



Original Research article

Metal-organic Framework MIL-53(Fe) as a Highly Efficient Reusable Catalyst for the Synthesis of 2-aryl-1H-benzimidazole



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KEYWORDS

Metal-organic framework MIL-53(Fe)

2-Aryl-1H-benzimidazole

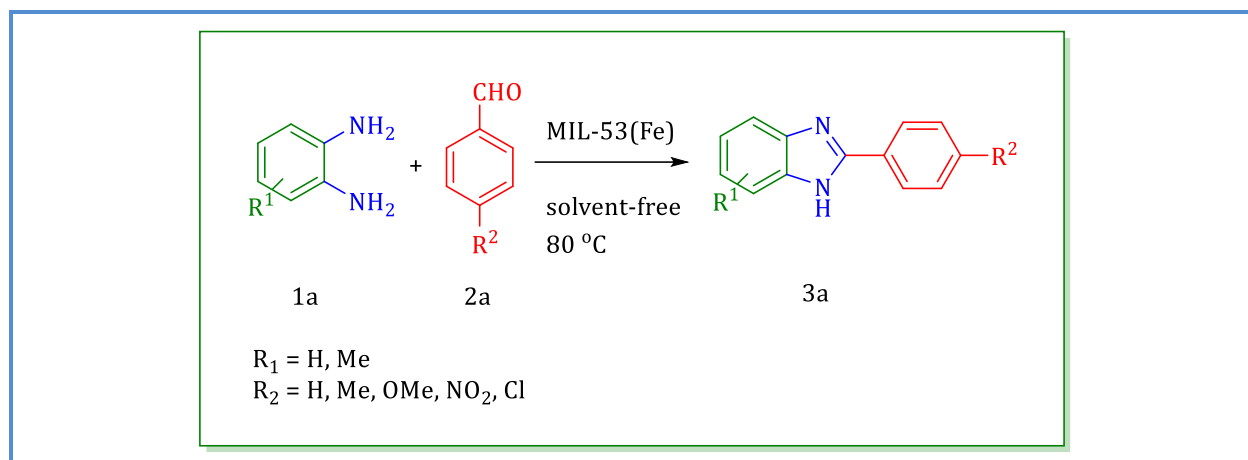
Aldehydes

o-Phenylenediamine

ABSTRACT

Metal-organic framework MIL-53(Fe) (MIL = materials of institute lavoisier) as a recyclable and heterogeneous catalyst efficiently catalyzed the synthesis of 2-aryl-1H-benzimidazole derivatives from *o*-phenylenediamine and aldehydes in solvent-free condition. This method provides benzimidazole in with good to excellent yields and little catalyst loading. Furthermore, the catalyst can be readily isolated by filtering as no obvious loss of activity can be observed when the catalyst was reused in five consecutive runs.

Graphical Abstract



Introduction

Metal-organic frameworks (MOFs) are important crystalline materials *via* inherent surface area and versatility in properties of the materials [1-4]. Some of the applications of metal organic frameworks MOFs include their use as heterogeneous catalysts with high internal surface area, microporosity, storage of gases, acid sites, base sites, solar energy, super-capacitors, stability, diffusion, and high metal content [5]. This material can be easily synthesized *via* the conventional strategies, such as microwave or solvothermal method. MOFs catalyze many reactions such as Knoevenagel condensation, cyclopropanation of alkene, oxidation of organosulfide, *N*-methylation of aromatic primary amines, Sonogashira reaction, cycloaddition of CO₂ with epoxides, Suzuki cross-coupling, trans esterification reaction, hydrolysis of ammonia borane, Friedel-Crafts alkylation and acylation, three-component coupling reaction of aldehyde, alkyne, and amine, alkene epoxidation, oxidation of homocoupling of phenylboronic acid, the Biginelli reaction, aza Michael condensation and 1,3-dipolar cycloaddition reactions [6-20].

Benzimidazoles have attracted much attention because of their applications/properties as anti-HIV, antitumor, cardiotoxic, antitubercular, antiulcer, antiallergic, antihistamines, antimicrobial, neuroleptic, immunosuppressant and anticonvulsant properties [21-22]. The high profile of biological applications of the benzimidazole compounds has prompted the emergence of extensive studies of their syntheses. During the past decades, many methods have been reported for the synthesis of these heterocycles; including, condensation of *o*-phenylenediamines with carboxylic acids their derivatives (the condensation of *o*-phenylenediamine with carboxylic acid often requires strong acidic conditions and high

temperatures), [25] transition metal catalyzed coupling reactions to construct benzimidazole nucleus [26] the condensation of aldehyde with *o*-phenylenediamine [27] which are traditional methods for the synthesis of these compounds.

MIL-53 (Fe) or Fe(III) (OH) (1,4-BDC) is a typical class of MOFs generated by a combination between Fe(III) cations and 1,4-dicarboxylic acid (Figure 1) [28, 29]. This structure consists of FeO₆ hexagonal chains connecting to dicarboxylate anions to form the three-dimensional networks or secondary building units [30, 31]. MIL-53(Fe) is chemically stable and constitutes of lower toxic metal centers and thus has gained much attention [32].

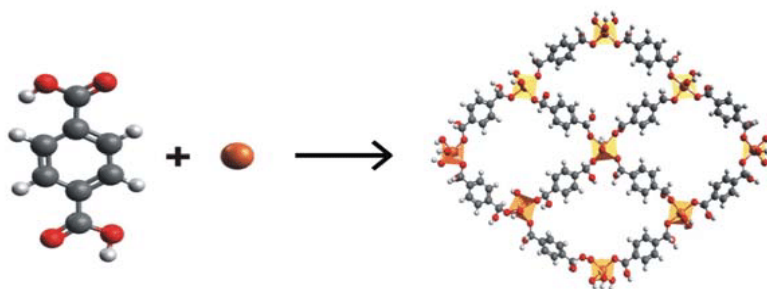


Figure 1. Structure of metal-organic framework MIL-53(Fe)

In this research study, we tested and analyzed metal-organic framework MIL-53(Fe) as a heterogeneous catalyst to synthesize benzimidazole derivatives under solvent and solvent-free conditions at 80 °C.

Experimental

Materials and methods

All reagents and solvents used in this work were obtained from Merck and were used without further purification. Analytical thin layer chromatography was performed using Merck silica gel GF₂₅₄ plates. Plate chromatography was performed using silica gel 60 PF₂₅₄₊₃₆₆. All products are known and characterized by comparison of their spectra (¹H NMR, ¹³C NMR, and FT-IR) and physical data with those of authentic samples.

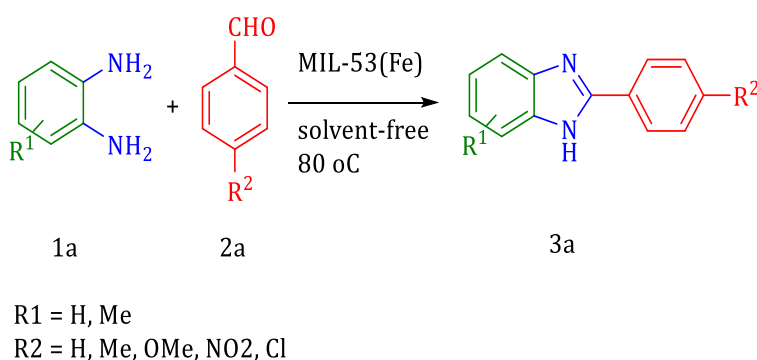
Synthesis of MIL-53(Fe)

MIL-53(Fe) was prepared according to the previously reported work [33]. FeCl₃·6H₂O (1 mmol), terephthalic acid (TPA, 1 mmol), and HF (1 mmol) were mixed in a solvent of *N,N*-dimethylformamide (5 mL). The precursor solution was transferred to a Teflon lined stainless steel autoclave and heated at 150 °C for 3 days. The synthesized yellow MIL-53(Fe) solid was washed with methanol to remove the DMF solvent from the pores of the material, and, then the methanol

was substituted with water (1 g of MIL-53 in 0.5 L of water) and, finally, this yellow powder was then dried naturally.

Typical procedure for synthesis of benzimidazoles

A mixture of aldehyde (1.2 mmol) and *o*-phenylenediamine (1.0 mmol) in the presence of MIL-53(Fe) (10 mgr) was heated at 80 °C until completion (Scheme 1). The progress of the reaction was monitored by TLC. After completion of the reaction as indicated by TLC, the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate and washed with water. The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude products were purified by column chromatography.



Scheme 1. Synthesis of benzimidazoles by using MIL-53(Fe)

Results and discussion

Characterization of catalyst

MIL-53(Fe) was successfully synthesized using described method and characterized using various techniques.

The FT-IR spectra of MIL-53(Fe) displayed a stretching vibration at about 3440 cm⁻¹ for g vibrations of O–H from the surface adsorbed water, 1543 and 1396 cm⁻¹ for carbonyl group of asymmetric C–O and symmetric C–O in order. The peak at 750 cm⁻¹ corresponds to the C–H bending vibrations of benzene. The intense peak at 540 cm⁻¹ is related to the Fe–O vibrations. The FT-IR spectrum in this Figure is similar to previous reports [34].

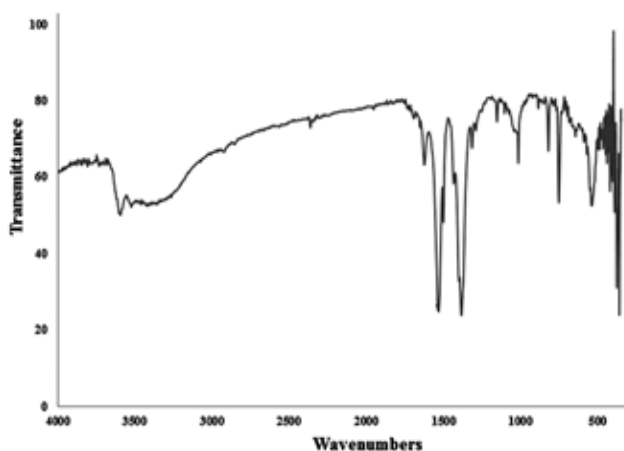
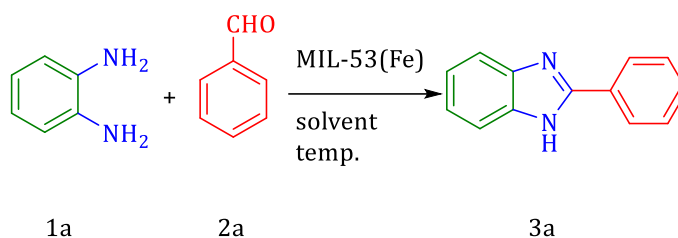


Figure 2. FT-IR spectrum of MIL-53(Fe)

Table 1. Optimization of reaction conditions^a



Entry	Amount of catalyst (mg)	Solvent	Time (min)	Yield (%) ^b
1	10	H ₂ O	40	80
2	10	EtOH	40	77
3	10	CH ₃ CN	50	71
4	10	CH ₂ Cl ₂	55	70
5	10	Solvent-free	30	94
6	4	Solvent-free	50	78
7	7	Solvent-free	35	60
8	12	Solvent-free	30	95

^aReaction conditions: *o*-phenylenediamine (1.0 mmol) and benzaldehyde (1.2 mmol) in the presence of catalyst and solvent (2.0 mL).

^bIsolated yield

After successful characterization of the prepared metal organic framework MIL-53(Fe), the catalytic activity of MIL-53(Fe) in the synthesis of 2-aryl-1*H*-benzimidazole was studied. To the first step amount of catalyst, and kind of solvent were tested. In the preliminary experiment, the reaction between *o*-phenylenediamine (**1a**) and benzaldehyde (**2a**) was studied in the presence of MIL-53(Fe). According to the results **3a** was obtained in 94% yield in solvent free condition (Table 1, entry 5). Results shown, the yield of production **3a** was depended on amount of MIL-53(Fe).

When the amount of MIL-53(Fe) was decreased to 7.0 and 4.0 mgr, the reaction was yielded 78% and 60%, respectively (Table 1, entries 6 and 7). According to Table 1, the highest yield and shortest reaction time of product **3a** are obtained in the presence of 10 mg of MIL-53(Fe) in solvent-free condition at 80 °C.

After optimizing the conditions, to explore the generality of these conditions and limitation of this catalytic system, different aromatic aldehydes were subjected to the reaction with *o*-phenylenediamine converted to the corresponding (Table 2).

The results show that this protocol efficiently generated the corresponding products for both electron-withdrawing groups and electron-donating groups or electron-rich substituents on the aromatic ring in the ortho, meta and para positions which are successfully subjected to the same reaction as the corresponding benzimidazole derivatives are obtained in excellent yields (86–94%) in short reaction times (less than 60 min).

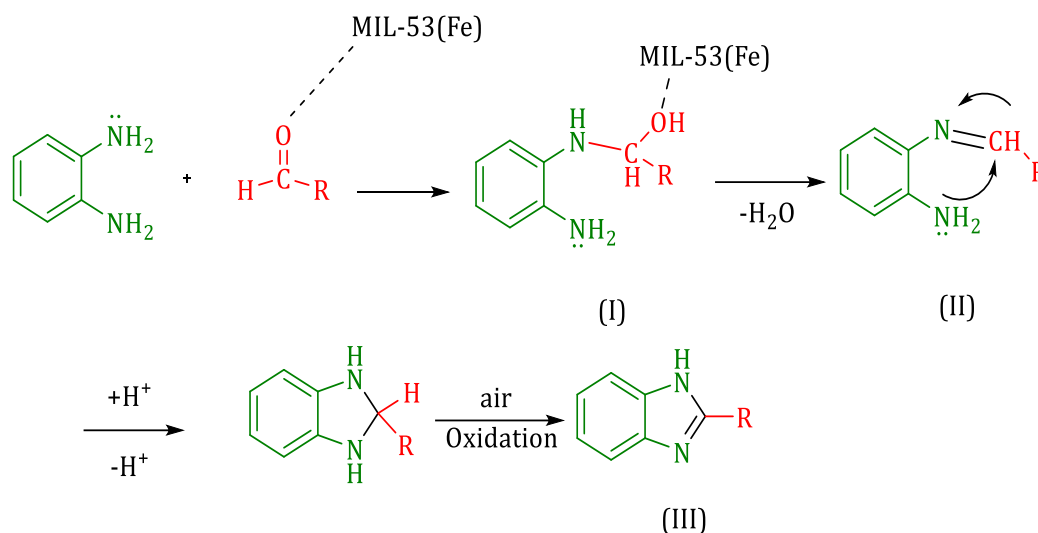
Table 2. Synthesis of benzimidazoles catalyzed by MIL-53(Fe)^a

Entry	R ¹	R ²	Product	Time (min)	Yield (%) ^b
1	H	H	3a	30	94
2	H	4-Me	3f	30	90
3	H	3-NO ₂	3d	80	91
4	H	4-NO ₂	3c	40	88
5	H	4-OMe	3e	90	86
6	H	4-Cl	3b	40	89
7	Me	H	3g	60	89
8	Me	Me	3h	50	86
9	Me	4-NO ₂	3i	40	89
10	Me	2-Cl	3j	65	89
11	Me	4-Cl	3k	80	88
12	Me	CHO	3l	80	86

^aReaction conditions: aldehyde (1.2 mmol), *o*-phenylenediamine (1.0 mmol) in the presence of MIL-53(Fe) and in solvent-free condition at 80 °C.

^bIsolated yield.

The proposed mechanism of the reaction supported by previous research [35] probably involves the interaction of MIL-53(Fe) with the aldehyde acting as an acid and also playing a complex role as shown in Scheme 2.



Scheme 2. The plausible mechanism of 2-aryl-1*H*-benzimidazole synthesis

As can be seen in Table 3, MIL-53(Fe) as a catalyst afforded good results in comparison to the other catalysts.

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

Entry	Catalyst	Conditions	Time (h)	Yield (%) ^a	Ref.
1	Fe ₃ O ₄ magnetic nanoparticles	EtOH, reflux	2-5	83-98	36
2	Yb(OTf) ₃ (0.5 mol%)	Solvent-free, 90 °C	1-6	40-92	37
3	Fe ₃ O ₄ -IL	H ₂ O or Solvent-free, 80 °C	20-75 min	84-92	38
4	H ₂ O ₂ /SiO ₂ -FeCl ₃ (0.1 gr)	Solvent-free, 150 °C	30 min	25	39
5	Cu(OAc) ₂ .H ₂ O (7 gr)	MeOH / H ₂ O, reflux	3	72	40
6	Zn ₃ (BTC) ₂	EtOH, r.t.	10-60 min	91-97	41
7	MIL-53(Fe)	Solvent-free, 80 °C	30-90 min	86-94	This work

The recovery and reusability of the catalyst was studied. the reusability of MIL-53(Fe) in the syntheses of product **3a** was investigated by repeatedly separating the MIL-53(Fe) from the reaction mixture, washing it and then reusing it over five successive runs. The catalytic activity was studied for several successive runs, showing similar activity (Table 4).

Table 4. The catalyst reusability of MIL-53(Fe) in 5 cycles

Run	1	2	3	4	5
Yield (%)	94	92	90	88	87

Conclusions

In this study, we have developed a simple and an efficient protocol for the preparation of benzimidazole from *o*-phenylenediamine and aldehydes in the presence of MIL-53(Fe) in solvent-free condition at 80 °C. All products were obtained in good to excellent yields. The advantages of this procedure include using MIL-53(Fe) as a recyclable and porous catalyst, high catalytic activity, very short reaction times and high yields.

Acknowledgement

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Conflict of Interest

We have no conflicts of interest to disclose.

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