Metal–organic frameworks as a very suitable reaction inductor for selective solvent-free multicomponent reaction: IRMOF-3 as a heterogeneous nanocatalyst for Kabachnik–Fields three-component reaction

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ABSTRACT

IRMOF-3 is found to be an active, selective and stable solid catalyst for three-component, one-pot reaction of amines, aldehydes and dimethyl phosphite to form the corresponding α -aminophosphonates in high yields. The catalyst can be isolated from the reaction mixture and reused at least four times.

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1. Introduction

Metal–organic frameworks (MOFs) have been the focus of increasing attention during the past decade [1]. MOF-based structures demonstrate various advantages such as high surface areas, adjustable pore sizes, and the simplicity of processability, tunable, and stable alternative materials [2,3]. MOFs and functionalized- or modified-MOFs have been utilized as solid catalysts in Friedel–Crafts alkylation and acylation [4], Sonogashira [5], alkene epoxidation [6], aldol [7], Suzuki [8], Biginelli [9], aza-Michael [10] and Knoevenagel [11,12], condensation or reactions. Recently, unfunctionalized IRMOF-3 has been used as heterogeneous catalyst by Gascon et al. In their investigations, IRMOF-3 catalyst contain non-coordinated amino groups demonstrates that the basicity of the aniline-like amino group is enhanced when incorporated inside the pores of MOF channels [11]. Gascon et al., have also reported a thermal and chemical stable MIL-101(Al) material containing amine functional groups. Their NH_2 -MIL-101(Al) has shown a high activity in the basic catalyzed Knoevenagel condensation [12]. On the other hand, when Xamena and Corma have reexamined the catalytic properties of unfunctionalized IRMOF-3 for the Knoevenagel condensation, to aiming at determining the

actual origin of the outstanding catalytic performance of IRMOF-3 (Scheme 1), they found that besides the amino groups presented as responsible active sites in the Gascon report, the presence of structural defects and the presence of extra framework ZnO species can also contribute to the Knoevenagel reaction [13].

Organic–inorganic hybrid porous IRMOF-3 would make the materials hydrothermal stable and hydrophobic and thus provide the materials with improved catalytic properties during applications for organic small molecules [11–17]. For these reasons and in our continuing interest in the synthesis and application of the organic–inorganic hybrid nanoporous material in catalyst and multicomponent reactions fields [18–24], we report herein our results for the application and direct using of the unfunctionalized IRMOF-3 as an suitable, efficient and green catalyst for the three-component condensation (3-CRs) of an amine, aldehyde and phosphite without any solvent, salts and additives with excellent yields of biological and medicinal [25–27] interest α -aminophosphonates (Scheme 1).

2. Experimental

2.1. Preparation of IRMOF-3

IRMOF-3 ($\text{Zn}_4\text{O}(\text{H}_2\text{N-TA})_3$) was synthesized according to the procedure from literature with slight modifications [11,13]. In a

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Scheme 1. Bifunctional acid base IRMOF-3 porous solid-catalyst.

typical catalyst preparation, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ (12.5 mmol) and H_2ATA (4.1 mmol) were dissolved in 100 ml DMF and stirred for 20 min at room temperature. The solution was transferred and sealed in a Teflon-lined autoclave, and kept at 100 °C for 20 h. The resulting brown solid was collected and washed with DMF and CHCl_3 , and the solid was finally dried in vacuum at 60 °C.

2.2. General procedure for Kabachnik–Fields reaction

A mixture of aldehydes (2.2 mmol), amines (2 mmol), dimethyl phosphite (2 mmol) and MOF (0.04 g) under solvent free condition, was stirred at 40 °C for 2 h. After completion the reaction, as indicated by TLC, the reaction mixture was cooled to room temperature and CH_2Cl_2 was added. The catalyst was separated by filtration. The CH_2Cl_2 was evaporated.

Dimethyl phenyl(phenylamino)methylphosphonate (**3a**) ^1H NMR (300.13 MHz, CDCl_3): 3.47 (d, $^3J_{\text{HP}} = 10.5$, 3 H), 3.78 (d, $^3J_{\text{HP}} = 10.5$, 3 H), 4.84 (d, $^2J_{\text{HP}} = 24.3$, 1 H), 5.02 (br, 1 NH), 6.51–7.51 (m, 10 H).

Dimethyl (3-nitrophenyl)(phenylamino)methylphosphonate (**3b**) ^1H NMR (300.13 MHz, CDCl_3): 3.64 (d, $^3J_{\text{HP}} = 10.8$ Hz, 3 H), 3.83 (d, $^3J_{\text{HP}} = 10.4$, 3H), 5.00 (d, $^2J_{\text{HP}} = 25.1$, 1 H), 5.25 (br, 1 NH), 6.62–8.41 (m, 9 H).

Dimethyl (4-chlorophenyl)(phenylamino)methylphosphonate (**3c**) ^1H NMR (300.13 MHz, CDCl_3): 3.55 (d, $^3J_{\text{HP}} = 10.8$, 3 H), 3.77 (d, $^3J_{\text{HP}} = 10.8$, 3 H), 4.52 (br, 1 NH), 4.79 (d, $^2J_{\text{HP}} = 24.3$, 1 H), 6.59–7.44 (m, 9 H).

Dimethyl (p-tolylamino)(4-nitrophenyl)methylphosphonate (**3d**) ^1H NMR (300.13 MHz, CDCl_3): 2.24 (m, 3 H), 3.50 (d, $^3J_{\text{HP}} = 10.5$, 3 H), 3.78 (d, $^3J_{\text{HP}} = 10.5$, 3 H), 4.80 (d, $^2J_{\text{HP}} = 24.3$, 1 H), 6.02 (br, 1 NH), 6.54–7.38 (m, 8H).

Dimethyl (p-tolylamino)(2-methoxyphenyl)methylphosphonate (**3e**) ^1H NMR (300.13 MHz, CDCl_3): 2.18 (m, 3 H), 3.45 (d, $^3J_{\text{HP}} = 10.5$, 3 H), 3.82 (d, $^3J_{\text{HP}} = 10.5$, 3 H), 3.93 (s, 3 H), 4.06 (br, 1 NH), 5.43 (d, $^2J_{\text{HP}} = 24.0$, 1 H), 6.54–7.49 (m, 8 H).

Dimethyl (p-tolylamino)(2-chlorophenyl)methylphosphonate (**3f**) ^1H NMR (300.13 MHz, CDCl_3): 2.16 (m, 3 H), 3.43 (d, $^3J_{\text{HP}} = 9.9$, 3 H), 3.83 (d, $^3J_{\text{HP}} = 9.9$, 3 H), 4.85 (br, 1 NH), 5.39 (d, $^2J_{\text{HP}} = 24.9$, 1 H), 6.49–7.56 (m, 8 H).

Dimethyl (2-methoxyphenyl)(pyrrolidin-1-yl)methylphosphonate (**3g**) ^1H NMR (300.13 MHz, CDCl_3): 1.69 (m, 4 H), 2.16 (m, 2 H), 2.64 (m, 2 H), 3.46 (d, $^3J_{\text{HP}} = 6.3$ Hz, 3 H), 3.77 (d, $^3J_{\text{HP}} = 6.3$ Hz, 3 H), 3.85 (s, 3 H), 4.66 (d, $^2J_{\text{HP}} = 18.0$ Hz, 1 H), 6.89–7.75 (m, 4 H).

Dimethyl (N,N-diethylamino)(3-nitrophenyl)methylphosphonate (**3h**) ^1H NMR (300.13 MHz, CDCl_3): 0.95 (t, $^3J_{\text{HH}} = 7.2$ Hz, 6 H), 2.21 (m, 2 H), 2.88 (m, 2 H), 3.37 (d, $^3J_{\text{HP}} = 9.3$ Hz, 3 H), 3.77 (d, $^3J_{\text{HP}} = 9.3$ Hz, 3 H), 4.12 (d, $^2J_{\text{HP}} = 24.9$ Hz, 1 H), 7.17–7.38 (m, 5 H).

Dimethyl 1-(phenylamino)cyclohexylphosphonate (**3i**) ^1H NMR (300.13 MHz, CDCl_3): 1.13–2.13 (m, 10 H), 3.45 (br, 1 NH), 3.55 (d, $^3J_{\text{HP}} = 10.5$ Hz, 6 H), 6.66–7.06 (m, 5 H).

3. Results and discussion

3.1. Catalyst synthesis and characterization

The nanoporous metal–organic framework IRMOF-3 was prepared by refluxing of 2-aminoterephthalic acid (H_2ATA) and zinc nitrate hexahydrate in DMF by a solvothermal method, according to a literature procedure [11,13]. In a typical catalyst preparation, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ (3.75 g) and H_2ATA (0.75 g) were dissolved in 100 ml *N,N*-dimethylformamide (DMF) and the mixture was transferred to Teflon-lined autoclave. The mixture of the reaction kept for 1 h at 25 °C and then at 100 °C for 17 h. The resulting brown solid was collected and washed thrice with CHCl_3 , and the solid was finally dried in vacuum at 60 °C. The IRMOF-3 structure is made of Zn_4O tetranuclear clusters connected by rigid NH_2 -benzenedicarboxylic linkers to generate a cubic framework (Fig. 1).

The IRMOF-3 was then characterized using a variety of different techniques. The IR spectra of IRMOF-3 show two peaks in 3470 and 3359 cm^{-1} due to the existence of the amino groups of the NH_2 -TA ligand [24]. The two sharp bands at 1575 and 1385 cm^{-1} corresponds to asymmetric ($\nu_{\text{as}}(\text{C}-\text{O})$) and symmetric ($\nu_{\text{s}}(\text{C}-\text{O})$) vibrations of carboxyl groups, respectively [25]. And the peaks centered at 1656, 1496, and 1421 cm^{-1} was ascribed to $\text{C}=\text{C}$ stretching vibration of the aromatic. The 1257 cm^{-1} frequency can be assigned to C–N vibrations. Diffraction peaks at around $2\theta = 6.8^\circ$ and 9.6° are readily recognized from the XRD pattern (Fig. 2d). The observed diffraction peaks agree with the IRMOF-3

Fig. 1. Preparation process of unfunctionalized IRMOF-3.

Fig. 2. (a) Optical microscope photograph of IRMOF-3, (b) The nitrogen adsorption–desorption isotherms at 77 K of IRMOF-3, (c) SEM images and (d) X-ray diffraction patterns of IRMOF-3.

Fig. 3. Reaction scale: aniline (2 mmol), benzaldehyde (2.2 mmol), dimethyl phosphite (2 mmol) and catalysts (4 mol%) in 3 mL MeCN. Aminophosphonate **3a** (green) and hydroxy phosphonate **4a** (red). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

[11]. The crystal structure of IRMOF-3 seems changed to amorphous through the reusing after 4 times (see SI).

The nitrogen adsorption–desorption isotherms of the solvothermal synthesized IRMOF-3 are displayed in Fig. 2b. The optical microscope photograph and SEM images (Fig. 2a and c), together

Table 1

Study of the solvent and temperature on the model reaction.^a

Solvent	Temp (°C)	Time (h)	Yield% 3a
THF	60	4	93
CH ₃ CN	60	2	72
CH ₃ CN	r.t.	2	40
Toluene	60	4	90
Solvent-free	60	2	94
Solvent-free	40	2	91
Solvent-free	r.t.	3	87

^a Reaction scale: aniline (2 mmol), benzaldehyde (2.2 mmol), dimethyl phosphite (2 mmol) and catalysts (4 mol%) in 3 mL solvent.

Fig. 4. Catalyst amounts study of IRMOF-3 in synthesis of **3a**.

Scheme 2. Expected products from the reaction of dimethyl phosphite, amines and aldehydes.

Table 2
Synthesis of α -amino phosphonates.

with the XRD patterns showed that the IRMOF-3 was highly crystalline.

3.2. Catalytic studies

As expected, in which adduct of amines and aldehydes was treated with phosphites under the reaction conditions [25–27], led to the products α -aminophosphonates **3**, and α -hydroxy phosphonates **4** (Scheme 2). For our study, aniline, benzaldehyde and dimethyl phosphite were chosen as the benchmark substrates in the model reaction.

Due to the fact that the nature of the IRMOF-3 nanoreactor or its synthetic component may play an important role in the synthesis of aminophosphonate **3a**, and based on our previous experience about porous nanoreactor in organic process, the initial reaction was carried out using 4 mol% H_2ATA , $\text{Zn}(\text{NO}_3)_2$, 2-aminoterephthalic ester (NH_2 -TE) and IRMOF-3 catalyst at 60 °C for 2 h in acetonitrile. The IRMOF-3 was assessed for its catalytic activity in the Kabachnik–Fields by studying the model reaction to produce of α -aminophosphonate **3a** as the principal product and α -hydroxy phosphonate **4a** as the by-product (Fig. 3). When the model reaction was run using IRMOF-3, the product **3a** was obtained 72% yield and **4a** was not observed.

The model reaction was screened in polar and nonpolar solvents using 4% mol of IRMOF-3. When the reaction was run under

solvent-free condition, the product was obtained in 91% yield at 40 °C in 2 h (Table 1).

The model reaction was carried out using different amounts of IRMOF-3 nanoreactor as the catalyst (Fig. 4). A high yield of α -aminophosphonate **3a** (91%) was obtained with 4 mol% of the catalyst. A further increase in the amount of catalyst (6–10 mol%) did not have any significant effect on the product yield or reaction time.

In order to examine the scope of this process, and to demonstrate the diversity of the IRMOF-3, the optimized conditions were applied to a series of substrate as shown in Table 2.

In a comparative study to show the chemoselectivity, dimethyl phosphite was treated with the mixture of aniline, benzaldehyde and cyclohexanone. Analysis of the mixture after 2 h shows that only benzaldehyde reacted with aniline to corresponds **3a** (Scheme 3).

The possibility of recycling and reusing the catalyst was then examined. In this case, after completion of the reactions (TLC), hot ethanol or CH_2Cl_2 was added and the catalyst was filtered and reused for four times (Fig. 5).

To the best of our knowledge, our results also show that the catalytic activity and selectivity of IRMOF-3 are higher than porous SBA-15/ SO_3H (model reaction). When the model reaction was performed in the presence of the SBA-15 sulfonic acid, although benzaldehyde was almost consumed soon, but a mixture of **3a** and **4a** was formed [28].

In summary, we reported Kabachnik–Fields three-component coupling of amines, aldehydes, and dimethyl phosphite to produce pharmacy and biological interest α -aminophosphonates catalyzed by IRMOF-3, in high yields under solvent-free conditions. This method has many advantages such as short reaction time, small amount of catalyst used and facily recycled, especially the abstaining from toxic organic solvents in the reaction, which provides a green and effective method for synthesis of α -aminophosphonates.

Fig. 5. Recyclability of MOF on the synthesis of **3a**.

Scheme 3. Chemoselective addition of phosphite to aldehyde and ketone.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.micromeso.2013.05.009>.

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