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A rare (3,4,5)-connected metal-organic framework featuring an unprecedented 1D + 2D → 3D self-interpenetrated array and O-atom lined pore surface: structure and drug controlled release†

Di-Chang Zhong,*[a] **Lie-Qiang Liao,**[a] **Ji-Hua Deng,**[a] **Qing Chen,***[b] **Ping Lian,**[a] and **Xu-Zhong Luo***[a]

A rare (3,4,5)-connected self-interpenetrated metal-organic framework with O-atom lined pore surface has been constructed from Zn(II) and H_4L (H_4L = 5,5'-(1,3,6,8-tetraoxobenzo[lmn][3,8]phenanthroline-2,7(1H,3H,6H,8H)diyl)-diisophthalic acid), which features an unprecedented 1D + 2D → 3D self-interpenetrated array and shows good property in drug controlled release.

Metal-organic frameworks (MOFs) continue to attract extensive interest because of their variety of architectures and intriguing topologies, as well as potential applications in fields of chemistry, material, biology, and medicine.[1] Several sepecial issues in journals of *Chem. Soc. Rev.* and *Chem. Rev.* have been devoted to concluding the research progresses of this currently hot field from several aspcects.[2] To well describe the structures of complicated MOFs, node and net approach, pioneered by Wells, has been extensively used to simplify the structures of MOFs.[3] Usually, networks with high symmetry are more likely to be found in nature, and node correspondences and a sequence of transformations often derive new networks from a given network. As a result, a large number of derived uninodal/binodal nets have been produced. Besides MOFs with uninodal net such as 3-connected *srs*, 4-connected *dia* and 6-connected *pcu* nets,[5] as well as those with binodal nets such as (3,8)-, (4,8)-, (3,9)-, (3,12)-connected nets[6] have been high-frequently reported, MOFs with special topological structures such as polycatenation, polythreading, polyknotting and so on have also been fabricated and reported with the rapid development of the crystal engineering.[7] However, to the best of our knowledge, (3,4,5)-connected network featuring an unprecedented 1D + 2D → 3D self-interpenetrated array has not been reported in MOF materials so far.

In applications, due to the high and regular porosity associated to important volumes and surface areas, MOFs have been explored as biomaterials used for drug delivery, drug controlled release, and so on.[8] MIL-101(Cr), with unsaturated Lewis acid metal sites on pore surface, can load up to 1.4 g of ibuprofen per gram, much higher than the amounts of ibuprofen incorporated into other MOFs without function group on pore surface.[9] This observation clearly shows that delicate design of inner surface of MOFs is very important for creation of an efficient MOF-based material for drug controlled release. To find out more other functional groups in MOFs that may benefit for drug controlled release, recently, we synthesized a series of MOFs with functional pore surface and investigated their properties in drug controlled release. Herein, we report a Zn(II) MOF based on H_4L (Scheme S1; H_4L = 5,5'-(1,3,6,8-tetraoxobenzo[lmn][3,8] phenanthroline-2,7(1H,3H,6H,8H)-diyl)diisophthalic acid), $\{[NH_2(CH_3)_2]-[Zn_2(HL)L_{0.5}]\}_n \cdot n(8DMF \cdot 5H_2O)$ (**1**), which features an unprecedented 1D + 2D → 3D self-interpenetrated array and O atom lined pore surface. In this communication, we report the synthesis and novel structure of **1**, and it's function for controlled release of ibuprofen.

The ligand H_4L was synthesized by method reported in literature.[10] Solvothermal reaction of $Zn(NO_3)_2 \cdot 6H_2O$ with H_4L in DMF in a molar ratio of 1:1 at 110 °C for 72h led to the formation of brown block-shaped crystals of **1** in 55 % yield (ESI†). Infrared spectra of **1** shows an intense peak at 1713 and 1676 cm^{-1}, corresponding to the stretching vibration of uncoordinated and coordinated carboxylate group respectively. The broad peak at 3431 cm^{-1} indicates the existence of H_2O molecules in **1** (ESI†, Fig. S1).

Single crystal X-ray diffraction analysis indicates that **1** crystallizes in a *C2/c* space group.‡ As shown in Fig. 1a, the asymmetric unit contains two crystallographically independent Zn(II) ions. Both of them coordinate with four O atoms from four individual L ligands, resulting in a ZnO_4 tetrahedral geometry. The ligand H_4L exhibits two species, one is L^{4-} in which four carboxylate groups are fully deprotonated, and the other is HL^{3-} where three of carboxylate groups are deprotonated (ESI†, Scheme S1), which is consistent with the IR result. L^{4-} and HL^{3-} anion ligands adopting symmetrical and asymmetrical coordination mode, respectively, coordinate to six and five Zn(II) ions (ESI†, Scheme S1). The Zn-O distances, ranging from 1.863(9) to 1.946(8) Å, are similar to these reported in IRMOF-5 containing $Zn_4O(CO_2)_6$ tetrahedral cluster,[11] while slightly longer than those reported in MOFs with typical $Zn_2(CO_2)_4$

[a] *Key Laboratory of Organo-Pharmaceutical Chemistry of Jiangxi Province, Key Laboratory of Jiangxi University for Functional Material Chemistry, and College of Chemistry & Chemical Engineering, Gannan Normal University, Ganzhou 341000, China.*
E-mail: zhong_dichang@hotmail.com, luoxuzhong@hotmail.com
[b] *Institute of Chinese Materia Medica, Guangxi University of Chinese Medicine, Nanning, 530001, China. E-mail: qing0082@163.com*

† Electronic Supplementary Information (ESI) available: Synthesis, crystallographic data in CIF, topological analysis, supplementary figures, and TGA, XRPD results (PDF). See DOI: 10.1039/b000000x/

paddle-wheel structural unit.[12] Three carboxylate groups from one L^{4-} and two HL^{3-} ligands, empolying the *syn-syn* bridging mode, connect Zn1 and Zn2 together, generating a binuclear Zn structural unit (Fig. 1a). The distance between Zn1 and Zn2 is 3.344(2) Å, much longer than the value reported in MOFs with typical $Zn_2(CO_2)_4$ paddle-wheel structure (*ca.* 2.92 Å).[12] The binuclear Zn cluster units are further linked together by L^{4-} and HL^{3-} ligands, resulting a 3D porous framework with the pore size of 14.2 Å × 4.3 Å (Fig. 1b). It needs to mention that the pore surface is lined with carboxylic O atoms. The counterions $[NH_2(CH_3)_2]^+$, originated from the decomposition of some DMF molecules, fill in the pore together with the lattice DMF and H_2O molecules. About 45% solvent accessible volume is estimated by PLATON procedure. Due to the great disorder of the guest molecules, they could not be well assigned from the difference map. The number of guest molecules were estimated from the results of elemental analysis (EA) and thermogravimetric analysis (TGA) (ESI[†]).

The most striking feature in **1** is the unprecedented 1D + 2D → 3D self-interpenetrated array constructed from Zn(II) and HL^{3-}/L^{4-} ligands. As shown in Fig. S2a (ESI[†]), HL^{3-} ligands link Zn1 and Zn2 together to form a 2D layer. Each layer contains 38-membered $Zn_4(HL)_2$ rhombuses, where two binuclear Zn(II) structural units are bridged by two HL^{3-} ligands with the length and width of *ca.* 12.532(5) and 9.039(7) Å respectively (ESI[†], Fig. S2a). The L^{4-} ligands thread through the rhombuses and connect Zn1 and Zn2 together to generate a 1D chain (Fig. 1c, ESI[†], Fig. S2b). By sharing the metal centers (Zn1 and Zn2), the 1D chain and 2D layer are not isolated but incorporated together, resulting in a 3D network containing 1D + 2D → 3D self-interpenetrated array (Fig. 1d). To the best of our knowledge, among thousands of MOFs, **1** represents the first example that contains 1D + 2D → 3D self-interpenetrated array.[7]

From the perspective of topology, the 3D framework of **1** can be described as a trinodal (3,4,5)-connected network. The binuclear Zn(II) structural unit, connecting three HL^{3-} and two L^{4-} anions, should be considered as a 5-connected node (ESI[†], Fig. S3a). The HL^{3-} anion, linking three binuclear Zn(II) structural units, can be regarded as a 3-connected node (ESI[†], Fig. S3b), and the L^{4-} anion, connecting four binuclear Zn(II) structural units, can be viewed as a 4-connected node (ESI[†], Fig. S3c). Therefore, the structure of **1** belongs to a (3,4,5-*c*) connected topological net with the Schläfli symbol of $\{4.8^2\}_2\{4^2.8^3.10\}\{4^2.8^8\}_2$ (ESI[†], Fig. S3d). The trinodal (3,4,5-*c*) connected self-interpenetrated array and O-atom lined pore surface, reveal that **1** is an unprecedented MOF among thousands of reported MOFs.

The bulk phase purity of **1** was examined by powder X-ray diffraction. As shown in Fig. S4 (ESI[†]), all the peaks displayed in the measured pattern (ESI[†], Fig. S4b) closely match to those in the simulated one generated from single-crystal diffraction data (ESI[†], Fig. S4a), which indicates single phase of **1** has been formed. The thermogravimetric (TG) curve of **1** shows a weight loss of 39.1% from room temperature to 205 °C, corresponding to the removal of all the guest molecules of each formula unit (calcd 38.8%). The desolvated framework is stable up to 325 °C, then begin to

decompose through another three steps of weight losses upon further heating (ESI[†], Fig. S5).
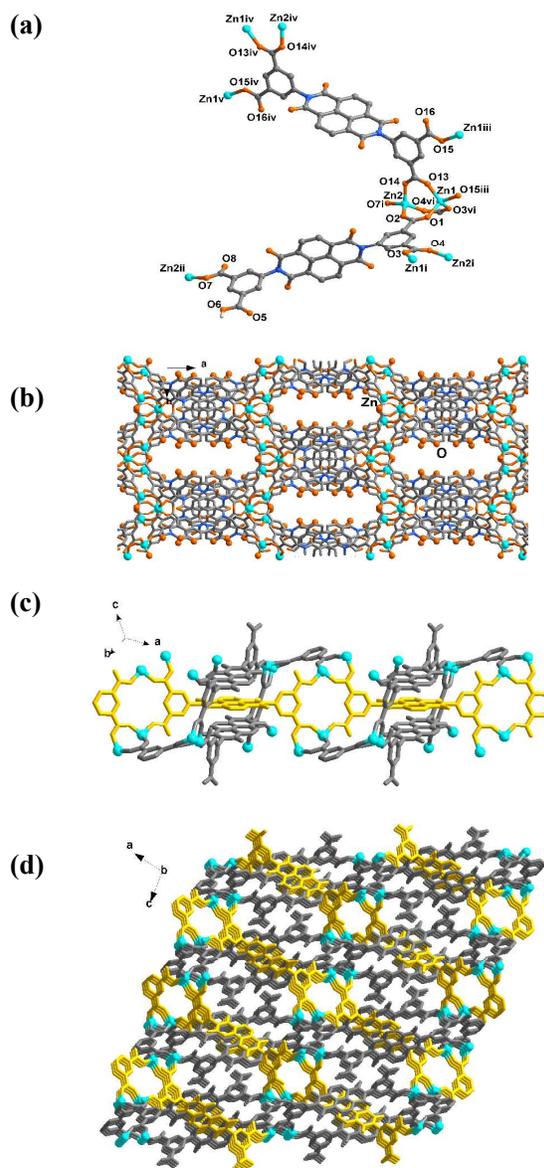
Fig. 1 (a) Coordination environments of Zn(II) ions, and symmetrical/asymmetrical coordination modes of L^{4-}/HL^{3-} anion ligands in **1** (Symmetric codes: *i* = 0.5-*x*, -0.5+*y*, 0.5-*z*; *ii* = -*x*, 2-*y*, -*z*; *iii* = 0.5-*x*, 1.5-*y*, 1-*z*; *iv* = -*x*, 2-*y*, 1-*z*; *v* = -0.5+*x*, 0.5+*y*, *z*; *vi* = 0.5-*x*, 0.5+*y*, 0.5-*z*). (b) 3D porous structure of **1** with O-atom lined pore surface. (c) Part of structure in **1**, to well show the self-interpenetrated array in **1**. (d) 3D self-interpenetrated structure of **1**.

To examine the possible permanent porosity in **1**, freshly prepared **1** was soaked in methanol solution to exchange the guest DMF molecules in the pores of **1**. The resulted product shows similar XRD pattern to that of freshly prepared **1**, indicating the framework can keep stable after exchanged by methanol (ESI[†], Fig. S4c). However, after further activation by removal of the methanol, the framework collapses, which is evidenced by the markedly changed XRD pattern (ESI[†], Fig. S4d) and the N_2 adsorption isotherms (ESI[†], Fig. S6). This may be ascribed to the fragile binuclear Zn(II) structural unit, not strong enough to strut such a large framework after removing the guest inside the cavity.

Considering the pore surface of **1** is lined with carboxylic O atoms, we have investigated the possible function of **1** in drug controlled release. Ibuprofen, a nonsteroidal anti-inflammatory drug structurally containing carboxylate group that may strongly interact with the pore surface by hydrogen bond, was selected. The ibuprofen was incorporated into methanol-exchanged sample of **1** by an impregnation method (ESI†). The pore window of **1** is large enough to allow ibuprofen molecules freely enter the channel through a side-entering mode. Powder XRD measurement shows that some peaks of ibuprofen-loaded **1** are slightly dissimilar to those of the simulated due to the flexibility of the framework induced by the incorporation of ibuprofen. However, most of the peaks of ibuprofen-loaded **1** are closely match to those of the simulated, which indicates the framework can keep stable after incorporation of ibuprofen (ESI†, Fig. S4e). Elemental analysis (EA) and TG were used for determination of the loading amount of ibuprofen (ESI†). The result obtained from EA reveals that 0.5075 g of ibuprofen has been incorporated into per gram of **1** (ESI†, Table S1). TG analysis indicates that 0.3870 g of ibuprofen, calculated from the first weight loss (corresponding to the departure of ibuprofen), has been loaded into per gram of **1** (ESI†, Fig. S5). This value is smaller than the one obtained from the EA results, which may be ascribed to the incomplete removal of ibuprofen in the first weight loss stage.

The ibuprofen release experiments, monitored by UV-Vis spectra, were further conducted in methanol solution to evaluate the property of drug controlled release (**1** is unstable in simulated body fluid). The results demonstrated in Figs. S7a and S7b show that the ibuprofen molecules slowly release from the pore of **1** due to the concentration diffuse mechanism. The steady hyperchromicity is observed. After 96 h, the absorbance reaches the largest value, corresponding to 44.5 mg of ibuprofen, calculated using the UV-Vis quantitative method (Fig. S7c), released. This value corresponds to 0.445 g of ibuprofen per gram of **1**, which is smaller than the one obtained from the EA results. This may be attributed to the incomplete release of ibuprofen in the final releasing experiment. The amount of ibuprofen incorporated into **1** is larger than these loaded in most MOF materials,[9b,9c] while lower than that loaded in MIL-101(Cr), the famous MOF showing the largest encapsulation capacity for ibuprofen.[9a] It should be noted that it takes over four days to release most of the ibuprofen inside of **1**. The slow release rate may be ascribed to the strong hydrogen-bond interactions between **1** with O-atom lined pore surface and ibuprofen molecules with carboxylate groups. This result elucidates that **1** has good capacity of ibuprofen controlled release, and reveals that hydrogen-bond interaction can be applied to design materials used for controlled release of ibuprofen-like drugs in future.

In conclusion, we for the first time demonstrate here a rare (3,4,5)-connected metal-organic framework, which features unprecedented 1D + 2D → 3D self-interpenetrated array and O-atom lined pore surface, and shows good controlled release of ibuprofen.

Notes and References

‡ Crystallographic data for **1** ($C_{53}H_{38}N_6O_{20}Zn_2$), Monoclinic, *C*2/*c*, *a* = 38.596(8), *b* = 15.279(3), *c* = 23.600(5) Å, *β* = 101.29(3)°, *V* = 13648.4(5) Å^3, *Z* = 8, *µ* = 0.769 mm^{-1}, D_c = 1.177 Mg/m^3, *F*(000) = 4944, 5974 unique (R_{int} = 0.099), R_1 = 0.0783, wR_2 = 0.1782 ($I > 2\sigma(I)$), GOF = 0.973. For crystallographic data in CIF or other electronic format, see DOI: 10.1039/b000000x/

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TOC graphic for

A rare (3,4,5)-connected metal-organic framework featuring an unprecedented 1D + 2D → 3D self-interpenetrated array and O-atom lined pore surface: structure and drug controlled release

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A rare (3,4,5)-connected self-interpenetrated metal-organic framework has been constructed from Zn(II) and H$_4$L ligand (H$_4$L = 5,5'-(1,3,6,8-tetraoxobenzo[lmn][3,8]phenanthroline-2,7(1H,3H,6H,8H)-diyl)diisophthalic acid), which features an unprecedented 1D + 2D → 3D self-interpenetrated array and O-atom lined pore surface, and shows good controlled release of ibuprofen.