Spontaneous chiral resolution directed by symmetry restriction and $\pi-\pi$ interaction

Jin-Tao Yu1,2, Yan-Yan Shi1,2, Junliang Sun1,3, Jianhua Lin1,3, Zhi-Tang Huang1,2 & Qi-Yu Zheng1,2

1Beijing National Laboratory for Molecular Sciences, Beijing, PR China, 2CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, PR China, 3College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, PR China.

In order to understand and rationally construct homochiral self-assembled structures from racemic molecules, two novel crystalline metal-organic frameworks with chiral cavities were developed. The homochirality of the layers in both MOFs was achieved by forming strong coordinate bonds between the C3-symmetric cyclotriveratrylene and Zn4O(CO2)6 cluster. By changing weak $\pi-\pi$ interactions between organic building blocks, the achiral assembly of ZnCTV-1 was successfully transformed into a chiral assembly in ZnCTV-2. This study demonstrated a possible route for designing the synthesis of chiral MOF through weak interactions.

Chirality is a common phenomenon in nature, and represents the evolution of matters towards more complicated cases. Many chiral systems achieve their functions through the interaction with other chiral molecules or the environment (chiral recognition or chiral assembly)1–3. However, the rules controlling (a)chiral interactions, such as chiral symmetry breaking, self-resolution, supramolecular chirality formed by achiral molecular aggregation, etc. remain relatively poorly understood. Therefore, the understanding and rational construction of chiral structures from achiral or racemic molecules are still challenging4,5.

Metal-organic frameworks (MOFs), an important class of self-assembled materials, built by organic linkers and metal ions or clusters have attracted great attention over the past decades due to the structural diversity and outstanding properties6–20. Chiral MOFs are more attractive because of their additional properties for asymmetric catalysis, enantioselectivity, chiral molecular imaging, etc14–18. To prepare homochiral MOF materials, three complimentary approaches have been widely used19: direct synthesis from enantiopure ligands or via self-resolution process, chiral-templated synthetic procedures and post-synthetic modification approaches. Among these, spontaneous resolution during crystallization is of higher interest.

Cyclotriveratrylene (CTV) is a rigid cyclic macromolecule with a shallow electron-rich cavity20–22. New progress in the domain of macrocyclic CTV-based hosts includes applications in material science, sensing and separations23–28. Owing to a pyramidal shape and convergent binding modes, CTV itself and CTV-based ligands are capable of forming coordination complexes with group one elements and transition metals29–44. Hardie et al. conducted excellent works on pyridyl decorated CTV derivatives that form discrete or infinite metallo-supramolecular assemblies33–38. When it comes to carboxylic acid decorated CTV ligands, only a few structures have been reported39–44, and their transition metal complexes are even rarer42–44. We recently reported the first CTV based 1D ternary independent nanotubular framework with permanent porosity44. In this work, C3-symmetric tritopic corner ligands tri-(4-carboxyl)-trimethoxycyclobenzylebe ($H_3L_1$) and tri-(4-carboxy-phenyl)-trimethoxy-cyclobenzylebe ($H_3L_2$) were used for the construction of chiral MOFs (Fig. 1a). As far as we know, there is no CTV-based infinite coordination polymer with chiral cavities reported until now.

Here, six-coordinated octahedral Zn$_2$O(CO$_2$)$_6$ clusters were selected as inorganic nodes due to a relative easy formation as well as good thermal stability. According to the principles of reticular chemistry, (6,3)-coordinated networks are expected. Yaghi et al. have reported two kinds of 3D (6,3)-coordinated networks (known as pyr and qom topology) with flat three-connected organic linkers and Zn$_2$O(CO$_2$)$_6$ clusters, which show ultrahigh porosity than most MOFs. While, due to the concave and bowl-shape structure of CTV type ligands, different topologies are formed as we will discuss below.
Results

Synthesis and crystal structure of ZnCTV-1. A preliminary experiment resulted in the formation of ZnCTV-1, which is synthesized from the solvothermal reaction of Zn(NO$_3$)$_2$·6H$_2$O and H$_3$L$_1$ in N,N’-dimethylformamide (DMF) at 95 °C (Fig. 1b). The colourless hexagonal plate crystals of ZnCTV-1 are insoluble in water and common organic solvents (DMF, alcohol, THF, etc), elemental analysis gave a formula of [Zn$_4$O((L$_1$)$_2$)]·DMF·EtOH·H$_2$O. Single crystal X-ray diffraction analysis showed that ZnCTV-1 is a stacking of 2D (6,3)-coordinated layers in the space group of P31c. Each layer can be considered as a fused honeycomb bilayer in eclipsed mode shown in Fig. 2a & 2b. In each layer, face-to-face arranged ligands of the same enantiomer link to Zn$_4$O(CO$_2$)$_6$ clusters through their carboxylates, forming rigid chiral capsules with C$_3$ symmetry and a cavity volume of 167 Å$^3$. The homochirality in each bilayer is due to symmetry restriction and the chirality was transferred from one ligand to another through the rigid Zn$_4$O(CO$_2$)$_6$ cluster. Unfortunately, the adjacent bilayers are symmetrically related by the c-glide and contain the opposite enantiomers (Fig. 2c).

Based on the analysis of ZnCTV-1, we could devise two possible ways to obtain a chiral MOF. The first consists in using a homochiral CTV ligand to exclude the formation of the layers with the opposite chirality. However, with the present solvothermal synthetic conditions, ligand molecules could easily flip to their enantiomers during the reaction process$^{47}$. A new synthetic route with milder conditions is under investigation. The alternative route is to keep the homochiral layer but modify the interaction between layers to assemble the homochiral layers selectively. In ZnCTV-1, the main interaction between layers is the π-π interaction in a parallel-displaced mode with a plane distance of about 3.2 Å (Supplementary Fig. S2). In order

Figure 1 | Ligands and crystal images. (a), Chemical structures of the two ligands based on C$_3$-symmetrical CTV, H$_3$L$_1$ and H$_3$L$_2$. (b), Crystal image of ZnCTV-1. (c), Crystal images of ZnCTV-2.

Figure 2 | Layered crystal structure of ZnCTV-1. (a), One 2D (6,3)-coordinated bilayer of real structure (top view). (b), Topology of eclipsed 2D structure. (c), Two adjacent bilayers with opposite enantiomers (side view). (Zn, green tetrahedron; O, red; C, gray; H atoms were omitted for clarity.)
to modify the possible \( \pi-\pi \) interaction, our strategy is to insert a phenyl group between the CTV-skeleton and the carboxylate group with the \( \text{H}_3\text{L}_2 \) shown in Fig. 1.

**Synthesis and crystal structure of ZnCTV-2.** Similar solvothermal reactions of \( \text{ZnCl}_2 \) and \( \text{H}_3\text{L}_2 \) in \( \text{N},\text{N}''\)-diethylformamide (DEF) produced beautiful octahedral crystals, ZnCTV-2 (Fig. 1c), with a yield of 86%. The product was formulated as \( \text{Zn}_4\text{O}(\text{L}_2)_2 \cdot 13\text{DEF} \cdot 3\text{H}_2\text{O} \) on the basis of elemental analysis. Single crystal X-ray diffraction revealed also a layered \((6,3)\)-connected framework but with the topology shown in Fig. 3b with space group \( \text{R}3\text{2} \). This layer can also be considered as a fused honeycomb bilayer but in a staggered mode (Fig. 3a & 3b). Although the geometry restriction here is weaker than that in ZnCTV-1 structure due to the longer CTV arms, all CTV molecules in each layer still have the same chirality as those in ZnCTV-1. However, in stark contrast with ZnCTV-1, the ligands of adjacent layers in ZnCTV-2 have the same chirality and the whole structure is in a chiral space group (Fig. 3c). Note that due to the racemic nature of the reactant, the whole batch of materials are considered as a mixture of homochiral left and right-handed crystals.

**Weak interactions in ZnCTV-2.** To understand the formation of homochiral ZnCTV-2, the interaction between the honeycomb bilayers were examined carefully. There are two types of bilayer interfaces. At \( z = 0 \), two CTV molecules are symmetry related by the 2-fold rotation, and their two pairs of phenyl groups have a plane distance about 3.4 \( \text{Å} \), showing typical \( \pi-\pi \) interactions in a parallel-displaced mode (Fig. 4a & Supplementary Fig. S3). At \( z = 0.5 \), two CTV molecules are also symmetry related by the 2-fold rotation, while the two pairs of phenyl groups have a typical \( \pi-\pi \) interaction in a T-shaped mode\(^{48} \) with a C-Centroid distance of about 3.9A (Supplementary Fig. S3). Thus, in both cases, the interactions are
about twice as strong as those in ZnCTV-1 (only one pair of π–π interaction). This may explain why the ZnCTV-2 crystals are much thicker than ZnCTV-1 along the c-axis. Moreover, as we expected, the stronger interaction between the bilayers in ZnCTV-2 may increase the chiral recognition and result in a spontaneous self-organization of chiral functional materials. According to TGA, the weight loss of 44% below 270°C corresponds to the release of 13 DEF molecules together with three water molecules and the framework is stable up to 410°C. The PXRD pattern of the desolvated sample reveals that, upon guests exchange and evacuation, the desolvated materials have much lower crystallinity and its structure cannot be obtained (Supplementary Fig. S10 & S12). N$_2$ gas adsorption isotherms of desolvated ZnCTV-2 at 77K shows a reversible type I behaviour without hysteresis upon desorption, indicating an open framework with accessible microporosity (Supplementary Fig. S13–S16).

Discussion

CTV analogues are a type of macrocyclic molecule with convergent binding modes, which can be easily functionalized to construct amazing structures. By using reticular chemistry, we prepared two novel crystalline MOFs with chiral cavities based on C$_3$-symmetric macrocyclic CTV ligands and the octahedral Zn$_4$(CO$_2$)$_6$ clusters. We showed our strategy to understand and to construct homochiral MOFs from racemic C$_3$-symmetrical linkers. In the layer, the rigid Zn$_4$(CO$_2$)$_6$ cluster guides the selection of enantiomers through strong coordination bonds, while between layers, the relatively weak π–π interaction plays a great role in directing the formation of chiral MOFs. This approach contributes a new guidance in the construction of chiral functional materials.

Methods

Materials. All reagents and solvents used in synthetic studies were commercially available and used as supplied without further purification unless stated otherwise. Ligand H$_3$L$_1$ and H$_3$L$_2$ were synthesized according to the method as shown in Supplementary or according to the literature procedure 32,44.

Synthesis of ZnCTV-1. A mixture of H$_2$L$_1$ (9 mg, 0.018 mmol), and Zn(NO$_3$)$_2$·6H$_2$O (19 mg, 0.064 mmol) was dissolved in a 20 mL Teflon vial containing 1 mL DMF, 1 mL ethanol, and 0.5 mL H$_2$O. The vial was sealed and heated at 95°C for 48 h. The resulting colorless hexagonal plate crystals were collected and washed with DMF and ethanol, dried in air overnight (10 mg, 77%). Elemental analysis (%): calcld. for [Zn$_4$(OH)$_2$]$_2$·DMF·4EtOH·H$_2$O (C$_{120}$H$_{132}$N$_{24}$O$_{72}$Zn$_4$): C, 50.84; H, 4.12; N, 1.10; found: C, 50.84; H, 4.14; N, 1.06.

Synthesis of ZnCTV-2. A mixture of H$_2$L$_2$ (10 mg, 0.014 mmol), and ZnCl$_2$ (115 mg, 0.84 mmol) was dissolved in a 20 mL Teflon vial containing 1 mL DEF, 1 mL ethanol, and 0.2 mL H$_2$O. The vial was sealed and heated at 105°C for 48 h. The resulting small colorless octahedron like crystals were collected, washed with DEF dried in air overnight (18 mg, 86%). Elemental analysis (%): calcld. for [Zn$_2$(OH)$_2$]$_2$·13DEF·3H$_2$O (C$_{353}$H$_{372}$N$_{18}$O$_{117}$Zn$_2$): C, 40.40; H, 7.03; N, 5.91; found: C, 40.16; H, 6.48; N, 6.08.

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Author contributions

J.-T.Y., J.S., Z.-T.H. and Q.-Y.Z. designed the study, analyzed the data and wrote the 

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