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The synthesis of a bifunctional copper metal organic framework and its application in the aerobic oxidation/Knoevenagel condensation sequential reaction

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A novel one-pot aerobic oxidation/Knoevenagel condensation reaction system was developed employing a Cu(II)/amine bifunctional, basic metal-organic framework (MOF) as the catalyst. The sequential aerobic alcohol oxidation/Knoevenagel condensation reaction was efficiently promoted by the Cu_3TATAT MOF catalyst in the absence of basic additives. The benzylidenemalononitrile product was produced in high yield and selectivity from an inexpensive benzyl alcohol starting material under oxygen atmosphere. The role of the basic functionality was studied to demonstrate its role in the aerobic oxidation and Knoevenagel condensation reactions. The reaction progress was monitored in order to identify the reaction intermediate and follow the accumulation of the desired product. Lastly, results showed the yield was not significantly compromised by the reuse of a batch of catalyst, even after more than five cycles.

Introduction

Multicomponent reactions are attractive and practical tools in chemistry as two or more synthetic steps are combined into one. Compared to multi-step synthetic processes, one-pot reactions improve efficiency, reduce production of waste, and enable the rapid construction of more complex molecules from simple, readily available starting materials.[1] Several catalytic systems have been designed to achieve efficient one-pot reactions. However, homogeneous catalysts, which are commonly used in one-pot multicomponent reactions, often suffer from catalyst contamination and poor recyclability.[2] Therefore, the development of heterogeneous catalysts that may be systematically designed and facilely recycled is currently one of the major foci of research on one-pot multicomponent reactions,, specifically for synthetic procedures, such as the Knoevenagel condensation, which furnish synthetically useful products.[3]

Recently, metal-organic frameworks (MOFs), have drawn great interest in several research areas because of their unique and attractive properties, such as their highly-ordered porous structure, high specific surface areas and great structural tunability.[4] Several utilizations, like gas storage, medical diagnostics, gas separation, optics, biosensing and catalysis, have been achieved employing MOF materials.[5] As one of the most promising inorganic-organic hybrid materials for catalysis, MOFs have emerged as highly practical and efficient platforms to engineer multifunctional catalysts for multistep organic transformations.[6] MOF materials can function as ideal solid platforms for catalytic design since both components, the metal and the organic ligand, can be functionalized with many advantageous features.[7] So far, the utilization of MOF catalysts in one-pot multicomponent reactions is limited in the literature.[8] Although several multifunctional heterogeneous catalysts have been obtained employing a "site-isolation" strategy, several drawbacks during their application in catalysis strongly limit further utilization. The current multifunctional catalytic systems in fact suffer often from weak catalytic activity; the need for an extra light source, as well as tedious preparation procedures.[9] In addition, one-pot multicomponent reactions should exclude the use of expensive starting materials.[10] For example, despite being more expensive than benzaldehyde itself, benzaldehyde acetal often serves as a precursor for the generation of benzaldehyde.[11] It would be much more practical to use inexpensive starting materials to initiate multistep reactions.

In this study, a multifunctional Cu_3TATAT catalyst was designed, synthesized, and employed in an efficient one-pot multicomponent reaction involving an aerobic oxidation/Knoevenagel condensation sequence of reactions (Scheme 1). The Cu_3TATAT catalyst was prepared in four different morphologies and sizes to study the relationship between its structure and catalytic activity. The novel utilization of a Cu(II)-promoted aerobic oxidation for the formation of aldehyde intermediates in a one-pot reaction from

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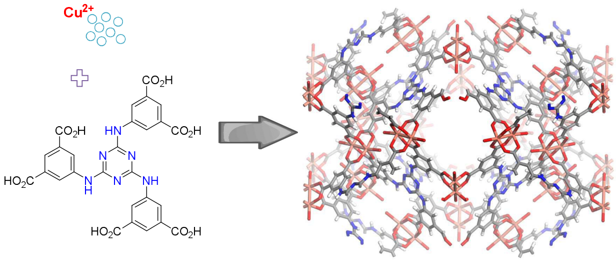

Scheme 1. The design and synthesis of Cu_3TATAT MOF with dual functionalities.

inexpensive aromatic alcohol starting materials has not been previously reported in the literature. This newly developed Cu_3TATAT catalyst is compatible with various aromatic alcohols under the studied conditions; it allows to convert them to the desired Knoevenagel condensation products in good yields and excellent selectivities. Furthermore, this one-pot reaction strategy can be extended to generate a nitro-vinyl substituted Henry reaction product via nitromethane nucleophilic addition.

Results and discussion

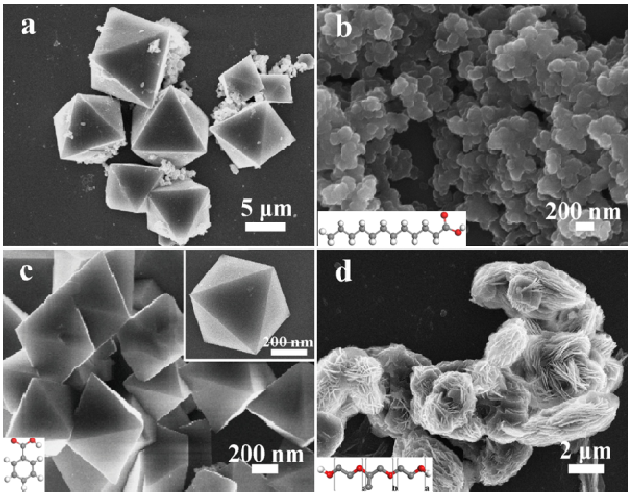

Fig. 1 SEM of Cu_3TATAT produced with different additive: (a) Cu_3TATAT-1 (No additive), (b) Cu_3TATAT-2 (Dodecanoic acid additive), (c) Cu_3TATAT-3 (Benzoic acid additive), (d) Cu_3TATAT-4 (Pluronic® F127 additive).

Nanosized MOF architectures have attracted much attention as they typically offer significantly improved chemical and physical properties and reactivity compared to the bulk ones. The nanomorphology of a solid catalyst takes advantage of its increased and accessible textural porosity; this leads to increased activity in the catalytic system.[12] As a result, the preparation of MOFs with controllable size and morphology via a facile route is crucial. Herein, we successfully synthesized a series of Cu_3TATAT in various sizes and morphologies employing morphology control reagents. As shown in Fig. 1a, the octahedral Cu_3TATAT crystal at approximately 10 µm scale was obtained in the absence of an additive.[13] In order to achieve Cu_3TATAT crystals at the nanoscale level, different mediators have been added during the synthetic process, which could strongly influence the dimension as well as the morphology. When dodecanoic acid was employed as the additive, uniform nanospheres with a diameter of 100 nm were observed by SEM (Fig. 1b). While replacing dodecanoic acid with benzoic acid as the additive gave a highly ordered crystalline Cu_3TATAT morphology, uniform and monodispersed octahedral crystals with a diameter of 600 nm were observed(Fig. 1c). In addition, a surfactant additive such as Pluronic® F127 provided a flower-like Cu_3TATAT crystal (Fig. 1d). The flower-like crystals were assembled from a thin nanoplate at the size of about 5 µm.

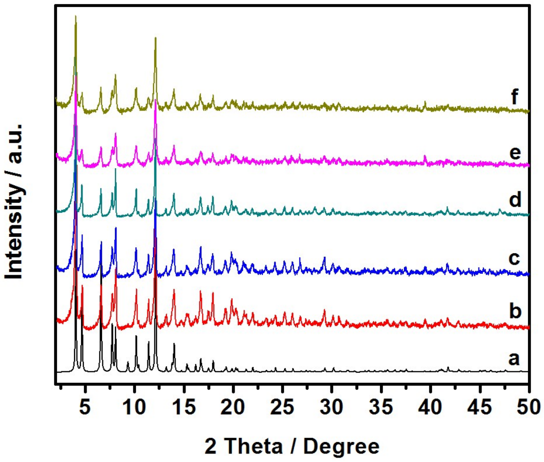

Fig. 2 PXRD of copper MOFs: a) Simulated Cu_3TATAT using its single crystal structure, b) Cu_3TATAT-1, c) Cu_3TATAT-2, d) Cu_3TATAT-3, e) Cu_3TATAT-4, f) Cu_3TATAT-3 after 5 recycles.

The crystallinity, structure and composition of the prepared Cu_3TATAT samples were characterized by powder X-ray diffraction (PXRD). The addition of different categories of mediators during the synthetic process does not affect the internal crystalline structure, as shown in Fig. 2. All PXRD patterns of the Cu_3TATAT were measured at solvated state. The patterns are in agreement with the simulated PXRD using Accelrys Materials Studio using CIF file from CCDC 831219. The PXRD results exclude the possibility that additional Cu carboxylate complexes/clusters were being formed inside the pores. Furthermore, the PXRD pattern results also indicate that the internal crystal structures of Cu_3TATAT samples 1-4 are the same, despite the fact that different additives were employed (Figure 2b-2e). However, the existence of crystalline defects is possible inside of Cu_3TATAT samples 2-4 due to the addition of external chemical additives. The characteristic diffraction peaks at 2 theta values of about 4.05°, 4.66°, 6.61°, 7.68°, 8.09°, 10.16°, 12.13° and 13.24° are assigned to the (101), (110), (112), (103), (202), (213), (303) and (224) planes of the Cu_3TATAT crystal, which is consistent with the literature.[14]

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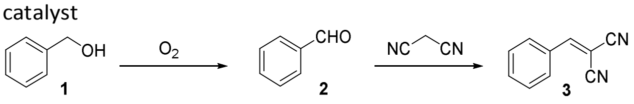
Table 1 The N_2 Adsorption/desorption Isotherms of Cu_3TATAT MOFs

Sample	S_{BET} (m^2g^{-1})	$S_{Langmuir}$ (m^2g^{-1})	V_{pore} (cm^3g^{-1})	$D_{Average\ pore}$ (nm)
Cu_3TATAT-1	1307(35)	1393(40)	0.69	2.12
Cu_3TATAT-2	1518(45)	1613(60)	0.72	1.91
Cu_3TATAT-3	1520(45)	1620(60)	0.77	2.03
Cu_3TATAT-4	1202(35)	1356(40)	0.62	1.94

The N_2 adsorption/desorption isotherms of various Cu_3TATAT samples synthesized using different additives were measured and the data is summarized in Table 1. The additive free Cu_3TATAT-1 sample gave a BET surface area of 1307.5 m^2g^{-1}. It was observed that nanoscaled samples Cu_3TATAT-2 and CuTATAT-3 had increased surface area (Table 1). Cu_3TATAT-2 with dodecanoic acid showed the BET area of 1518.1 m^2g^{-1}, while switching the additive to benzoic acid in Cu_3TATAT-3 gave a BET surface area of 1520.9 m^2g^{-1}. It was expected that the flower-morphology assembled from nano-plates could further increase the BET surface area. However, the corresponding BET area decreased to 1202.9 m^2g^{-1}; we attribute this unexpected result to the low crystalline integrity of Cu_3TATAT-4.

Table 2 One-pot multicomponent reaction using various catalyst



Entry	Catalyst	Base additive (mol%)	Conv. of 1 (%)	Yield (%) 2	Yield (%) 3
1	-	-	0	0	0
2	$Cu(NO_3)_2$	Na_2CO_3 (8)	23	8	11
3	$Cu(PhCOO)_2$	Na_2CO_3 (8)	46	16	27
4	$Cu_3(BTC)_2$	Na_2CO_3 (8)	53	17	32
5	$Cu_3(BTC)_2$	Na_2CO_3 (50)	86	0	82
6	$Cu_3(BTC)_2$	-	<5	<5	<5
7	$Cu(PhCOO)_2$	Melamine (2.7)	18	3	12
8	$Cu(PhCOO)_2$	Melamine (10)	57	6	50
9	$Cu_3(BTC)_2$	Melamine (10)	65	5	58
10	$Cu(PhCOO)_2$	UiO-66-NH_2 (8)	18	12	5
11	Cu_3TATAT-1	-	87	<5	85
12	Cu_3TATAT-2	-	91	<5	87
13	**Cu_3TATAT-3**	**-**	**95**	0	95
14	Cu_3TATAT-4	-	74	<5	70
15	-	Melamine (50)	0	0	0
16	-	TEMPO (50)	0	0	0

[a] Reaction conditions: catalyst (8 mol% based on copper), benzyl alcohol (1.0 mmol), malononitrile (1.5 mmol), TEMPO (0.5 equiv.), and base additive were stirred in 5 mL CH_3CN at 75 °C using 1 atm O_2 balloon for 12 h.

Among the Cu_3TATAT substrates studied, Cu_3TATAT-3 demonstrated the optimal material morphology and largest BET surface area. A quick catalytic survey of the as-prepared Cu_3TATAT materials revealed that Cu_3TATAT-3 provides the highest yield and best recyclability. Cu_3TATAT-4 only showed moderate yield (70%) and poor recyclability due to the relatively low crystalline structure and low BET surface area. Furthermore, Cu_3TATAT-1 and Cu_3TATAT-2 were not as good as Cu_3TATAT-3 in terms of catalytic yield and recyclability. As a result, Cu_3TATAT-3 proved to be the optimal copper MOF material for further catalytic evaluation taking advantage of its high crystalline structure, large BET surface area and efficient catalytic performance.

The aerobic oxidation/Knoevenagel condensation sequential reaction was systematically investigated employing various catalysts and base additives and the results are summarized in Table 2. No background reaction was observed in absence of the catalyst and/or basic additive; an O_2 balloon was used as the oxygen source (Table 1, entry 1). Employing 8 mol% of Na_2CO_3 as the base additive under mild reaction conditions, a Cu(II) salt achieved 23% conversion of benzyl alcohol, leading to 11% yield of the desired benzylidenemalononitrile product (Table 2, entry 2). $Cu(PhCOO)_2$ showed a much improved conversion under the same reaction conditions, which gave a 32% yield of the benzylidenemalononitrile product (Table 2, entry 3). This significant improvement in reaction efficiency is observed for copper complex with carboxylate ligand, which was also observed in our previous studies.[15] Interestingly, the $Cu_3(BTC)_2$ MOF promotes the one-pot multicomponent reaction efficiently in the presence of Na_2CO_3 (Table 2, entries 4 and 5). The use of $Cu_3(BTC)_2$ in the oxidation of benzyl alcohol was studied in detail during our previous investigation when 1.0 equiv. of Na_2CO_3 was used.[15] The alcohol conversion was compromised with only 0.08 equiv. of Na_2CO_3 due to its low protonation/deprotonation equilibrium constant (Table 2, entry 4). The conversion went up to 86% when increasing the amount of Na_2CO_3 to 0.5 equiv. (Table 2, entry 5). In addition, the conversion of benzyl alcohol was extremely low in the absence of Na_2CO_3, which indicated the base additive plays a crucial role (Table 2, entry 6). It would be ideal to employ an amine organic base to serve as the base for the aerobic alcohol oxidation, as well as the basic catalyst for the promotion of the Knoevenagel condensation. The water by-product generated during the oxidation and condensation reaction has no negative impact on the catalytic activity of our catalyst.

Melamine was chosen as the organic base candidate, proceeding in low yield using the combination of 8 mol% $Cu(PhCOO)_2$ and 2.7 mol% melamine (8 mol% based on aromatic nitrogen) in the one-pot multicomponent reaction (Table 2, entry 7). The nitrogen-based organic base is less efficient than the Na_2CO_3 inorganic base during the alcohol aerobic oxidation step. Increasing the melamine loading to 10 mol% improved the conversion of benzyl alcohol to 57%, which corresponds to a 50% yield of the desired condensation product (Table 2, entry 8). The use of both $Cu_3(BTC)_2$ and 10 mol% melamine further increased the yield to 58% (Table 2, entry 9). The successful implementation of melamine as the

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organic base provides the opportunity for organic base integration into a catalyst structure. However, the use of basic UiO-66-NH_2 MOF as the basic additive was not successful due to its weak basicity (Table 2, entry 10). This observation excludes the possibility of using an aromatic amine on the MOF structure as the base for the Knoevenagel condensation reaction.[16] In addition, it is also difficult to recycle the homogeneous $Cu(PhCOO)_2$ catalyst. Our Cu_3TATAT-3 solid catalyst was tested as a bifunctional catalyst with the incorporation of both Cu(II) and melamine catalytic moieties (Table 2, entires 11-14). Cu_3TATAT-3 gave a conversion of 95 % in the absence of base additive, taking advantage of the basicity of the H_6TATAT ligand (Scheme 1 and Table 2, entry 13). This result was better than its analogs, which gave 85 %, 87 % and 70 % yield, for sample 1, 2 and 4, respectively. We believe that the relatively larger surface area and the more unified crystalline structure assisted the catalytic process. The aerobic oxidation reaction initiated from the deprotonation of the benzyl alcohol, as promoted by the base. The further deprotonation of the benzylic position was achieved using a combination of copper(II), base, TEMPO and molecular oxygen. The $Cu_3(BTC)_2$ and the Cu_3TATAT promoted aerobic oxidation reactions shared similar mechanisms, with the only difference of employing different basic additives. Lastly, base additive and TEMPO alone were shown to have no catalytic oxidation activity to initiate the first step of the one-pot multicomponent reaction, even at 0.5 equiv. (Table 2, entries 15 and 16). The role of TEMPO in the Cu(II) promoted oxidation has already been thoroughly studied in Semmelhack's studies.[17] TEMPO was being oxidized to nitrosonium ion while Cu(II) was reduced to Cu(I). At this stage, the nitrosonium ion generated from TEMPO oxidized benzyl alcohol to form the corresponding aldehyde product. The regeneration of TEMPO and Cu(II) was promoted by the oxygen in solution.

With the optimal catalytic reaction conditions in hand, the one-pot multicomponent reaction pathway was further investigated by tracing the product distribution versus the reaction time, while employing 8 mol% of Cu_3TATAT-3 as the catalyst (Fig. 3). According to GC-MS monitoring over the reaction progress, the one-pot reaction took place in two steps . Inspection of the amount of reactant and product in the solution as shown in Fig. 3 indicates that benzylidenemalononitrile was efficiently generated via the oxidation of benzyl alcohol. The concentration of the benzaldehyde intermediate went up initially to reach a maximum after 6 h. Then the generation of benzylidenemalononitrile became the dominant reaction pathway and the one-pot reaction was finished after 12 h. According to the information reported in Fig. 3, intermediate and product distribution exhibited a typical behavior of one-pot sequential reactions. The turnover number (TON) of Cu_3TATAT-3 was calculated to be 11.9, which is significantly higher than other literature reported systems, in which the reaction is performed in the absence of base additive(Table S3).[18]

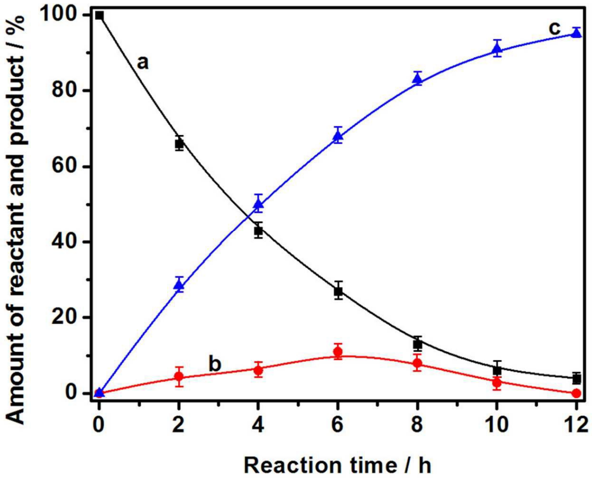

Fig. 3 Results of the catalytic activity of the Cu_3TATAT-3 catalyst for the aerobic oxidation/Knoevenagel condensation tandem reaction. Conversion vs reaction time of (a) benzyl alcohol, (b) benzaldehyde and (c) benzylidenemalononitrile.

The role of basic additives during the nucleophilic addition to the benzaldehyde intermediate has been further studied employing various aromatic organic bases. These tests were carried out under the optimal reaction conditions employing 8 mol% of the copper MOF catalyst, 10 mol% of base additive (based on nitrogen), 1.0 mmol benzaldehyde, and 1.5 mmol malononitrile, in 5 mL CH_3CN. Melamine **B1** was used first as a basic catalyst for the Knoevenagel condensation reaction of benzaldehyde and malononitrile. As shown in Fig. 4, melamine demonstrated good catalytic activity for the benzaldehyde conversion, by taking advantage of the large number of aromatic amine and triazine moieties (Fig. 4, **B1**). Catalyst Cu_3TATAT-3 **B5** was evaluated in the absence of the $Cu_3(BTC)_2$ MOF and giving a slightly higher yield of **B1**; this is likely due to the similarity of the core structure of Cu_3TATAT-3 to melamine.

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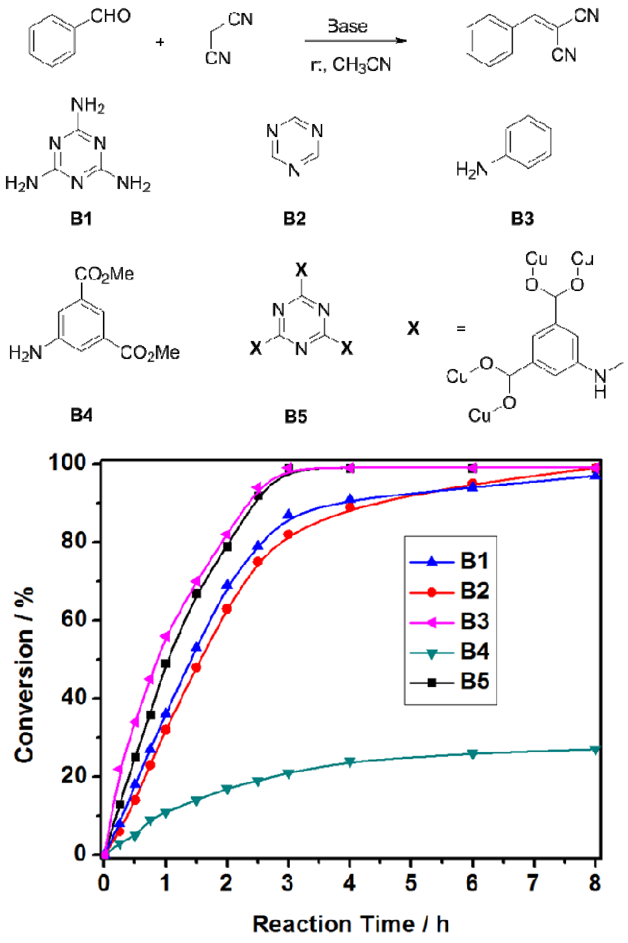
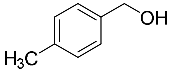
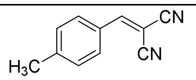
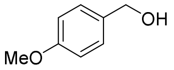
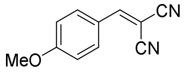
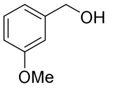
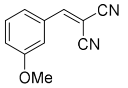
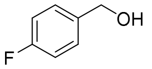
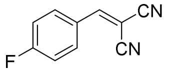
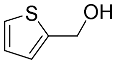
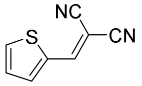
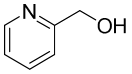
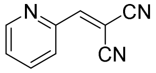
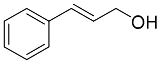
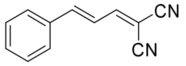
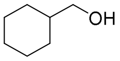
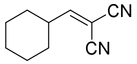


Fig. 4 The effect of organic bases in the Knoevenagel condensation reaction; conversion vs time of the Knoevenagel condensation catalyzed by various bases.

However, whether or not the aromatic amine or triazine moiety is responsible for the catalytic activity remains unclear at this stage. 1,3,5-Triazine **B2** was evaluated to determine the basic catalytic activity of the triazine core in bases **B1** and **B5**. A slightly diminished reaction rate was observed in comparison to the use of **B1** as the base (Fig. 4, **B2**). This observation strongly suggests the high activity and crucial role of the triazine moiety during the Knoevenagel condensation reaction, despite the fact that the triazine moiety is less efficient than the aromatic amino moiety. Furthermore, aniline **B3** was also tested to study the catalytic activity of aromatic amines (Fig. 4, **B3**). Aniline **B3** showed the highest reaction efficiency when it was employed in the same molar amount of nitrogen. This observation also explains how melamine **B1** behaved more efficiently than triazine **B2**. Even though aniline showed good activity in the Knoevenagel condensation reaction, the deactivation of aniline through carboxylate groups significantly reduced the catalytic efficiency during the condensation reaction (Fig. 4, **B4**).

Table 3 One-pot reaction of various alcohols using Cu_3TATAT-3 catalyst^a

Entry	Substrate	Product	Conv. %	Sel. %
1			90	99
2			97	99
3			86	99
4			78	99
5			72	99
6			93	99
7			69	99
8			12	99

^{a}Reaction conditions: Cu_3TATAT-3 catalyst (8 mol% based on copper), alcohol (1.0 mmol), malononitrile (1.5 mmol), and TEMPO (0.5 equiv.), in CH_3CN (5 mL) were stirred at 75 °C using a 1-atm O_2 balloon for 12 h.

With this information in hand, we can conclude that the aromatic amino functional group in Cu_3TATAT-3 does not function effectively as a base. As a result, the triazine moiety in Cu_3TATAT-3 is responsible for the majority of reactivity in the Knoevenagel condensation of the one-pot multicomponent reaction. A variety of primary alcohols were evaluated employing the synthesized Cu_3TATAT-3 as the catalyst under the optimal reaction conditions (Table 3). A methyl substituted aromatic alcohol was compatible under the optimal reaction conditions, providing 90% yield of the desired product (Table 3, entry 1). Electron-rich aromatic alcohols, such as 4-methoxybenzyl alcohol and 3-methoxybenzyl alcohol, were compatible with the Cu_3TATAT-3 catalyst under the homogeneous reaction conditions.

Conversions of 97% and 86% were achieved for methoxy substitutions at the *para*- and *meta*-positions respectively (Table 3, entries 2 and 3). An aromatic alcohol containing a *para* electron-withdrawing group also performed well under the optimal reaction conditions despite its electron-deficient nature (Table 3, entry 4). Furthermore, heteroaromatic thiophen-2-ylmethanol reacted smoothly with malononitrile in the presence of Cu_3TATAT-3 and a moderate yield of 2-(thiophen-2-ylmethylene)malononitrile was obtained (Table 3, entry 5). Similar reactivity was expected for pyridin-2-ylmethanol, which provided the malononitrile functionalized pyridine ring in 93% conversion and 99% selectivity (Table 3, entry 6). Furthermore, *trans*-cinnamyl alcohol was evaluated and only a

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moderate yield was achieved, presumably due to the poor electron density of the hydroxyl group since it is relatively far from the aromatic ring (Table 3, entry 7). Lastly, an alkyl alcohol such as cyclohexane methylalcohol was also compatible with the malononitrile nucleophile under the optimal reaction conditions, despite the fact that the reaction rate was slow and only a yield as low as 12% was achieved after 12 hours of reaction time (Table 3, entry 8).

The recyclability of the Cu_3TATAT-3 catalyst was evaluated to demonstrate the advantage of bifunctional solid catalysts. The reaction was carried out using benzyl alcohol and malononitrile in presence of Cu_3TATAT-3 under the optimal reaction conditions as reported in Table 1. The recycled catalyst showed no loss of reactivity over five runs (Fig. 5); the yield of the desired 2-benzylidenemalononitrile product remained in fact over 90% after five runs. The supernatant of the CH_3CN suspension after completion of the reaction showed no reactivity to the benzyl alcohol in the presence of malononitrile and further addition of melamine did not raise the consumption of benzyl alcohol. This result suggests that there is no leakage of the copper content. Addition of benzaldehyde to the filtered supernatant did not lead to formation of benzylidenemalononitrile, indicating good stability of Cu_3TATAT-3 without detectable H_6TATAT ligand leakage. This further shows that only the H_6TATAT ligand on the heterogeneous Cu_3TATAT-3 is responsible for the Knoevenagel condensation reactivity.

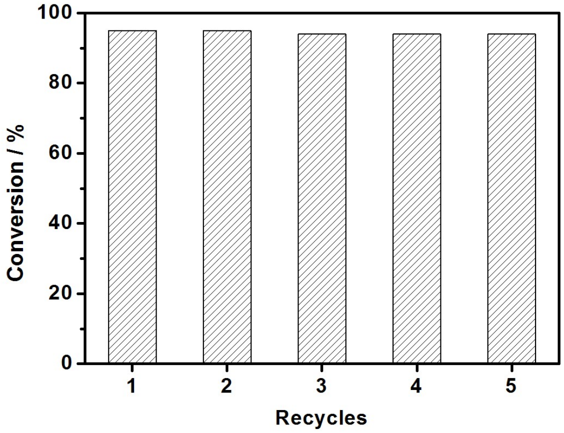

Fig. 5 Recyclibility test of Cu_3TATAT-3 in the one-pot reaction of benzyl alcohol and malononitrile.

To further study the possibility of catalyst leaching of Cu_3TATAT-3 during the Knoevenagel condensation reaction, a hot filtration test was performed and the catalytic reaction was stopped after 4 h. Then the reaction solution was centrifuged and the supernatant was further stirred for an additional 8 h. The result in Fig. 6 shows the conversion of benzyl alcohol paused after 4 h after the centrifugation of the solid catalyst. This observation indicates the advantage of the stable covalently bonded structure of the Cu_3TATAT-3 MOF and that there was no leakage of the copper or TATAT ligand. The Cu_3TATAT-3 catalyst was assessed by PXRD and FTIR before and after one-pot catalysis, to evaluate its structural integrity.

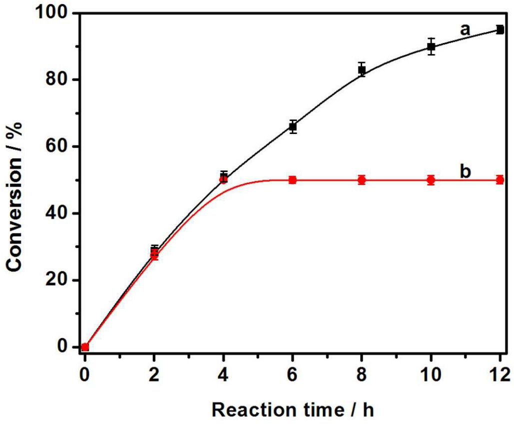

Fig. 6 Conversion of benzyl alcohol as a function of reaction time in a one-pot multicomponent reaction over: (black curve) Cu_3TATAT-3 and the reaction system after Cu_3TATAT-3 was filtered (red curve).

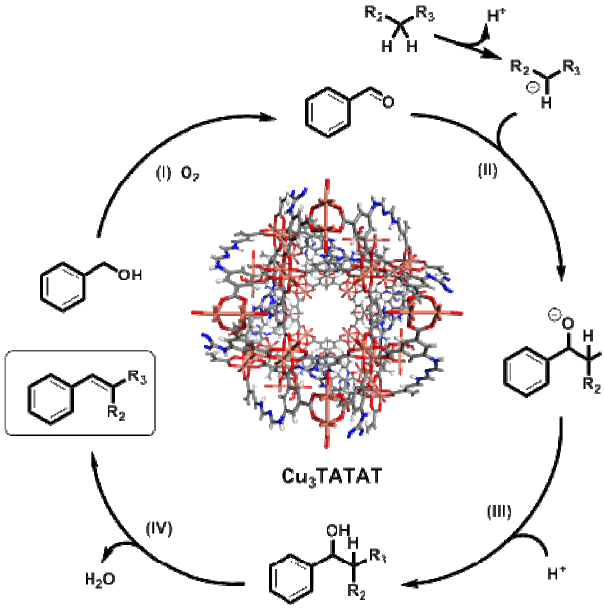

Fig. 7 Proposed mechanism of the one-pot multicomponent reaction.

Powder X-Ray Diffraction characterization of the recovered Cu_3TATAT-3 catalyst was carried out on fresh and recycled catalysts, showing almost identical PXRD (Fig. 2f) profiles. Furthermore, the FT-IR spectra of the fresh and recovered Cu_3TATAT-3 samples were also identical; we can conclude that there is no structural alteration of the MOF framework (Fig. S1). In addition, the BET surface area remained at 1514.9 m^2g^{-1} after 5 catalytic cycles (Fig S2).

A mechanism for the one-pot multicomponent reaction between aromatic alcohols and methylene nucleophiles has

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been proposed (Fig. 7). The reaction initiates from the aerobic oxidation of an aromatic alcohol using a Cu(II) catalyst in the presence of the basic H_6TATAT ligand (step I). The aromatic aldehyde is formed efficiently using the Cu_3TATAT catalyst, through the first aerobic oxidation step. Secondly, the as-formed aromatic aldehyde can further react with a methylene nucleophile through a condensation reaction in the presence of the basic triazine moiety in the Cu_3TATAT MOF. The initial step of the Knoevenagel condensation reaction involves the base-promoted deprotonation of the active methylene group for the generation of a carbanion intermediate. This newly formed carbanion will react with the carbonyl group on the aromatic aldehyde via nucleophilic attack (step II). Lastly, the addition intermediate will quickly be converted to the benzylidenemalononitrile product after the absorption of one proton and loss of water (steps III and IV).

Experimental

Preparation of H_6TATAT ligand.

H_6TATAT (H_6TATAT = 5,5',5''-(1,3,5-triazine-2,4,6-triyl)tris (azanediyl)triisophthalate) was synthesized according to literature procedures.[19] In a typical process, a 250-mL three-necked round bottom flask was charged with 7.6 g of 5-aminoisophthalic acid (0.042 mmol), 2.68 g of NaOH (0.067 mmol) and 4.37 g of $NaHCO_3$ (0.052 mmol). Then 70 mL of H_2O was added and the mix was vigorously stirred at 0 °C for 1 h. Then, a mixture of 1.84 g of cyanuric chloride (0.01 mmol) in 35 mL of 1,4-dioxane was added dropwise, followed by heating to, and maintaining at 100 °C for 24 h. The resulting mixture was acidified to pH=2 with a hydrochloric acid solution. The product was collected by filtration and washed with distilled water 3 times. Finally, the H_6TATAT was dried under vacuum at 40 °C for 24 h.

Preparation of Cu_3TATAT MOFs.

In a typical process, Cu_3TATAT-1 was synthesized by completely dissolving $Cu(NO_3)_2$ (0.164 g, 0.68 mmol) in a mixture of DMA (2.0 mL), DMSO (2.0 mL), H_2O (10 μL) and HBF_4 (0.9 mL). Subsequently, H_6TATAT (0.030 g, 0.049 mmol) was added. The mixture was transferred to a small vial and stirred at 90 °C for 3 days. The blue crystal was collected by filtration and washed with DMA 3 times. Finally, the obtained product was dried under vacuum at 40 °C for 24 h. In order to tune the diameter and morphology of Cu_3TATAT, dodecanoic acid, benzoic acid and Pluronic® F127 were employed as additives.

In a typical process, Cu_3TATAT-2 was synthesized by completely dissolving dodecanoic acid (0.060 g, 0.3 mmol) and $Cu(NO_3)_2$ (0.164 g, 0.68 mmol) in a mixture of DMA (2 mL), DMSO (2 mL), H_2O (10 μL) and HBF_4 (0.9 mL). Then, H_6TATAT (0.030 g, 0.049 mmol) was added. The mixture was transferred to a small vial and heated at 90 °C for 3 days. The blue crystal was collected by filtration and washed with DMA 3 times. Finally, the obtained product was dried under vacuum at 40 °C for 24 h.

Similarly, the syntheses of Cu_3TATAT-3 and Cu_3TATAT-4 were achieved using benzoic acid or Pluronic® F127 as an additive instead of dodecanoic acid and following a similar procedure to that reported for Cu_3TATAT-2.

Characterization.

The morphologies of the resulting products were characterized by scanning electron microscopy (SEM, ZEISS SUPRA55). The samples for SEM detection were dispersed in ethanol and sonicated for several minutes followed by supporting onto the silicon slice. The composite and structure of the crystals were demonstrated by wide-angle X-ray powder diffraction (XRD, M21X) with Cu Kα radiation at a scanning rate of 2 degrees per minute (λ=0.154178 nm). The specific surface areas were obtained through the Brunauer–Emmett–Teller (BET) method (Micromeritics ASAP 2420 adsorption analyzer). All samples were dried under vacuum at 120 ºC for 12 h before the measurement. The porosity properties of the obtained samples were determined by the adsorption branches of isotherms by using the Barrett-Joyner-Halenda (BJH) model. Fourier transform Infrared spectra (FT-IR) were also obtained using a Nicolet 6700 spectrometer and the samples were prepared using the potassium bromide (KBr) pellet technique. The thermal decomposition characteristics of the samples were carried out using thermogravimetric analysis (TG) by a Netzsch STA449F3 instrument at a heating rate of 10 °C/min, under a dry N_2 flow. The element content of the samples was tested by inductively coupled plasma-atomic emission spectrometry (ICP-AES, 715-ES). The chemical composition of the products was analyzed by X-ray photoelectron spectrometry (XPS, ESCALAB 250Xi), and the catalytic products were analyzed by Gas Chromatography-Mass Spectrometry (Agilent 7890A/5975C-GC/MSD) with dodecane as an internal standard.

Conclusions

In summary, a general copper/amine bifunctional Cu_3TATAT MOF catalyst was developed for an efficient one-pot multicomponent reaction. An aerobic oxidation/Knoevenagel condensation reaction sequence was optimized in presence of the bifunctional Cu_3TATAT catalyst. Four different morphologies and sizes were achieved employing organic additives and their corresponding catalytic activities were studied in detail. Furthermore, the aromatic alcohol oxidation and Knoevenagel condensation of the resultant aromatic aldehyde with malononitrile were explored in a one-pot sequential reaction and it was found that various aromatic alcohols are tolerated under the optimized reaction conditions. The copper site was found to be responsible for the alcohol oxidation and the organic amino functional group was found to serve as a base in both, the aerobic oxidation and the condensation reaction. The catalytic reactivity was further

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extended to a one-pot reaction involving a nucleophilic Henry reaction to demonstrate the high efficiency and general applicability of the synthesized Cu_3TATAT catalysts. The Cu_3TATAT catalysts can be recycled up to five times while showing no significant loss of activity in the one-pot oxidation/Knoevenagel condensation reaction.

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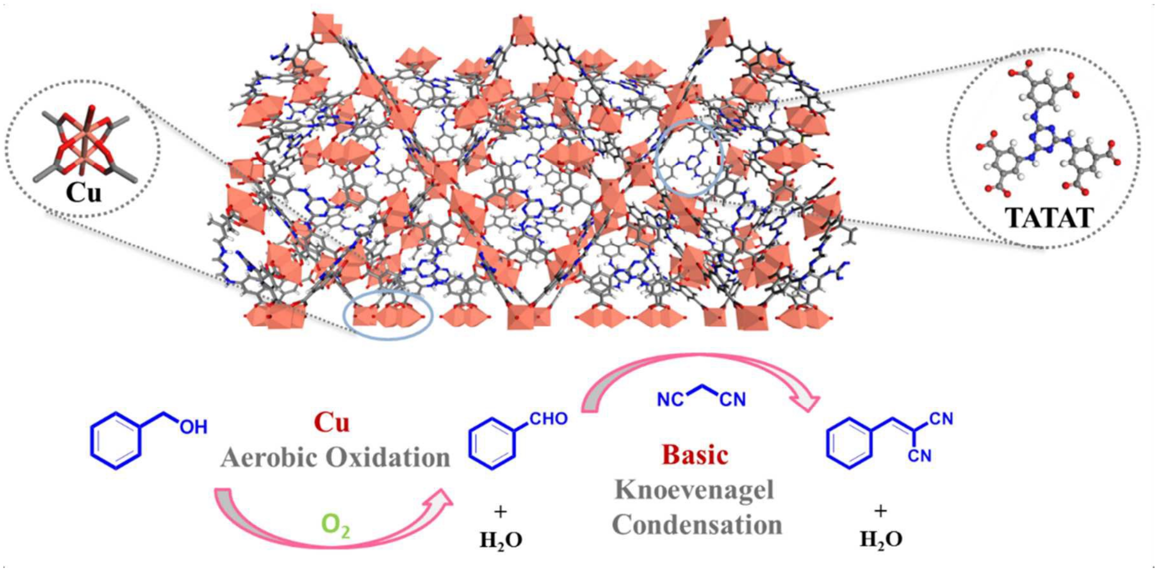

A novel one-pot aerobic oxidation/Knoevenagel condensation reaction system is developed employing a Cu(II)/basic bifunctional metal-organic framework (MOF) as the catalyst. The sequential aerobic alcohol oxidation/Knoevenagel condensation reaction can be efficiently promoted by the Cu$_3$TATAT MOF catalyst in the absence of base additives. The benzylidenemalononitrile product was produced in high yield and selectivity from an inexpensive benzyl alcohol starting material under oxygen atmosphere. The role of the basic functionality has been systematically studied to demonstrate its utility in the aerobic oxidation and Knoevenagel condensation reactions. The reaction progress has been monitored in order to reveal the reaction intermediate and accumulation of the desired product. Lastly, this newly developed catalytic system shows excellent recycling performance without significant compromise of the reaction yield after five runs.