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Defect-Engineered Chiral Metal–Organic Frameworks for Efficient Asymmetric Aldol Reaction

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ABSTRACT: By employment of a mixed truncated chiral ligand synthetic strategy, a defect-engineered chiral metal–organic framework with hierarchical micro/mesoporous structure was prepared, and it exhibited efficient heterogeneous catalytic activity and enantioselectivity for asymmetric aldol reaction.

hirality is an important property of nature that is increasingly considered to be significant in numerous fields especially for asymmetric catalysis. Chiral metal-organic frameworks (CMOFs), constructed by metal nodes or metal clusters with organic ligands featured in chiral groups, offer great potential in heterogeneous asymmetric catalysis because of their periodic porous structure, high surface area, and adjustable chiral functionality.¹⁻⁴ Many CMOFs have been prepared directly or indirectly by introducing chiral functional groups into the frameworks.⁵⁻¹⁰ However, most of reported CMOFs to date are microporous structures with pore sizes below 2 nm, which not only hinder the fast diffusion and mass transfer of reactants or products but also inhibit the stereogenic effect for chiral catalysis.¹¹⁻¹⁶ Recently, a few CMOFs based on mesoporous MOFs such as UiO-67, UiO-68, and MIL-101 have been reported.¹⁷⁻²⁰ However, the introduction of chirality to those parent mesoporous MOFs usually adopts the methods of chiral preliminary treatment of the ligands or postsynthetic modification of MOFs. The chiral active molecule suffered from such covalent or coordinated modification would not only block the pores of MOFs but also reduce their chiral degree of freedom.

The defect engineering theory of MOFs might provide a new avenue for the rational synthesis of CMOFs with larger cavities. By the incorporation of missing linker and missing node defects into MOFs, some bigger cavities can be generated in the defect sites without losing long-range-order MOFs, producing a larger catalytic space. In fact, a homochiral zinc-containing MOF, MOF-5@imidazolium iodide, has been achieved via the defect engineering synthetic strategy. However, the defect engineering approach they adopted to obtain the CMOF is to in situ replace the terephthalic acid linker and coordinated N.N-dimethylformamide (DMF) by chiral-functionalized imidazolecarboxylic acid. The chiral groups block the windows of the cavities, and the detachment of coordinated DMF leads the partial collapse of the framework, resulting in a dramatic decrease in the Brunauer-Emmett-Teller (BET) surface area from 4000 $m^2 \cdot g^{-1}$ of the parent MOF-5 to 280 m²·g⁻¹. Therefore, MOF-5@imidazolium iodide shows no enantioselectivity for asymmetric catalytic reaction.

Herein, we developed a simple and effective method: a mixed truncated chiral ligand synthetic strategy to construct defective

CMOFs (DCMOFs) with a hierarchical micro/mesoporous structure.²¹ As shown in Scheme 1, the construction building





unit of C3-symmetric ligands for parent MOFs is partially replaced by a truncated ligand-functionalized chiral active group. The truncated ligand would generate a linker defect and produce mesopores, leading to the formation of defective structures of the MOFs. Thus, the larger pore volume could maintain the stereogenic configuration freedom of the larger chiral active molecules, which is conducive to free chiral transfer from chiral catalysts to reactants. More importantly, the secondary building units of the DCMOFs are the same as those of the parent MOFs with high hydrothermal stability to ensure that they carry out asymmetric catalytic reactions under harsh conditions. Inspired by these considerations, CuBTC, a well-known Cu-MOF that is constructed from a copper(II) paddlewheel cluster and a 1,3,5benzenetricarboxylate (BTC) ligand and has been extensively studied because of its facile synthesis and potential commercialization, was chosen as the parent MOF.^{22,23} By the mixing of chiral (S)-5-[1-(tert-butoxycarbonyl)pyrrolidine-2-

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carboxamido]isophthalic acid (IPA-L-Pro-BOC) and BTC ligands with different ratios into the synthetic system, a series of defective chiral CuBTC compounds (denoted as DC-CuBTC) were prepared and exhibited efficient asymmetric catalytic activities and good recyclability for aldol reactions at room temperature.

The as-synthesized DC-CuBTC-decorated proline chiral active group showed green-blue polygonal microcrystals. As can be seen from Figure 1a, DC-CuBTC-0.17 and DC-CuBTC-



Figure 1. (a) PXRD patterns of the simulated CuBTC and assynthesized DC-CuBTC samples. (b) ¹H NMR spectra of the mixed ligand DC-CuBTC samples digested in deuterium chloride/dimethyl sulfoxide- d_6 . Blue triangles and black circles stand for the characterization peaks of the BTC and IPA-L-Pro ligands, respectively. (c) N₂ sorption isotherms of CuBTC and DC-CuBTC. (d) Pore-size distribution data of CuBTC and DC-CuBTC calculated using the DFT method.

0.27 exhibit powder X-ray diffraction (PXRD) patterns identical with that of simulated CuBTC, but the diffraction peak of DC-CuBTC-0.6 at 5.8° attributed to the 111 crystal plane is very weak. We presume that axial growth of the crystal along the 111 plane changed with an increase of the chiral ligands, which is also evidenced by the slightly distorted octahedron and rough surface of crystal morphology (Figure S5c). However, the other characteristic diffraction peaks of DC-CuBTC-0.6 are consistent with the simulated one, indicating that all DC-CuBTC compounds have a framework connection similar to that of the parent CuBTC. This could be attributed to the geometry similarity between IPA-L-Pro and BTC, resulting in maintenance of the overall CuBTC framework topology even after incorporation of the IPA-L-Pro moieties. It is noteworthy that the BOC group is necessary to protect the chiral proline unit of the IPA-L-Pro-BOC ligand, which prevents its protonation or coordination to copper(II) under the condition of synthesis of DC-CuBTC.¹⁸ Deprotection of the proline ligand can be triggered by heating at 100 °C to generate the final DC-CuBTC product.^{24,25} The successful incorporation of IPA-L-Pro into DC-CuBTC was further confirmed by the ¹H NMR spectra of the digested MOFs (Figures 1b and S1 and S2). The incorporated amount of IPA-L-Pro can be adjusted by applying different feed molar ratios of IPA-L-Pro to BTC. According to integration of the assigned peaks, the incorporated ratios are

0.17, 0.27, and 0.6 for the feed ratios of 1, 2.5, and 4, respectively. Therefore, the resulting MOFs were named as DC-CuBTC-0.17, DC-CuBTC-0.27, and DC-CuBTC-0.6.

The N₂ adsorption experiment at 77 K shows that the porosity of DC-CuBTC depends on the functionalization degree (Figure 1c and Table S1). The parent Cu-BTC has a type I isotherm with a BET specific surface area of 1470 $m^2 \cdot g^{-1}$, indicating its microporous structure. Additionally, with an increase of the molar ratio of IPA-L-Pro/BTC from 0.17 to 0.6, the BET surface areas of the DC-CuBTC samples gradually decrease from 1274 to 863 m²·g⁻¹. In particular, the N₂ sorption data of DC-CuBTC-0.6 apparently displayed a type IV isotherm at relative P/P_{0} , indicating that it has a mesoporous existence. As can be seen from the results of nonlocal density functional theory (DFT) calculation (Figure 1d), the pore-size distribution of CuBTC features two sizes of 8.6 Å (major) and 6.8 Å (minor), which match quite well with its crystal structure. In addition, the DC-CuBTC samples exhibit smaller micropore sizes, of ca. 5.6 Å (major) and ca. 8 Å (minor), than those of CuBTC possibly because of the introduction of chiral moieties into the frameworks. The DFT desorption models reveal that mesopores with pore sizes from 24 to 40 Å readily developed in the DC-CuBTC samples, confirming that their hierarchical porous structures contain both micropores and mesopores, which might enhance reactant diffusion and mass transport in asymmetric catalytic reactions. Moreover, through scanning electron microscopy (SEM; Figure S3), the modified DC-CuBTC sample morphology did not change significantly.

The optical activity of the as-synthesized MOFs was confirmed by solid-state circular dichroism (CD) spectroscopy equipped with an integrating sphere. As shown in Figure 2, there



Figure 2. Solid-state CD spectra of IPA-L-Pro, IPA-D-Pro, CuBTC, DC-CuBTC-0.6, and DC-CuBTC-D-0.6.

is no dichroism signal in the parent CuBTC because it does not have a chiral nature. However, the Cotton effect can be observed in the curve of DC-CuBTC-0.6, which is consistent with the signal of the powder sample of the IPA-L-Pro ligand. This demonstrated that IPA-L-Pro was successfully anchored on the wall of DC-CuBTC and intact during the whole mixed truncated chiral ligand synthetic procedure. In addition, DC-CuBTC-D-0.6, the counterpart of DC-CuBTC-0.6, presents nearly mirror images of DC-CuBTC-0.6, indicating the enantiomeric nature of the two materials. All of the above characterizations demonstrated the successful syntheses of DC-CuBTC, further pubs.acs.org/IC

proving the possibility of this mixed truncated chiral ligand synthetic strategy for the synthesis of DCMOFs.

The chiral property with microporous/mesoporous structure prompted us to explore DC-CuBTC utilization as a heterogeneous asymmetric catalyst for aldol reaction. As listed in Table 1,

Table 1. Catalyst Screening for the Asymmetric Aldol Reaction^a



^{*a*}The asymmetric aldol reaction was carried out with 4-nitrobenzaldehyde (0.66 mmol) and acetone (5 mL) as solvents, a catalyst (25 mol % chiral ligand), and trifluoroacetic acid (additive, $6 \,\mu$ L),²⁸ at 25 °C for 2 days. ^{*b*}Isolated yield of the purified material. ^{*c*}The enantiopurity was determined by high-performance liquid chromatography. ^{*d*}The catalyst was DC-CuBTC-0.6. ^{*e*}The products are in the S configuration.

the homogeneous catalyst IPA-L-Pro achieved 98.9% conversion with 51.1% enantiomeric excess (ee) of the R-configured enantiomer and IPA-D-Pro 96.7% conversion with 53.9% ee of the S-configured enantiomer. When using DC-CuBTC as the catalyst, as listed in entries 4-6, their conversion rate and ee values saw an increase with the addition of chiral ligands. Among them, DC-CuBTC-0.6 achieved the highest conversion of 66.5% and especially an ee of 56.5% similar to that of the primitive chiral ligand IPA-L-Pro. In addition, data analogous to those of the counterpart configuration appeared on its enantiomers (DC-CuBTC-D-0.6, entry 9). We summarized the performance of the reported proline-functionalized CMOFs with only microporous structure, such as MIL-53(Al), UiO-66, H-DÚT-5(Al), and MIL-101(Al).^{12,26,27} As listed in entries 10–13, although those microporous CMOFs exhibited acceptable conversion, their ee values were far below that of DC-CuBTC-0.6. It is noteworthy that the increase of the ee value seems to be determined by the pore size of the CMOF. For MIL-53, UiO-66, and DUT-5 with

small pore sizes (their maximum pore diameters are about 8.5, 10, and 11.1 Å, respectively), they only gave 2%, 5%, and 13% ee values, respectively. For a MIL-101 structure with a larger pore diameter of 34 Å, 95% conversion with 29% ee can be achieved. In our work, DC-CuBTC-0.6 has a mesopore with a diameter of about 40 Å and exhibits the highest ee value of 56.5%. This is distinct evidence that the pore size of the CMOF is conducive to the stereogenic effect of aldol reaction. The larger pore volume could maintain the stereogenic configuration freedom of the larger chiral active molecules, which is conducive to free chiral transfer from the chiral catalysts to the reactants.

In order to prove that no leaching occurs, the catalysts were separated by centrifugation and filtration. In the case of DC-CuBTC-0.6, the catalyst was filtered off after 24 h of reaction and the filtrate mixture was then stirred for a duration of up to 72 h. No significant progress was observed in the results, which proved the true heterogeneous nature of catalysis over the catalyst (Figure S3). The synthesized L-proline-functionalized MOFs were also tested for catalyst recycling over three runs. The results are illustrated in entries 7 and 8 in Table 1 and Figure S4. DC-CuBTC-0.6 shows constant conversion and ee values. Even after the third run, DC-CuBTC-0.6 converts 60.6% of 4nitrobenzaldehyde. The selectivity with respect to the addition product does not change within experimental error. PXRD and SEM (Figure S5) characterizations also demonstrated that the recovered catalyst maintained its crystallinity. Finally, the substrate scope of the direct asymmetric aldol reaction of various aldehydes with acetone was investigated, and the results are summarized in Table S2. It was found that the conversion decreased gradually with an increase of the aldehydes' size, indicating the molecular sieving capabilities of DC-CuBTC.

In conclusion, we have applied a mixed truncated chiral ligand synthetic strategy to construct defective chiral MOFs with mesopores of up to 40 Å. Compared to microporous CMOFs, DC-MOFs exhibited higher enantioselectivity for asymmetric reaction because the larger pore volume could maintain the steregenic configuration freedom of the chiral active molecules, which is conducive to free chiral transfer from the chiral catalysts to the reactants. These findings delineated an explicit blueprint to the synthesis and application of promising defect-engineered chiral MOFs and other porous materials.

ASSOCIATED CONTENT

③ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.inorgchem.1c00141.

Experimental details, structural description of DC-CuBTC, and additional tables and figures (PDF)

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Z.C. and X.Y. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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