$Zn_3(BTC)_2$ as a Highly Efficient Reusable Catalyst for the Synthesis of 2-Aryl-1*H*-Benzimidazole

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 $Zn_3(BTC)_2$ metal-organic frameworks as recyclable and heterogeneous catalysts were effectively used to catalyze the synthesis of benzimidazole derivatives from *o*-phenylendiamine and aldehydes in ethanol. This method provides 2-aryl-1*H*-benzimidazoles in good to excellent yields with little catalyst loading. The catalyst was characterized using different techniques such as X-ray diffraction (XRD), energy dispersive X-ray (EDX) analysis, scanning electron microscopy (SEM), and Fourier transform infrared (FT-IR) spectroscopy.

Keywords: Zn₃(BTC)₂; Benzimidazoles; *o*-Phenylendiamine; Aldehydes; Metal-organic frameworks.

INTRODUCTION

Metal-organic frameworks (MOFs) are important crystalline materials used as heterogeneous catalysts or catalyst supports in a variety of organic transformations.¹⁻⁴ MOFs open up the possibility to design and synthesize a variety of new porous materials. Some of the features of MOFs for their use as heterogeneous catalysts are their high internal surface area, microporosity, ease of separation of the product, acid sites, base sites, stability, diffusion, and high metal content.⁵ MOFs catalyze many reactions such as the oxidation of organosulfides. cyclopropanation of alkene, Nmethylation of aromatic primary amines, Sonogashira reaction, Suzuki cross-coupling, Friedel-Crafts alkylation and acylation, three-component coupling reaction of aldehyde, alkyne, and amine, the Biginelli reaction, Knoevenagel condensation, cycloaddition of CO2 with epoxides, alkene epoxidation, oxidation of homocoupling of phenylboronic acid, transesterification reaction, hydrolysis of ammonia borane, aza-Michael condensation, and 1,3-dipolar cycloaddition reactions.^{6–16}

Benzimidazoles have attracted much attention because of their various applications.^{17,18} For instance, they have been shown to exhibit fungicide, antitumor, immunosuppressant, and anticonvulsant properties.¹⁹ They have also been used as ligands for asymmetric catalysis.²⁰ Benzimidazoles and their derivatives represent one of the most biologically active classes of compounds. The high profile of biological applications of the benzimidazole compounds has prompted extensive studies of their syntheses. During the past decades, many methods have been reported for the synthesis of these heterocycles including (1) condensation of o-phenylenediamines with carboxylic acids and their derivatives (the condensation of o-phenylenediamine with carboxylic acid often requires strong acidic conditions and high temperatures),²¹ (2) transition-metalcatalyzed coupling reactions to construct the benzimidazole nucleus, 2^{22} and (3) the condensation of aldehydes with o-phenylenediamine, ²³ which are traditional methods for the synthesis of these compounds. Though efficient, most of these methods have significant drawbacks such as the use of harsh conditions, expansive reagents, low isolation yields, laborious work-up and purifications, special oxidation process, and long reaction times. Partially due to the availability of a large number of aldehydes, method (3) has been extensively used. In this regard, a large number of reagents have been used and reported in the literature.^{24–28}

Indeed, the design of eco-friendly and economical processes, more efficient systems, and new protocols to improve these methods are considered of high practical value. Here, we describe a simple, mild, and efficient procedure for the synthesis of 2-aryl-1*H*-benzimidazole

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Fig. 1. Synthesis of Zn₃(BTC)₂.

in the presence of Zn₃(BTC)₂ MOF as an efficient heterogeneous catalyst.

RESULTS AND DISCUSSION

Characterization of catalyst

 $Zn_3(BTC)_2$ was successfully synthesized using strategy depicted in Figure 1 and characterized using different analysis techniques including Fourier transform infrared (FT-IR) spectroscopy, scanning electron microscopy (SEM), and X-ray diffraction (XRD). The FT-IR spectra (Figure 2) displayed a peak at about 3447 cm⁻¹ due to the stretching of the water molecul and peaks at 1642 and 1446 cm^{-1} due to the carbonyl group of benzenetricarboxylic acid (BTC) and double bonds of benzene, respectively. The FT-IR spectrum in this figure is similar to those in previous reports²⁹ with no change in the position or shape of the bands, which indicates that the structure of the compound is preserved.

The particle morphology and textural properties of the nanoporous catalyst were studied using SEM.



Fig. 3. Surface morphology of Zn₃(BTC)₂.

The SEM images of Zn₃(BTC)₂ at different magnifications are displayed in Figure 3. These images of the synthesized nanoporous material confirm the formation of nanoparticles with high quality and of conical shape. From this analysis, it is evident that the catalyst is made up of uniform particles, with the average size of $Zn_3(BTC)_2$ being ~100 nm.

EDX is an effective technique for studying the conformation of the metal inside the nanostructures. It shows the incorporation of Zn metal inside the organic framework and a uniform distribution of the particles throughout the framework (Figure 4).

Catalytic study in the synthesis of 2-aryl-1Hbenzimidazole

After successful characterization of the prepared MOF, the catalytic activity of $Zn_3(BTC)_2$ in the synthesis of 2-aryl-1H-benzimidazole was studied. Our first



800

2000

1500

nber cm-1

3000 2500

80

60

40

20

Transmittance [%]

Table 1. Optimization of reaction conditions	Table 1.	Optimization	of reaction	conditions
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	1a	2a	3a	
Entry	Amount of catalyst (mg)	Solvent	Time (min)	Yield $(\%)^2$
1	4	EtOH	25	65
2	6	EtOH	20	80
3	8	EtOH	10	97
4	10	EtOH	9	98
5	8	Acetone	30	85
6	8	EtOAc	45	75
7	8	CH ₃ CN	45	73
8	8	H_2O	60	70
9	8	CH_2Cl_2	30	60

^{*I*} Reaction conditions: *o*-phenylendiamine (1.0 mmol) and benzaldehyde (1.2 mmol) in the presence of catalyst and solvent (2.0 mL).

² Isolated yield.

step was to optimize the reaction under normal atmospheric conditions to achieve information about the amount of catalyst and determine the kind of solvent to be used. In a preliminary experiment, the reaction between o-phenylenediamine (1a) and benzaldehyde (2a) was studied in the presence of $Zn_3(BTC)_2$ in ethanol at room temperature. The kind of solvent was controlled. According to the results shown in Table 1, 2,phenyl-1H-benzo[d]imidazole 3a was obtained in 97% yield in ethanol (Table 1, entry 3). Afterward, the influence of the amount of Zn₃(BTC)₂ was also examined. As the results show, the yield of 3a depended on the amount of $Zn_3(BTC)_2$. When the amount of $Zn_3(BTC)_2$ was decreased to 6.0 and 4.0 mg, the reaction yield was 65% and 80%, respectively (Table 1, entry 1-2). Significant improvement of the reaction was also observed in the presence of 8.0 mg of $Zn_3(BTC)_2$, as the product yield was 97%. According to Table 1, the highest yield and shortest reaction time of product 3a are obtained in the presence of 8.0 mg of Zn₃(BTC)₂ in EtOH (2.0 mL) at room temperature (Table 1, entry 3).

With the optimized reaction conditions, to explore the scope and limitation of this catalytic system, a library of aromatic aldehydes (1.2 mmol) was subjected to react with o-phenylenediamine (1.0 mmol) for converting to the corresponding 2-aryl-1*H*-benzimidazole in the presence of $Zn_3(BTC)_2$ (8.0 mg) in EtOH at room temperature (Scheme 1). The results are summarized in Table 2.

The results show that this protocol efficiently generated the corresponding products for both electrondonating groups (EDGs) and electron-withdrawing groups (EWGs) or electron-rich substituents on the aromatic ring in the ortho, meta, and para positions when subjected to the same reaction conditions, and the corresponding 2-aryl-1*H*-benzimidazole derivatives were



Scheme 1. Zn₃(BTC)₂ cyclocondensation of *o*-phenylenediamine with aromatic aldehydes.

Entry	\mathbb{R}^1	R^2	Product	Time (min)	Yield $(\%)^2$	M.p. (°C)
1	Н	Н	3a	10	97	288–291 ³⁰
2	Н	4-C1	3b	15	91	285-288 ³⁰
3	Н	$4-NO_2$	3c	35	93	307-309 ³⁰
4	Н	3-NO ₂	3d	60	95	209-211 ³¹
5	Н	4-OMe	3e	15	91	225-228 ³²
6	Н	4-Me	3f	10	94	275-278 ³¹
7	Me	Н	3g	20	90	270-275 ³⁰
8	Me	Me	3h	30	90	258-262 ³⁰
9	Me	$4-NO_2$	3i	20	93	145–148 ³³
10	Me	2-C1	3j	45	93	263-268 ³³
11	Me	4-C1	3k	60	92	206-210 ³³
12	Me	CHO	31	60	90	$178 - 180^{34}$
13	Н	OH	3m	60	91	242-245 ³³
14	Me	N(Me) ₂	3n	60	90	232–235 ³⁴
15	Н	2-Cl	30	40	94	228-230 ³⁰

Table 2. $Zn_3(BTC)_2$ -catalyzed synthesis of 2-aryl-1*H*-benzimidazole in EtOH at room temperature¹

¹ Reaction conditions: aldehyde (1.2 mmol), *o*-phenylenediamine (1.0 mmol) in the presence of $Zn_3(BTC)_2$ and EtOH (2.0 mL) at room temperature.

² Isolated yield.

obtained in excellent yields (90–97%) in short reaction times (less than 60 min).

Recovery and reusability

Recovery and reusability of the catalysts are valuable advantages in catalysis research, which make them very favorable from the commercial and economic points of view. In this respect, the reusability of $Zn_3(BTC)_2$ in the syntheses of product **3a** was investigated by repeatedly separating the $Zn_3(BTC)_2$ from the reaction mixture, washing it, and then reusing it over five successive runs. After each run, the catalyst was separated from the reaction mixture by simple decantation, then washed with copious amounts of *n*-hexane to remove any physisorbed reagents, and dried. Then, the recovered catalyst was reused for a subsequent fresh batch of the reaction. The catalytic activity was studied for several successive runs, showing similar activity (Figure 5).

In order to determine whether active Zn species leached from the solid $Zn_3(BTC)_2$ catalyst could contribute to the total conversion of the reaction between *o*-phenylenediamine and 4-hydroxy benzaldehydes for the synthesis of 2-(4-hydroxyphenyl)-1,3-benzimidazole, an experiment was performed using simple centrifugation during the course of the reaction. The reaction was carried out under optimized condition using 8.0 mg $Zn_3(BTC)_2$ for the synthesis of 2-(4hydroxyphenyl)-1,3-benzimidazole, and then the nanocatalyst was removed from the reaction mixture after 10 min of reaction by simple filtration. The reaction solution was then transferred to a new flask, stirred for an additional 20 min with aliquots being sampled at different time intervals, and analyzed by gas chromatography (GC). The results confirmed that almost no further conversion was observed for the synthesis of 2-



Fig. 5. Catalyst recycling studies. Reaction conditions: benzaldehyde (1.2 mmol), *o*-phenylenediamine (1.0 mmol), Zn₃(BTC)₂ (8.0 mg), and EtOH (2.0 mL) at room temperature.



(4-hydroxyphenyl)-1,3-benzimidazole. Also, the synthesis of these compounds could only be performed in the presence of the $Zn_3(BTC)_2$ catalyst, and the contribution of leached active Zn species soluble in the solution, if any, was insignificant (Figure 6).

In order to show the efficiency of the synthesized catalyst, the results obtained for the synthesis of the products were compared with those of previously reported procedures (Table 3). The present protocol is found to be similar to some of the previously reported procedures in terms of product yield, reaction time, and reaction conditions.

CONCLUSIONS

To summarize, in this study, we have developed a straightforward synthetic method for the preparation of 2-aryl-1*H*-benzimidazole from aldehydes and *o*-phenylenediamine in the presence of $Zn_3(BTC)_2$ in

ethanol. It is noteworthy that all products were obtained in good to excellent yields. The important feature of this method is the use of $Zn_3(BTC)_2$ as a recyclable and porous catalyst. This protocol has several advantages such as high catalytic activity, simple operation, high yields, and the use of a minimum amount of catalyst, simple preparation of the catalyst from commercially available materials; also, the reactions can be carried out in EtOH as a green solvent instead of the usually used organic solvents.

EXPERIMENTAL

Synthesis of Zn₃(BTC)₂

Initially, zinc acetate dihydrate 1.2 g (5.4 mmol) was dissolved into 25 mL ethanol. It was followed by the addition of trimesic acid (benzene-1,3,5-tricarboxylic acid, 0.315 g (1.5 mmol)) in 5 mL of dimethylformamide (DMF) and mixing thoroughly until it was completely dissolved. It was kept at 100 °C for 12 h in an oven to yield small crystals. Then the autoclave was cooled down to room temperature naturally, and the white crystals were recovered by filtration. The suspension was washed with a mixture of DMF and ethanol (10:20) several times and then dried at 100 °C for 45 min.⁴⁷

Synthesis of 2-aryl-1*H*-benzimidazole

o-Phenylenediamine (1.0 mmol) and aldehyde (1.2 mmol) in the presence of $Zn_3(BTC)_2$ (8.0 mg) was

Table 3. Comparison of activity of various catalysts in the synthesis of 2-aryl-1H-benzimidazole

Entry	Catalyst	Conditions	Time (h)	Yield (%) ¹	Ref.
1	Ceric (IV) ammonium nitrate (50 mol%)	CH ₂ Cl ₂ , reflux	15-50 min	65–95	35
2	NaHSO ₄ -SiO ₂	EtOH, reflux	8	87–95	36
3	<i>p</i> -TsOH (10 mol%)	DMF, 80 °C	10-60 min	trace-85	37
4		PhNO ₂ ,150 °C	1	83-88	38
5	$LaCl_3$ (10 mol%)	CH ₃ CN, r.t.	2–4	85–95	23
6	Yb(OTf) ₃ (0.5 mol%)	Solvent-free, 90 °C	1–6	40-92	39
7	Dowex 50 W (10 mol%)	H_2O , reflux	4–16	75–93	40
8	T(o-Cl)PPFe ^{III a} (5 mol%)	EtOH, r.t.	1–5	90–97	41
9	TiCl ₃ OTf (5 mol%)	EtOH, r.t.	50-130 min	70–90	42
10	HBr (10 mol%)	CH_3Ph , reflux	5	77	43
11	$Cu(OAc)_2.H_2O(7 g)$	MeOH/H ₂ O, reflux	3	72	44
12	H_2O_2/SiO_2 -FeCl ₃ (0.1 g)	Solvent-free, 150 °C	30 min	25	45
13	$Er(OTf)_3$ (10 mol%)	H ₂ O, 1–2 °C	2–5 min	81–97	46
14	$Zn_3(BTC)_2$	EtOH, r.t.	10-60 min	91–97	This work

¹ meso-Tetrakis(o-chlorophenyl)porphyrinato)iron(III) chloride.

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added to a flask containing ethanol (5.0 mL) at room temperature until the reaction went to completion. thinlayer chromatography (TLC) was used to monitor the progress of the reaction. After completion of the reaction, the solvent was evaporated by a rotary evaporator and the residue was dissolved in ethyl acetate and washed with water. Then the organic layer and the aqueous layer were separated. The organic layer was dried by Na₂SO₄ and concentrated under a rotary evaporator. The crude products were separated by plate chromatography.

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