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A series of porous metal–organic frameworks with hendecahedron cage: Structural variation and drug slow release properties

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ABSTRACT

A series of porous MOFs with hendecahedron cage-liked cavity has been constructed from the $[Cu_2(COO)_4]$ secondary building unit, H_3L (H_3L = [1,1';3',1'']Terphenyl-4,5',4''-tricarboxylic acid) and pyrazine derivatives varied with different sizes; the structural evolving of the hendecahedron cage and the application in drug delivery and controlled release were presented.

1. Introduction

Metal–organic framework (MOFs), an emerging class of crystalline hybrid material, are built from the virtually limitless combinations of metals and ligands, which attracted extensive interest not only because of their intriguing varieties of architectures, but also due to the nature of their own performance, which can be reasonable tuning for specific applications [1–3]. Due to their high stability, high surface area, and large pore volume, large numbers of MOFs have shown various potential applications including gas storage [4], catalysis [5], nonlinear optics [6], separations [7], sensing [8] and biomedicine [9]. In view of molecular storage, the porous MOFs materials with cage-liked cavity, especially those with high-connectivity polyhedral cage, can afford the features of confined nanospace, extra-large surface area, different window size for guest molecule exchange as well as the delicate pore surface with functional group. Above characteristics make porous MOFs candidates for bio-molecule capsules [9], molecular carrier for molecule transporters [10] as well as platforms for drug molecules storage and controllable release [11–13].

The use of "paddle-wheel" Cu_2 carboxylate as secondary building unit (SBU) was a classic way to construct porous MOFs material [14]. In the view of the structure property of "paddle-wheel" Cu_2 carboxylate SBU, the strategy of combination of multi-connection aromatic carboxyl acid with pyridine-like secondary linker, represents an effective way to assemble MOFs with cage-like cavity [15]. In another hand, the MOF derivation by introducing the functional group into known MOF structures can lead to an improvement of host-guest interaction [16]. It was a good strategy to obtain MOFs with predicted properties, which could be used in the field of drug slow release by porous MOFs carrier.

In our previous work, $Cu(NO_3)_2{\cdot}3H_2O$, the triangle aromatic carboxylic acid of [1,1';3',1''] Terphenyl-4,5',4''-tricarboxylic acid (denoted as H_3L) and pyrazine are mixed in a solution composited of DMF and H_2O to yield a porous MOF with a formula of $[Cu_3L_2(pyrazine)(H_2O)]_n$ [13a] The hendecahedron-like cage present in this 3D structure bear three kinds of "windows" with different sizes. And this compound shows good controlled release performance for the release of ibuprofen over anethole and guaiacol. As a continuation of the work, here we present a series of porous MOF materials based on above hendecahedron cage-liked cavity, which were constructed from the paddle-wheel Cu_2 carboxylate SBU, H_3L and various pyrazine derivatives, with a formula of $[Cu_3L_2(X)(H_2O)]_n$, [X = pyrazine-2,3-diamine (**1**), quinoxaline (**2**) and H_2O (**3**)]. Drug molecule storage and release experiments were carried out based on the amino-pyrazine based MOF (**1**), which revealed that the framework of **1** achieved drug loading of $0.30\ g\ g^{-1}$ (ibuprofen), and $0.37\ g\ g^{-1}$ (guaiacol), respectively. Compound **1** showed the improved ability of slow release toward the small drug molecule of guaiacol than its pyrazine based prototype MOF.

2. Experimental

2.1. Materials and general methods

The reagents and solvents were commercially available and were

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used as received without further purification. ^1H NMR test spectra were recorded with a Bruker AV 400. IR spectra were recorded in the range of 4000–450 cm^{-1} on a Nicolet 6700 FT-IR spectrometer using the KBr disc technique. Elemental analyses (C, H, N) were performed on a Euro Vector EA3000 CHN elemental analyzer. Powder X-ray diffraction (PXRD) data were recorded on Philips PW-1710 or a Bruker D8 powder X-ray diffractometer with Cu-Kα_1 radiation (λ = 1.5406 Å). Nitrogen (N_2) adsorption measurement was performed on a Micromeritics ASAP 2020 surface area analyzer at 77 K. UV data were measured on an Agilent 8453 UV–Vis spectrometer.

2.2. Synthesis of [Cu_3L_2(pyrazine-2,3-diamine)(H_2O)]$_n$ (1)

$Cu(NO_3)_2·3H_2O$ (0.25 mmol), H_3L (0.125 mmol) were added in a solution of 6 mL DMF and 1 mL 1,4-dioxane, then and pyrazine-2,3-diamine (0.125 mmol) in 1 mL 0.1 M HCl was added under stirring; the solution was transferred in to a 15 mL autoclave. The system was heated at 80 °C in oven for 24 h and cooled to room temperature, where upon the blue bock-shaped crystals of **1** were produced (yield: 52 mg, 71.6% based on $Cu(NO_3)_2·3H_2O$). The solid product was washed with DMF, and dried in air.

2.3. Synthesis of [Cu_3L_2(quinoxaline)(H_2O)]$_n$ (2)

$Cu(NO_3)_2·3H_2O$ (0.25 mmol), H_3L (0.125 mmol) and quinoxaline (0.125 mmol) were added in a solution of 6 mL DMF, 1 mL 1,4-dioxane and 1 mL water under stirring; the solution was transferred in to a 15 mL autoclave. The system was heated at 80 °C in oven for 24 h and cooled to room temperature, where upon the blue bock-shaped crystals of **2** were produced (yield: 38.5 mg, 0.068 mmol, 62.6% based on $Cu(NO_3)_2·3H_2O$). The solid product was washed with DMF, and dried in air.

2.4. Synthesis of [$Cu_3L_2(H_2O)_2$]$_n$ (3)

3 was synthesized as the same way of **2**, excepted that the quinoxaline was replaced by quinoxaline-2,3-diol (0.25 mmol) (yield: 38.9 mg, 68.2% based on $Cu(NO_3)_2·3H_2O$). The solid product was washed with DMF and dried in air.

2.5. Drug loading experiment of 1

Compound **1** was exchanged with CH_2Cl_2 for one week, then **1** was heated under vacuum condition in 100 °C for 1.5 h to get the activated sample, and then the activated samples of **1** were immersed in a hexane solution of ibuprofen (0.012 g/mL) and guaiacol solution to get the drug loading samples: **1**@ibuprofen and **1**@guaiacol, respectively.

2.6. Drug release experiment of 1

The drugs release experiments were performed in the media of water solution, the drugs release processes were monitored by UV–Vis spectroscopy. The dosage of the drug-loading samples were unified in 3 mg and the volume of the solution is 3 mL.

2.7. X-ray crystallography

The diffraction data of **1–3** was collected on an Oxford Xcalibur, Sapphire3, Gemini ultra CCD diffractometer, equipped with monochromatic Cu Kα radiation (λ = 1.54178 Å) at 173(2) K or room temperature. The intensity data were corrected for Lorentz and polarization effects (SAINT), and empirical absorption corrections based on equivalent reflections were applied (SADABS) [17]. The structures ware solved by direct methods and refined by the full-matrix least-squares method on F^2 with SHELXTL program package [18]. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were calculated and refined as a riding model. The hydrogen atoms of coordinated water molecules were located from difference maps. The disordered guest molecules in **1–3** could not be modeled and were treated by the SQUEEZE routine [19]. The crystallographic details are provided in Table 1, and selected bond lengths and angles are given in Table S1.

Table 1
Single Crystal X-ray diffraction refinement data for **1–3.**

Compound	1	2	3
Empirical formula	C46H29Cu3N4O13	C50H29Cu3N2O13	C42H25Cu3O15
Formula weight	1036.35	1056.37	960.24
Temperature	173(2) K	296(2) K	296(2) K
Wavelength	1.54178 Å	1.54178 Å	1.54178 Å
Crystal system, space group	Tetragonal, *I41/amd*	Tetragonal, *I41/amd*	Tetragonal, *I41/amd*
Unit cell dimensions	*a* = *b* = 19.5046(2) Å, c = 60.444(3) Å, *α* = *β* = *γ* = 90°	*a* = *b* = 19.6856(6) Å, c = 59.9228(15) Å, *α* = *β* = *γ* = 90°	*a* = *b* = 19.8736(6) Å, *c* = 59.423(3) Å, *α* = *β* = *γ* = 90°
Volume	22,994.5(13) Å^3	23,221.5(12) Å^3	23,469.7(16) Å^3
Z	8	8	8
F(000)	4192	4272	3872
Completeness	98.8%	97.4%	98.1%
Goodness-of-fit on F^2	1.133	1.002	0.995
Final R indices [I > 2sigma(I)]	R1 = 0.0684, wR2 = 0.2001	R1 = 0.0761, wR2 = 0.1686	R1 = 0.0608, wR2 = 0.1356
R indices (all data)	R1 = 0.0777, wR2 = 0.2109	R1 = 0.1384, wR2 = 0.1840	R1 = 0.0870, wR2 = 0.1444

3. Results and discussion

3.1. Structural properties

The product of our previous work, [Cu_3L_2(pyrazine)(H_2O)]n [13a], was set as the prototype MOF (Cu-pyz-MOF) in this work, where a typical "saddle-shape" structural unit composited of four L^{3-}, five $Cu_2(COO)_4$ SBUs and four pyrazine ligands was found; the "saddle-shape" structural unit connected and thus made the 3D structure of Cu-pyz-MOF (Fig. 1a and b). The porosity of Cu-pyz-MOF was featured as a unique hendecahedron-liked cage which stacked in an "up-down" mode. The hendecahedron-liked cage possessed three kinds of "windows" with different sizes (Fig. 2a), including the hexagon-shaped I-window with dimensions of 17.2 Å × 12.7 Å, the pentagonal II-window with dimensions of 14.9 Å × 10.3 Å and the tetragonal III-window with dimensions of 7.1 Å × 6.4 Å (accounting of van der Waals radii). Different from the traditional way to construct the MOF derivatives by introducing functional group into the aromatic acid ligand [16], a strategy of varying pyrazine with different function group and size was taken to achieve the functionalized cage without breaking it. Four similar pyrazine derivatives were used as secondary ligand, including pyrazine-2,3-diamine, quinoxaline, quinoxaline-2,3-diol and phenazine (Fig. 1c and d).

Compound **1** and **2** were obtained by using pyrazine-2,3-diamine or quinoxaline to replace pyrazine during the hydrothermal synthesis, whose structures were the analogue of the Cu-pyz-MOF, and two amino group or a benzene group were successfully installed in the II-window of the hendecahedron cage (Fig. 1c). However, it should be mentioned that the difference came from the synthesis aspect: in the synthesis of **1**, the pyrazine-2,3-diamine must be used in its form of hydrochloride, to suppress the ability of 2,3-diamine group in pyrazine to chelate the Cu(II) in solution [20]; for **2**, it just needed a simple replacement of pyrazine by quinoxaline without any change of the synthesis method of