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COMMUNICATION TYPE

Chirality from substitution: enantiomer separation via a modified metal-organic framework

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A microporous MOF structure, D-his-ZIF-8, with chiral environment was synthesized via a simple ligand in-situ substitution (LIS) of 2-methyl imidazolate (mIm) with D-histidine. These chiral MOF composites show exceptional selective separation capability for the racemic alanine and glutamic acid with an ee value of 78.52% and 79.44%, respectively.

Metal-organic frameworks (MOFs) are a class of crystalline polymeric materials consisting of metal ions or metal clusters covalently jointed by organic links.[1] Apart from their potential applications in various areas,[2] MOFs are ideally suited to serve as adsorbents and separators, by virtue of their structural diversity, well-defined open channels, molecule-sized cavities, impressive internal surface area, and ease of modification.[3] As chiral molecules play an indispensable role in biological functions, pharmaceutical industries, agrochemical industries, and material sciences,[4] there is a growing demand for separating enantiomerically pure compounds from their racemates.[5] MOFs have been established as one of the most promising hosts for enantioselective adsorption and separation of racemic mixtures through the imbedded chiral functionalities.[6]

Distinct strategies have been applied for the construction of MOFs with homochirality for chiral resolution. In the first approach, chiral open frameworks are built from totally achiral components via self-resolution process.[7] Despite the simplicity of this approach, racemic conglomerates are always obtained even if each individual crystal is chirally pure itself, which remains of less practical use in an enantioselective process. In the second and most reliable approach, homochiral porous frameworks are constructed by using enantiopure molecules as primary linkers or auxiliary ligands.[8] This method suffers from tedious synthesis and high costs for obtaining enantiopure ligands. The third approach is based on the utilization of chiral solvent or chiral additives for directing the formation of bulk homochiralMOFs.[9] Although several illuminating works have been reported, this approach lacks universality for a given set of precursors. In addition, post synthetic modification strategy offers another powerful means to prepare chiral MOFs.[10] In spite of that the aforesaid pioneering methodologies have shed light on chiral resolution, it is still a long pursuit to develop facile protocol to afford MOFs with absolute chirality.

Zeolitic imidazolate frameworks (ZIFs) are a sub-class of MOFs that usually encompass large cavities interconnected by narrow windows. ZIF-8, as one of the representative ZIF materials, is composed of Zn ions interconnected with 2-methylimidazole (HMeIM), forming a fully symmetrical sodalite (SOD) zeolite-like structure.[11] Herein, we report a facile yet simple and economically feasible strategy to impart ZIF-8 with absolute bulk chirality through a one-pot approach by ligand in-situ substitution (LIS) with D-histidine (Fig. 1). Thus-obtained porous crystalline material (denoted as D-his-ZIF-8) adopts the ZIF-8-like SOD topology and is imbedded with chiral functionalities. The water stability and inherent chirality of D-his-ZIF-8 enables it efficiently and enantioselectively separate racemic alanine and glutamic acid from water/EtOH solution with high enantiomeric excess (ee) value (78.52% for alanine, 79.44% for glutamic acid). Furthermore, the frameworks can be easily recovered and reused without losing chiral separation activity.

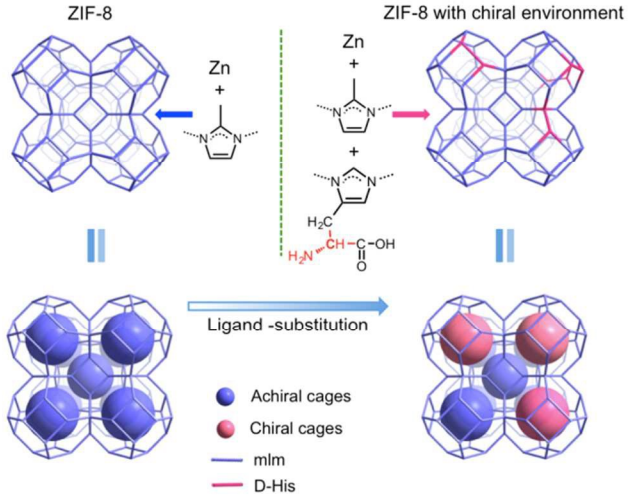

Fig. 1 The schematic representation of the synthetic route of D-his-ZIF-8.

As shown in Fig. 1, D-his-ZIF-8was synthesized via a simple LIS method. D-histidine was first dissolved in water (15 mL) followed by addition of methanol (MeOH, 85 mL) into the solution. Then, $Zn(NO_3)_2•4H_2O$ and 2-methylimidazole (HMeIM) was separately dissolved in the D-histidine MeOH/H_2O mixtures. Subsequently, the mixture of $Zn(NO_3)_2•4H_2O$and D-histidine was gradually added into the mixture of HMeIM and D-histidine. Upon stirring at room temperature for 24 h, the crude product was collected by centrifugation and extensively washed with large amounts of water and MeOH consecutively. The excessive D-histidine that was in between the particles and those

attached to the surface were thus removed and confirmed by UV-vis analysis of the washing residues. The powder X-ray diffraction (PXRD) patterns of D-his-ZIF-8 are in consistent with those of ZIF-8 with identical positions and relative intensities (Fig. 2a), which indicates ZIF-8-like architecture with SOD topology is formed in the network of D-his-ZIF-8.

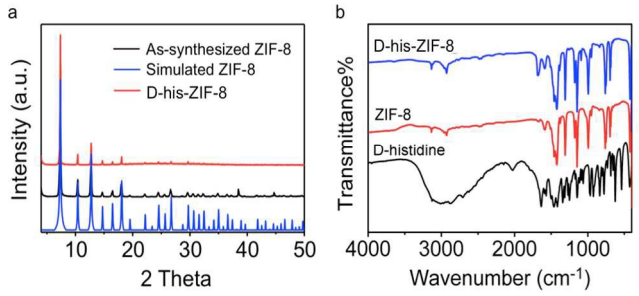

Fig. 2 a) PXRD patterns of simulated ZIF-8 (blue), as-synthesized ZIF-8 (black), D-his-ZIF-8 (red). b) FT-IR spectra of D-histidine (black), ZIF-8 (red), and D-his-ZIF-8 (blue).

There are five donor atoms in D-histidine: two nitrogen atoms in the imidazole ring, one N atom in amine group, and two O atoms in carboxylate group. These donor atoms are presumed to allow D-histidine to replace HMeIM in the skeleton via ligand substitution (Fig. S1).[12] We applied FT-IR spectroscopy, X-ray photoelectron spectroscopy (XPS), UV-vis spectroscopy, elemental analysis, and N_2 sorption isotherm measurement to verify this hypothesis.

UV-vis spectroscopy (Fig. S2) confirmed that there were no D-histidine molecules leaching out from the D-his-ZIF-8, even if the samples were soaked in water overnight and treated with ultrasonic for several times. In addition, we prepared Zn ion and D-histidine complex (denoted as Zn-D-his) and physical mixture of ZIF-8 and D-histidine (denoted as ZIF-8+D-histidine) as control experiments. In the FT-IR spectrum of histidine, the broad absorption between 3300 and 2200 cm^{-1} is assigned to the N-H groups and O-H stretching vibrations together with C-H stretching bonds, and the absorption at 2000 cm^{-1} is ascribed to the inner-salt vibrations. These absorption peaks, except for the one in C-H stretching bonds, disappear in the FT-IR spectra of D-his-ZIF-8 and Zn-D-his (Fig. 2 and Fig. S3). Meanwhile, the absorption peak at 1640 cm^{-1} attributed to C=O vibration for D-histidine shifts to 1680 cm^{-1} for D-his-ZIF-8 (Fig. S3b), and the peak at 925 cm^{-1} corresponding to N-H vibration vanishes for D-his-ZIF-8 and Zn-D-his (Fig. S3c). These results indicate the deprotonation of both imidazole groups and carboxyl groups in D-his-ZIF-8 and Zn-D-his.

To further examine whether the histidine is incorporated as part of the framework backbone or trapped in the pores, X-ray photoelectron spectroscopy (XPS) was employed. The deconvolution of N 1s spectrum of ZIF-8+histidine shows characteristic binding energies of imidazole =N- (399.3 eV), imidazole –NH- (400.4 eV), and -NH_2 (401.4 eV) groups (Fig. S4c). In contrast, the deconvolution of N 1s core-level spectrum of D-his-ZIF-8 results in two peaks: 399.7 and 401.3 eV, corresponding to coordinated imidazole =N- and amine moieties, respectively (Fig. S4a). Similar binding energies are found for Zn-D-his (Fig. S4b). Comparison of the O 1s core-level spectra of D-his-ZIF-8, Zn-D-his and ZIF-8+D-histidine (Fig. S5) reveals that the carboxyl groups in D-his-ZIF-8 and Zn-D-his partially participated in the formation of polymeric complexes. These results demonstrate that most of the donor atoms in D-histidine molecules are coordinately linked to Zn cations and tightly anchored to the framework (Fig. S1).

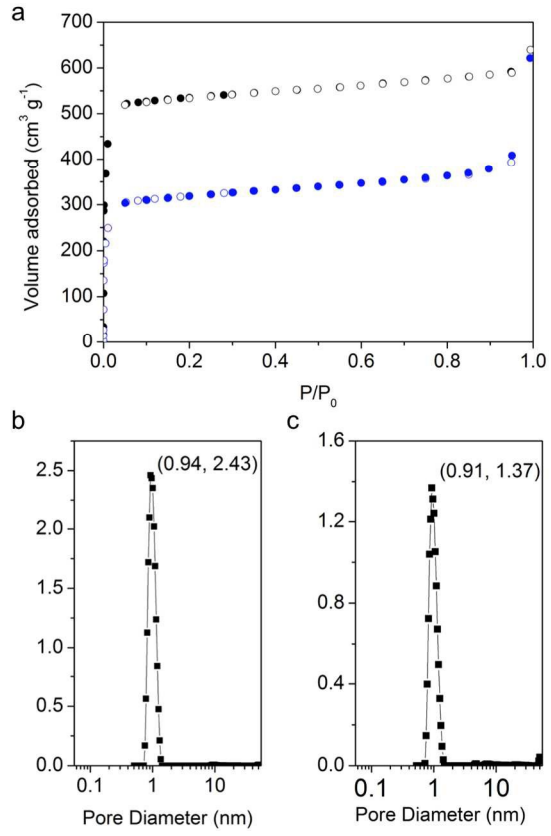

Fig. 3a) Nitrogen sorption isotherms of ZIF-8 (black) and D-his-ZIF-8 (blue) measured at 77 K. b) Pore size distribution profile of ZIF-8. c) Pore size distribution profile of D-his-ZIF-8.

On the basis of elemental analysis, the ratio of Zn, C, H, O, and N in the compound of D-his-ZIF-8 is calculated to be 6:54:69:2:27 (Table S1). The accessibility of the pore entrance has been studied by N_2 adsorption at 77 K. D-his-ZIF-8 shows typical type I adsorption isotherm (Fig. 3a), thus revealing microporous structure for this porous framework. Evaluation of pore size with a nonlocal density-functional theory (NLDFT) model indicates a narrow pore width distribution around 0.91 nm (Fig. 3b, 3c), the value of which is slightly smaller than that of ZIF-8 (0.94 nm). Analysis of the adsorption curve of D-his-ZIF-8 by Brunauer-Emmett-Teller (BET) method gives specific surface area of 1180.3 m^2 g^{-1}, whereas the BET surface area of ZIF-8 prepared under similar conditions is 2226.6 m^2 g^{-1} (Fig. 3a). Obviously, the BET surface area of D-his-ZIF-8 decreased significantly with the D-histidine loading. If we simply assume that D-histidine is physically mixed with the ZIF-8 particles, the surface area is calculated to be 1998.5 m^2 g^{-1} based on the mass factors contributed by each component (ZIF-8 and D-histidine). This result is far off the experimental data. Taken together with the former discussion about FT-IR, UV and XPS results, we can conclude that D-histidine and imidazole moieties are most likely

randomly distributed in the extended polymeric framework backbones of D-his-ZIF-8. The decreasing of the surface area is resulting from the relatively bulky groups in D-histidine moieties that partially block the pores.

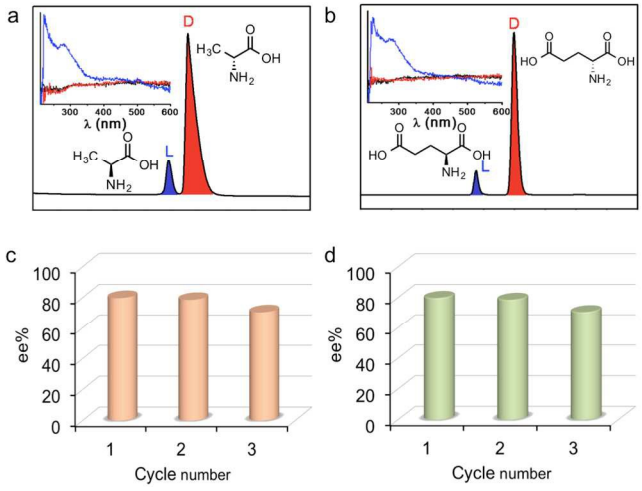

Fig. 4 Chromatogram of alanine a) and glutamic acid b) enantiomers using D-his-ZIF-8 as chiral resolving agent. Inset: CD spectra of leach liquor after soaking with ZIF-8 and D-his-ZIF-8 ((±)-alanine solution (black); solution after soaking with ZIF-8 (red); (±)-glutamic acid solution after soaking with D-his-ZIF-8 (blue)). ee% of alanine c) and glutamic acid d) in recycle experiments.

Circular dichroism (CD) spectrum of D-his-ZIF-8 suspensions in ethanol shows a positive dichroic signal at ca. 235 nm (Fig. S7), demonstrating that bulk D-his-ZIF material is endowed with absolute chirality. Two racemic amino acids, (±)-alanine and (±)-glutamic acid, were used to evaluate the chiral resolution property of D-his-ZIF-8. D-his-ZIF-8 was added into the racemic amino acid solution (H_2O:EtOH = 1:3) and stirred for 30 min. The mixture was left to stand at room temperature for 24 h, and then the solution was collected from the mixture through centrifugation and filtration. The positive dichroic signals in the CD spectra of the resulting solutions (Fig. 4a and 4b, insets, blue curves) indicate that D-alanine and D-glutamic acid are remained in the solutions, while S-alanine and S-glutamic acid are stuck in the pores of D-his-ZIF-8 during the separation. In contrast, ZIF-8 cannot separate these racemic amino acids (Fig. 4a and 4b, insets, red curves). Determined by chiral chromatographic column (Fig. 4a and 4b), the ee values for the solutions of (±)-alanine and (±)-glutamic acid after enantioselective separation by D-his-ZIF-8 are 78.52% and 79.44%, respectively. The higher residue amount of D-amino acids after separation is contributed to the geometry-dependent H-bonding interactions between the optical isomer guests and the chiral channels (Fig. 5). It is easier for S-amino acids to enter the pores and then trapped in them. Furthermore, the D-his-ZIF-8 material can be recovered after separation through centrifugation and reactivated by ultrasonic washing with H_2O five times. Then the reactivated sample was further reused directly in the next round of chiral separation. The enantioselective separation activity did not decrease obviously after three cycles (Fig. S8-S9).

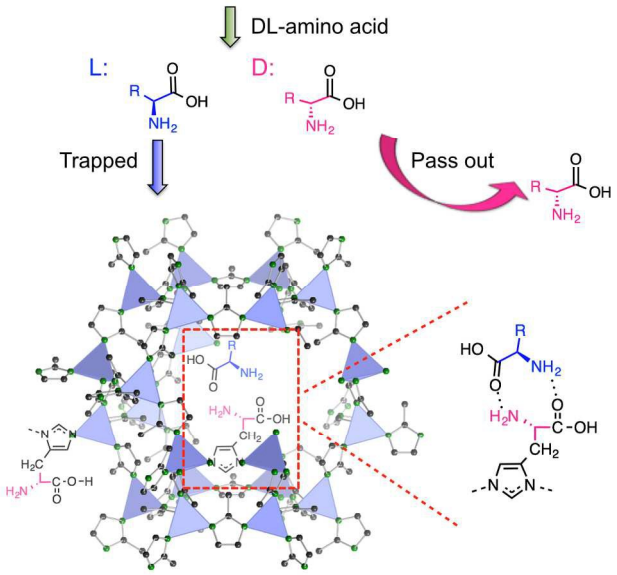

Fig. 5 The schematic representation of the enantioselective separation process by D-his-ZIF-8.

In summary, we have described a one-pot approach to the synthesis of a metal-organic framework, D-his-ZIF-8, with bulk chirality from readily available compounds. This crystalline material exhibits permanent porosity with narrow pore size distribution, excellent stability against water and organic solvents, enantioselective guest-sorption properties with high enantiomeric excess, and good reusability without losing its structural integrity and enantioselective separation activity. In principle, the present method takes advantages of applicable to other MOFs with particular composition or structure type. This LIS strategy can impart many achiral MOF structures with chiral properties and may expand enantiomer separation into unexplored microporous solid. Moreover, it may open great perspectives in terms of rendering MOFs with new functionalities.

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Notes and references

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† Electronic Supplementary Information (ESI) available: materials and instruments, synthetic methods, and experimentprocedures are included in the supporting information. See DOI: 10.1039/b000000x/

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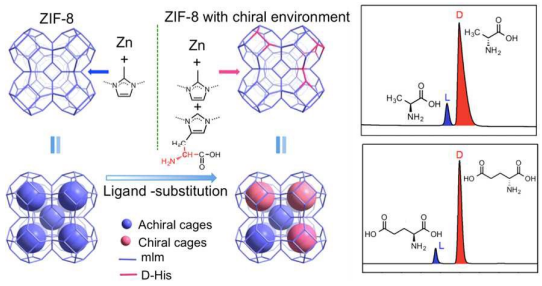

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