Heterogeneous Asymmetric Catalysis

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Heterogeneous Asymmetric Catalysis with Homochiral Metal–Organic Frameworks: Network-Structure-Dependent Catalytic Activity**

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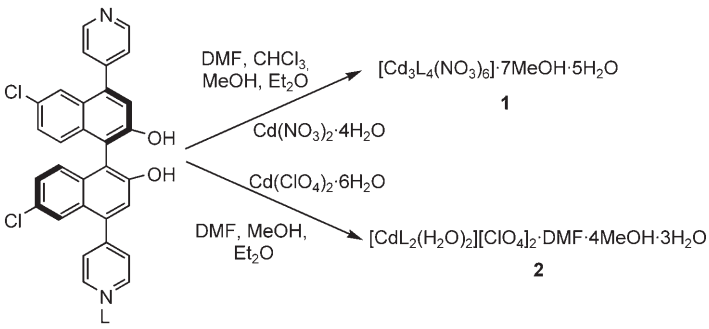
The prospect of generating functional solids by rational design has spurred a recent explosive growth of interest in research into metal–organic frameworks (MOFs).[1,2] A particular focus in this research area has been placed upon porous MOFs because of their intrinsic zeolite-mimicking, size- and shape-selective properties which make them potentially useful in a number of applications such as catalysis,[3] gas storage,[4] separation,[5] and ion-exchange processes.[6] By taking advantage of the mild conditions that are typically used for the synthesis of MOFs, we and others have successfully synthesized catalytically active homochiral porous MOFs by incorporating chiral constituent building blocks that contained orthogonal functionalities.[7] The single-crystalline nature of MOFs allows detailed structural interrogation, which makes it possible to examine the relationship between the structure and the catalytic activity of homochiral porous MOFs in great detail. A detailed understanding of the structure–activity relationship is key to further fine-tuning the catalytic performance of MOFs by judicious choice of building blocks. Herein we report two homochiral porous MOFs built from the same chiral bridging ligand and metal connecting point. Their drastically different catalytic activities are readily rationalized on the basis of their different framework structures.



Scheme 1. Synthesis of chiral MOFs **1** and **2**.

Colorless crystals of $[Cd_3L_4(NO_3)_6]\cdot 7MeOH\cdot 5H_2O$ (**1**) were synthesized by slow diffusion of diethyl ether into a mixture of $Cd(NO_3)_2\cdot 4H_2O$ and (*R*)-6,6′-dichloro-2,2′-dihydroxy-1,1′-binaphthyl-4,4′-bipyridine (L)[8] in DMF/$CHCl_3$/MeOH at RT (Scheme 1). Compound **1** crystallizes in the tetragonal $P4_122$ space group with 1.5 Cd^{II} centers in the asymmetric unit.[9] The first (half-occupied) Cd^{II} center is octahedrally coordinated to four L ligands (Cd–N = 2.310–2.317 Å) in the equatorial positions and to two nitrate oxygen atoms (Cd–O = 2.356 Å) in the axial positions, while the second Cd^{II} center is heptacoordinated to two bidentate nitrate groups (Cd–O = 2.317–2.552 Å), one nitrate oxygen atom (Cd–O = 2.299 Å), and two pyridyl groups (Cd–N = 2.286–2.330 Å) of two L ligands that are *cis* to each other. The L ligands thus link the first type of Cd^{II} centers into a 2D square grid of dimensions 20.305 × 20.305 $Å^2$ that is lying in the *ab* plane (Figure 1 A), and link the second type of Cd^{II} centers to form 1D zigzag polymeric chains that run along the 110 or 1–10 direction (Figure 1 B). The 2D grids and 1D zigzag polymeric chains are joined to each other by the bridging nitrate groups to form a 3D framework structure

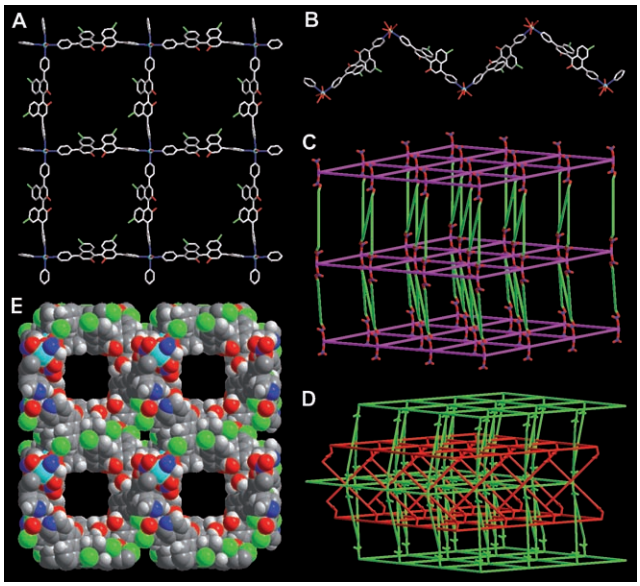


Figure 1. Crystal structure of **1**. A) The 2D square grid in **1**. B) The 1D zigzag polymeric chain in **1**. C) Schematic representation of the 3D framework of **1**. D) Schematic representation of the twofold interpenetration of **1**. E) Space-filling model of **1** as viewed down the *c* axis showing the chiral 1D channels of 13.5 × 13.5 $Å^2$ in dimensions. Color scheme for A), B), and E): cyan: Cd, green: Cl, red: O, blue: N, gray: C, and light gray: H.

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(Figure 1C). The 3D frameworks in **1** form twofold interpenetrated structures, presumably to avoid the formation of extraordinarily large open space (Figure 1D). The interpenetrated 3D networks are held together by strong π···π interactions between the pyridyl and adjacent naphthyl rings with shortest C···C distances of 3.399 Å. Even after twofold interpenetration, compound **1** still possesses very large interconnected channels that are occupied by the solvent molecules. The approximate dimensions of these channels are 4.9×13.1 Å^2 along the *a* and *b* axes and 13.5×13.5 Å^2 along the *c* axis.

Calculations performed using PLATON[10] showed that the effective volume for inclusion is about 10837.1 Å^3 per unit cell, which is about 53.0% of the crystal volume. Thermogravimetric analysis (TGA) of **1** showed a weight loss of 10.2% between 20 and 145 °C which corresponds to the loss of solvent molecules (calculated: 10.3%). The X-ray powder diffraction (XRPD) spectrum of a sample of **1** that had been ground and heated at 75 °C for 12 h under vacuum showed a sharp diffraction pattern similar to that of the pristine sample. This result indicated that the neutral chiral porous framework was maintained after removal of all the solvent molecules. CO_2 adsorption measurements showed that an evacuated sample of **1** possessed permanent porosity, with a Langmuir surface area of 772.3 m^{2}g^{-1} and a pore volume of 0.25 mL g^{-1}.[11]

Diffusion of diethyl ether into a mixture of $Cd(ClO_4)_2 \cdot 6H_2O$ and L in DMF and MeOH led to a 3D homochiral MOF with the formula $[CdL_2(H_2O)_2]$-$[ClO_4]_2 \cdot DMF \cdot 4MeOH \cdot 3H_2O$ (**2**; Scheme 1). Compound **2** crystallizes in the tetragonal $P4_32_12$ space group with each Cd^{II} center coordinating to four L pyridyl groups in the equatorial plane and two water ligands in the axial positions to form 2D rhombic grids lying along the (110) planes (Figure 2A). Interestingly, another set of crystallographically equivalent 2D rhombic grids lying along the (1−10) planes form a highly interpenetrated 3D network with the set of 2D grids lying along the (110) planes, presumably to avoid the formation of extremely large cavities (Figure 2B). Such a mode of interpenetration was previously observed in simpler iron–bipyridine MOFs.[12] A space-filling model shows that **2** possesses 1D channels with dimensions of approximately 1.2×1.5 nm^2, even after the interpenetration, which are filled by perchlorate anions and disordered DMF, MeOH, and H_2O solvent molecules (Figure 2C). PLATON calculations indicate that 59.4% of the crystal volume of **2** (6064.1 Å^3 out of 10211.2 Å^3) is accessible to solvents and anions. Thermogravimetric analysis showed a weight loss of 16.2% for **2** in the 20–125 °C range which corresponds to the loss of all the solvent molecules (calculated: 16.1%). CO_2 adsorption measurements indicated that an evacuated sample of **2** had a specific surface area of 370 m^{2}g^{-1} and a pore volume of 0.16 mL g^{-1}.

We have attempted to generate heterogeneous asymmetric catalysts by activating Lewis acidic metal centers (namely, $Ti(OiPr)_4$) with the chiral dihydroxy groups that are present as the orthogonal secondary functionalities in the porous solids **1** and **2**. It is well established in homogeneous systems that Ti^{IV}–binolate complexes are active catalysts for a range of organic transformations that are typically catalyzed by Lewis acids.[13] Treatment of **1** with excess $Ti(OiPr)_4$ in toluene indeed led to an active catalyst (**1**·Ti) for the addition of diethylzinc to aromatic aldehydes to afford chiral secondary alcohols upon hydrolytic workup. **1**·Ti generated chiral secondary alcohols in very high yields and enantioselectivities (Table 1). Specifically, **1**·Ti catalyzed the addition of diethylzinc to 1-naphthaldehyde to afford (*R*)-1-(1-naphthyl)-propanol with complete conversion and 90.0% *ee* (entry 1).

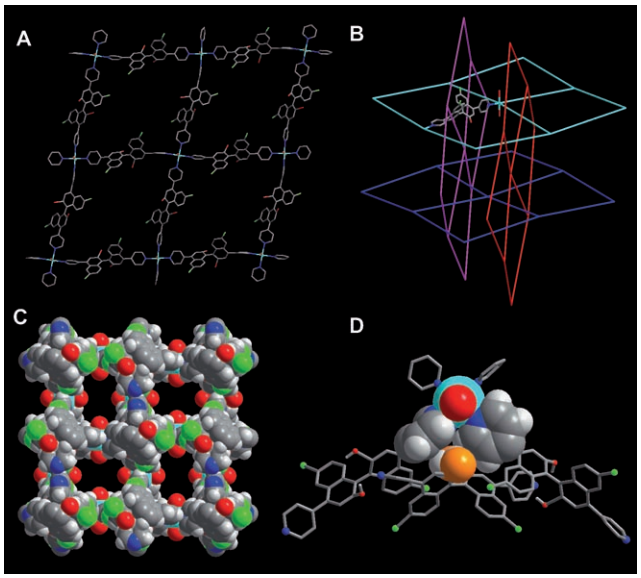
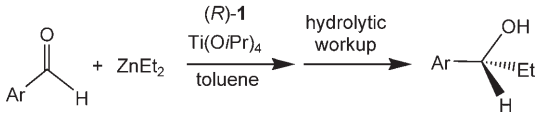


Figure 2. A) A view of the 2D rhombic grids of $[CdL_2(H_2O)_2]_n$ in the crystal structure of **2**. B) Schematic representation showing the interpenetration of mutually perpendicular 2D rhombic grids in **2**. C) Space-filling model showing the open channels running down the *c* axis. Rectangular channels with dimensions of approximately 1.2×1.5 nm run along the *c* axis. D) Schematic representation of the steric congestion around the chiral dihydroxy groups of L ligands (orange spheres) arising from the interpenetration of mutually perpendicular 2D rhombic grids through π···π stacking interactions. Color scheme in A), C), and D): cyan: Cd, green: Cl, red: O, blue: N, gray: C, and light gray: H.

Table 1: Addition of diethylzinc to aromatic aldehydes.[a]



Entry	Ar	Ligand	Loading [%]	Conv. [%]	*ee* [%]
1	1-naphthyl	**1**	12	>99	90.0
2	4-CH_3Ph	**1**	12	>99	84.2
3	4-CH_3Ph	**1**	25	>99	84.9
4	Ph	**1**	12	>99	81.9
5	Ph	L	20	>99	78.6
6	3-BrPh	**1**	12	>99	71.0
7	4-ClPh	**1**	12	>99	60.2
8	4-CF_3Ph	**1**	12	>99	45.0

[a] All reactions were conducted at room temperature for 15 h with **1** or L and excess amounts of $Ti(OiPr)_4$ in toluene. Conversion and *ee* values were determined by GC on a Supelco β-Dex 120 column for all of the secondary alcohols.

1·Ti also catalyzed the addition of diethylzinc to a range of other aromatic aldehydes with complete conversions and high *ee* values (entries 2–4 and 6–8). The conversions and *ee* values are only slightly affected by catalyst loadings (entries 2 and 3). No secondary alcohol product was obtained when 1-naphthaldehyde was treated with diethylzinc in the presence of the supernatant from a mixture of **1** and $Ti(OiPr)_4$ under otherwise identical conditions. This control experiment demonstrates the heterogeneous nature of the present catalyst system.

Interestingly, however, a mixture of **2** and $Ti(OiPr)_4$ under identical conditions did not catalyze the addition of diethylzinc to aromatic aldehydes, even though **2** possesses permanent porosity and chiral dihydroxy groups, just as in **1**. A closer examination of the structure of **2** reveals that the pyridyl and naphthyl rings from mutually perpendicular, interpenetrating 2D rhombic grids form strong π···π interactions, with a nearest C···C separation of 3.273 Å. As a result, all the chiral dihydroxy groups of the L ligands are held very close to the $\{Cd(py)_2(H_2O)_2\}$ hinges (Figure 2D). We believe that the lack of catalytic activity with the **2**/$Ti(OiPr)_4$ system is a result of the steric congestion around these chiral dihydroxy groups which prevents the substitution of two isopropoxide groups by the binolate functionality. We recently proved the inability of congested chiral dihydroxy groups to undergo substitution reactions with $Ti(OiPr)_4$ in a related homogeneous metallocyclophane system.[14]

The fact that complete conversions were observed for all of the small aromatic aldehydes used in the heterogeneous reactions demonstrates that **1**·Ti represents a unique highly enantioselective asymmetric catalyst derived from an interpenetrated homochiral MOF. However, the lack of catalytic activity with the **2**/$Ti(OiPr)_4$ system provides indirect proof for the heterogeneous nature of the **1**/$Ti(OiPr)_4$ system. The drastically different catalytic activities observed for the **1**/$Ti(OiPr)_4$ and **2**/$Ti(OiPr)_4$ systems is remarkable since **1** and **2** were built from exactly the same building blocks, and this finding highlights the important role of the framework structure in determining the catalytic performance.

In summary, we successfully synthesized a highly enantioselective asymmetric catalyst derived from an interpenetrated homochiral MOF. We have observed remarkable dependency of the catalytic activity on the framework structure for the heterogeneous asymmetric catalysts based on the two homochiral porous MOFs with the same building blocks.

Experimental Section

Synthesis of **1:** Slow diffusion of diethyl ether into a mixture of $Cd(NO_3)_2{\cdot}4H_2O$ (15.4 mg, 0.05 mmol) and L (25.5 mg, 0.05 mmol) in a mixed solvent of DMF (2 mL), $CHCl_3$ (3 mL), and MeOH (2 mL) afforded colorless crystals after one week. The crystals were filtered, washed with MeOH and then Et_2O, and dried at room temperature. Yield: 30 mg (79% based on L). Elemental analysis calcd for **1** (%): C 49.83, H 3.62, N 6.41; found: C 50.14, H 3.39, N 6.88. IR (KBr pellet): $\tilde{\nu}$ = 1663s, 1611s, 1544w, 1494w, 1425w, 1384m, 1290m, 1218w, 1180m, 1146w, 1090s, 1020w, 951m, 870w, 841m, 815 m, 772w, 655 m, 609w, 532w, 478w cm^{-1}.

Synthesis of **2**: Slow diffusion of diethyl ether into a mixture of $Cd(ClO_4)_2{\cdot}6H_2O$ (4.2 mg, 0.01 mmol) and L (5.1 mg, 0.01 mmol) in DMF (1 mL) and MeOH (3 mL) gave colorless crystals of **2** after one week. These crystals were filtered, washed with MeOH and then Et_2O, and dried at room temperature. Yield: 5 mg (67%). Elemental analysis calcd for **2** (%): C 50.76, H 4.13, N 4.42; found: C 49.21, H 4.63, N 3.91. IR (KBr pellet): $\tilde{\nu}$ = 1662s, 1609m, 1544w, 1494m, 1420w, 1383s, 1255w, 1220w, 1186w, 1101s, 951m, 870m, 843w, 772w, 655m, 623m, 533m, 460w cm^{-1}.

Asymmetric additions of diethylzinc to aromatic aldehydes using solid catalyst **1**·Ti: Solid **1** was placed in a 25-mL Schlenk flask and dried under vacuum at 70 °C for 4 h. Toluene (1 mL) was added by syringe, followed by $Ti(OiPr)_4$ (48 μL, 0.14 mmol) under argon. After the mixture had been stirred for 30 min, 1-naphthaldehyde (7 μL, 50 μmol) and diethylzinc (0.154 mmol) were added. This mixture was stirred under argon at RT for 15 h and then quenched with dilute hydrochloric acid. The organic phase was separated and passed through a short column of silica gel. An aliquot was analyzed by GC on a chiral stationary phase to give the conversion and *ee* values.

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[9] Crystal-structure determinations of **1** and **2** were performed on a Siemens SMART CCD. The data were collected using graphite-

monochromatic $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) at 173 K. The data sets were corrected by using the SADABS program.[15] The structures were solved by direct methods and refined by the full-matrix least-squares method with the SHELXTL-97 program package.[16] Crystallographic data for **1**: tetragonal, space group $P4_122$, $a = 20.305(1)$, $c = 49.641(4)$ Å, $V = 20466(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 0.993$ g cm^{-3}, $\mu(Mo_{K\alpha}) = 0.469$ mm^{-1}. Least-squares refinements based on 16912 reflections with $I > 2\sigma(I)$ and 866 parameters led to convergence, with a final $R1 = 0.0639$, $wR2 = 0.1798$, Flack parameter = 0.00(3), and GOF = 1.190. Crystallographic data for **2**: tetragonal, space group $P4_32_12$, $a = 17.962(1)$, $c = 31.649(1)$ Å, $V = 10211.2(6)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.031$ g cm^{-3}, $\mu(Mo_{K\alpha}) = 0.423$ mm^{-1}. Least-squares refinements based on 2254 reflections with $I > 2\sigma(I)$ and 201 parameters led to convergence, with a final $R1 = 0.1240$, $wR2 = 0.3090$, Flack parameter = 0.06(14), and GOF = 1.111. CCDC-609008 (**1**) and -261745 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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