Time (h)	m.p. (°C)	
									Found	Reported [Ref.]
1		***1a***	$(C_2H_5O)_3CH$	***2a***		***3a***	90	1.30'	172-173	171-173 [27]
2	***1a***		$(CH_3O)_3CH$	***2b***			78	2.30'		
3		***1b***	***2a***			***3b***	89	4	107-109	109-111 [27]
4	***1b***		***2b***				84	4.20'		
5		***1c***	***2a***			***3c***	75	5	149-151	149-150 [47]
6	***1c***		***2b***				70	5.30'		
7		***1d***	***2a***			***3d***	89	2	101-102	99-101 [48]
8	***1d***		***2b***				83	2.50'		

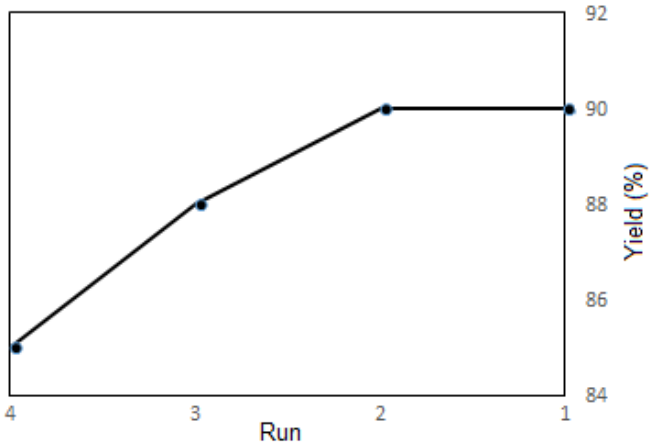


Figure 4. Reusability of $ZrOCl_2.8H_2O$@nano SiO_2 in the synthesis of ***3a***

Conclusion

In conclusion, we have developed an efficient method for the synthesis of benzimidazoles and benzoxazole in the presence of $ZrOCl_2.8H_2O$@nano SiO_2 as a newly synthesized, highly efficient, inexpensive, easy handling, non-toxic, and reusable nanocatalyst. Partial short reaction times, high yields of products, mild reaction conditions in the absence of any hazardous solvent, and reusability of the nanocatalyst are noteworthy advantages which would make this method attractive for chemists.

Acknowledgments

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