

Molecular tectonics: gas adsorption and chiral uptake of (L)- and (D)- tryptophan by homochiral porous coordination polymers

Received 00th January 20xx,
Accepted 00th January 20xx

Donata Asnaghi,^a Romain Corso,^b Patrick Larpent,^b Irene Bassanetti,^a Abdelaziz Jouaiti,^{*b} Nathalie Kyritsakas,^b Angiolina Comotti,^{*a} Piero Sozzani^{*a} and Mir Wais Hosseini^{*b}

DOI: 10.1039/x0xx00000x

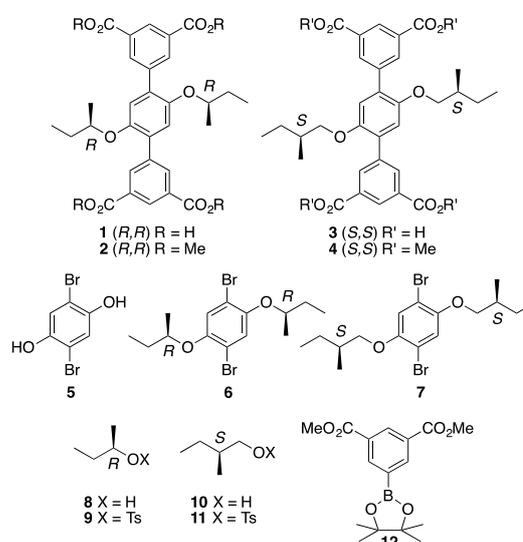
www.rsc.org/

Combinations of two enantiomerically pure organic tectons 1 and 3 with either Zn(II) or Cu(II) cations leads to the formation of four homochiral 3D networks among which two, 1-Cu and 3-Cu, are robust porous crystals displaying homochiral cavities and permanent microporosity. 3-Cu porous crystals capture 66% and 20% of L- and D-tryptophan, respectively, after 30 min adsorption.

Over the past two decades, Porous Crystalline Materials have attracted considerable attention owing to their applications in storage, separation, catalysis and drug delivery for example.^{1,2} Among these porous extended and periodic solid state architectures, coordination networks (PCPs), formed by self-assembly processes between organic tectons and metallic centres, are of particular interest.³ The design of porous systems with desirable functions and properties can be based on the molecular tectonics approach.^{4,5} Homochiral permanently porous crystalline materials represent an important sub-class of porous materials combining porosity and chirality. Examples of chiral extended architectures of the metal-organic frameworks (MOFs) or PCPs have been reported.⁶ Among the broad range of properties that PCPs can offer, chiral PCPs, offering tailored chiral pores and cavities, are of particular interest for enantiomeric separation.⁷ L-tryptophan is an essential α -amino acid, useful as precursor of important neurotransmitters such as serotonin and melatonin and thus the chiral separation of a racemic mixture by chromatography is a relevant issue especially for the industrial production.⁸

Herein, we report on the design and preparation of two homochiral PCPs 1-Cu and 3-Cu, their gas sorption properties and enantioselective adsorption of tryptophan in the solid state. Two isostructural compounds 1-Zn and 3-Zn were prepared for

comparison. The design of the 3D networks is based on the use of enantiomerically pure organic tectons 1 and 3 bearing two chiral side chains and four carboxylate coordinating groups (Scheme 1). Their combinations with Cu(II) lead to the formation of highly robust homochiral porous crystals displaying channels lined with homochiral alkyl moieties. Tectons 1 and 3 differ in both the connectivity of the alkyl fragment bearing the stereocenter (C*HMeEt for 1 and C*(CH₂)MeEt for 3) and their handedness, (*R,R*) enantiomer for 1 and (*S,S*) enantiomer for 3.



Scheme 1 Tectons 1 and 3 and synthetic intermediates

The common starting material for the synthesis of compounds 1 and 3 was the dibromo-dihydroxy-phenyl 5 (Scheme 1). The reaction of 5 with either the enantiomerically pure tosylate derivative 9 or 11 afforded the dibromo compounds 6 and 7, respectively. Compounds 9 and 11 were obtained upon tosylation of the enantiomerically pure commercially available alcohols 8 and 10. The coupling of the dibromo derivatives 6 and 7 with the boronic ester 12 afforded the tetraesters 2 and 4. Finally, the desired tectons 1 and 3 were

^a Department of Materials Science, University of Milano Bicocca, via R. Cozzi 55, Milan, Italy. E-mail: angiolina.comotti@unimib.it; piero.sozzani@mater.unimib.it

^b Molecular Tectonics Laboratory, UMR UDS-CNRS, 7140 & icFRC, University of Strasbourg, F-67000, Strasbourg, France. E-mail: hosseini@unistra.fr

* Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

obtained upon saponification of **2** and **4** (see ESI). As metallic centers Zn^{2+} and Cu^{2+} cations were chosen owing to their propensity to form paddlewheel-type nodes with carboxylate moieties.

The use of enantiomerically pure tectons for the preparation of chiral coordination networks has been employed by us⁹ and others.¹⁰

Under hydrothermal conditions, combinations of tectons **1** and **3** with $\text{Zn}(\text{NO}_3)_2$ in DMF at 100 °C afforded colourless single crystals of **1-Zn** and **3-Zn**, respectively (see ESI). Under similar conditions, combinations of **1** and **3** with $\text{Cu}(\text{NO}_3)_2$ in DMF at 85 °C and in the presence of HCl (1 drop, 3.7%) afforded, after 24h, blue microcrystalline powders of **1-Cu** and **3-Cu** (see ESI).

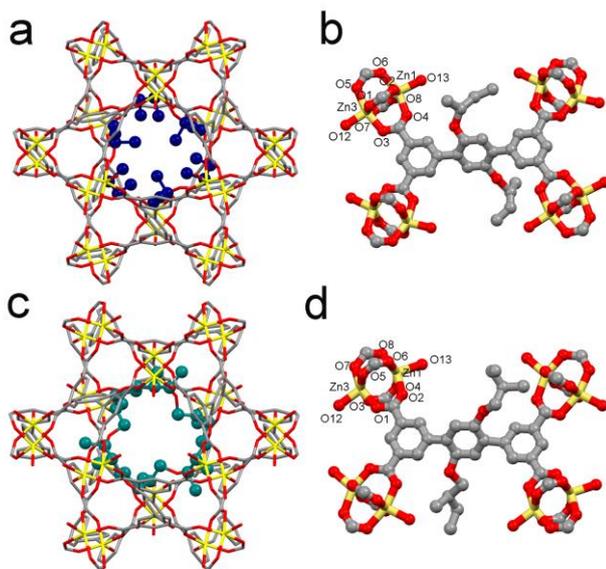


Fig. 1 Portions of the crystal structure of **1-Zn** (top) and **3-Zn** (bottom) showing the two types of channels along the *c* axis. The substituents bearing the stereogenic centres pointing towards the interior of channel are differentiated by color (blue for **1-Zn** and green for **3-Zn**). H-atoms and solvent molecules are omitted for clarity.

The solid state structures of **1-Zn** and **3-Zn** were elucidated by X-ray diffraction on single crystals (Figure 1). In both cases, crystals, in addition to **1** or **3** tectons and Zn^{2+} cation, contain solvent molecules. Solvent molecules were disordered and structures were refined using the squeeze command. Both coordination polymers crystallize in trigonal chiral space group $R\bar{3}$. In both cases, the tetranionic octadentate tectons act as connecting units, linking two distinct Zn(II) atoms through dimeric paddle wheel type motif with a Zn-Zn distance of *ca* 2.98 Å. The Zn(II) centers adopt a distorted square pyramidal geometry with average Zn-O (carboxylate) distances of 2.056 Å for **1-Zn** and 2.118 Å for **3-Zn**. The coordination sphere around each metal centre, composed of four O atoms belonging to carboxylate moieties, is completed with a water molecule. The 3D architectures form an interconnected network of cavities of two distinct sizes and shapes: a large ovaloid cavity (14 Å x 14 Å x 25 Å) and a smaller spherical cavity with 13 Å diameter. The free volumes explored by a sphere of 1 Å radius account for 53% (6280 Å³) and 52% (6148 Å³) of the unit cell volume for **1-Zn** and **3-Zn**, respectively. Interestingly, the larger ovaloid cavities are decorated with the chiral fragments pointing towards the centre of the cavity, thus modulating

the available empty space by the nature of the appended chiral fragments.

Unfortunately, no single-crystals suitable for XRD analysis could be obtained for the Cu-based architectures. However, comparisons (Figure 2) of Powder X-ray Diffraction (PXRD) patterns of polycrystalline powders of **1-Zn**, **3-Zn**, **1-Cu** and **3-Cu** with patterns simulated for **1-Zn** and **3-Zn** using the single crystal data (ESI Fig. S17 and S18), revealed a good match between them. Thus, it seems reasonable to assume that **1-Cu** and **3-Cu** 3D-networks are isostructural with **1-Zn** and **3-Zn**, respectively.

In order to establish the robustness of crystalline materials and their permanent porosity, they were activated by solvent exchange with methanol and dichloromethane, followed by heating at 120 °C under dynamic vacuum for 12h. Unfortunately, **1-Zn** and **3-Zn** crystals were found to be unstable in CH_2Cl_2 and thus it was not possible to perform solvent exchange to generate porous crystals. Interestingly, both **1-Cu** and **3-Cu** could be activated. This was established by PXRD which revealed minor changes of the unit cell parameters without loss of crystallinity (Figure 2). The thermal stability of the activated **1-Cu** and **3-Cu** crystals was studied by TGA which revealed that both materials were stable up to *ca* 300 °C (see ESI).

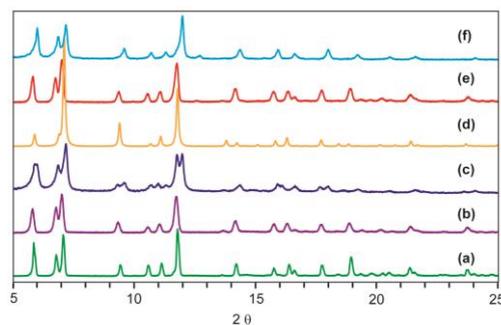


Fig. 2 XRPD patterns for **1-Zn** (a), **1-Cu** (b), activated **1-Cu** (c), **3-Zn** (d), **3-Cu** (e) and activated **3-Cu** (f).

The permanent porosity of the Cu-based PCPs was demonstrated by N_2 adsorption–desorption measurements performed at 77 K (Figure 3). The adsorption isotherms display a sharp uptake at low pressure and Type-I profiles, which are characteristic of microporous solids. The BET and Langmuir surface areas were determined to be 954 m²/g and 1198 m²/g for **3-Cu**, and 930 and 1102 m²/g for **1-Cu**. The porosity was confirmed by CO_2 adsorption isotherms at 195 K. Isotherms of both samples exhibited Langmuir profiles that reached plateau values of about 243 cm³(STP)/g at 1 bar. The measured CO_2 capacities correspond to an occupied volume of 0.62 cm³/g (CO_2 density (ρ) = 0.77 g cm⁻³ was used), which matches the pore volumes of 0.57 and 0.59 cm³/g for **3-Cu** and **1-Cu** respectively, as estimated by considering the crystal density and pore volume explored by a sphere having a radius of 1.2 Å. Collectively, these results indicate an almost complete filling of the empty spaces in the crystal structures and prove the easy accessibility of cavities to diffusing gases. Taking advantage of the microporous nature of **1-Cu** and **3-Cu** crystals, they have been tested for their storage capacities under mild conditions by collecting CO_2 and N_2 adsorption isotherms up to 10 bar and at

room temperature and at 273 K. Dealing with CO₂ capture, **1-Cu** shows Type-I isotherms and total absorbed amounts of 165 and 203 cm³(STP)/g, corresponding to 32% and 40% of the host weight at moderate pressure of 10 bar. Nitrogen adsorption experiments (Figure 3), revealed low uptake even at high pressure and the uptake was directly proportional to pressure in the covered range, indicating low nitrogen affinity. This observation may be exploited for selective separation of carbon dioxide in a mixture with nitrogen. Furthermore, the porous crystals were checked for methane storage. CH₄ isotherms exhibit Langmuir profiles reaching the value of 104 cm³(STP)/g at 273 K and 10 bar (extrapolated Q_{max}= 150 cm³(STP)/g. The isosteric heat of CO₂ adsorption, determined by applying the Van't Hoff equation, is 27 kJ/mol. This is in agreement with reported data for porous crystals and MOFs without open metal sites or specific interactions with pore's walls.^{2,14-16} However, the binding energy for CH₄ of 18 kJ/mol is rather high and may be accounted for by multiple van der Waals interactions between the hydrocarbon pendant groups and the gas.¹⁷ Similar values have been obtained for porous molecular crystals displaying pores lined with hydrocarbon moieties.¹⁸

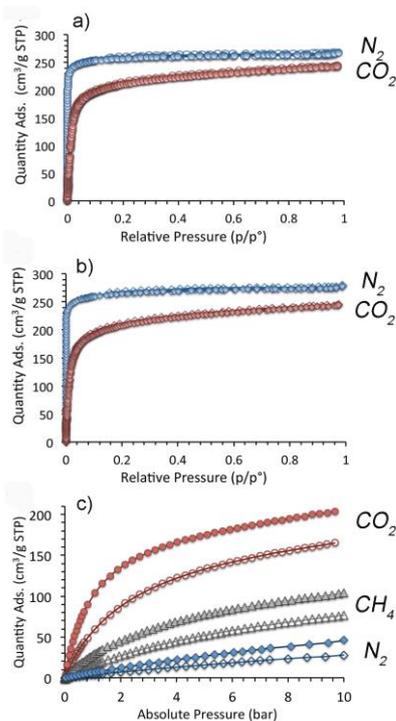


Fig. 3 CO₂ and N₂ adsorption isotherms at 195 K and 77 K for a) **3-Cu**, b) **1-Cu**, c) CO₂ (circles), CH₄ (triangles) and N₂ (diamonds) adsorption isotherms at 273 K (full symbols) and 298 K (empty symbols) for **1-Cu** compound.

The chiral and porous nature of **1-Cu** and **3-Cu** was exploited for chiral recognition and enantioselective adsorption.¹⁹⁻²² Based on the size of cavities and the nature of the chiral units pointing towards the interior of the empty chiral space, the adsorption of D- and L-tryptophan was investigated in water. Prior to adsorption studies, the stability and crystallinity of **1-Cu** and **3-Cu** in water at room temperature was investigated. After immersion in water for 24 h of the crystalline materials, the solvent was removed and the

microcrystalline powder was studied by PXRD which revealed the integrity of the both materials (See ESI Fig S25 and S26). For the uptake processes, enantiopure activated crystals of **1-Cu** or **3-Cu** were immersed in an aqueous solution containing pure L- or D-tryptophan and their absorption capacity was monitored by UV-Vis absorption spectroscopy by measuring the intensity of the band at 280 nm of tryptophan in solution as a function of time as reported in Figure 4 (see ESI for optical absorption measurement methods). From the concentration values, calculated by the calibration line, the enantioselective recognition was evaluated as a function of time (Figure 5). While enantioselective recognition was negligible in the case of **1-Cu**, **3-Cu** adsorbs preferably L-tryptophan: for instance after 30 mi. 66% of L- and 20% of D-tryptophan from solution were adsorbed with a ratio of 3.3. A higher ratio was obtained at shorter times and initial guest uptake. This is an indication that high enantioselectivity can be most favourably achieved far from the equilibrium conditions. The desorption process showed that, after 24 h, only 2.5-4.9% of guest is released from the adduct, indicating that strong host-guest interactions occur (Supporting Information). The higher stereoselectivity of **3-Cu** with respect to **1-Cu** can be explained by the longer pendants bearing the stereogenic carbons at their ends which protrude toward the center of the cavity and recognize more efficiently one of the enantiomers. However, the softness of the alkoxy chains does not allow high values of enantioselectivity.

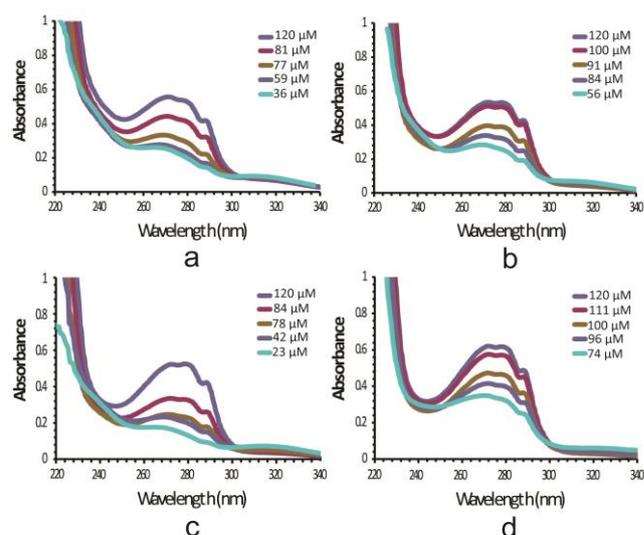


Fig. 4 UV-vis absorption spectra collected at different concentrations containing enantiopure D-tryptophan (a and c) and L-tryptophan (b and d) and **1-Cu** (a and b) and **3-Cu** (c and d), respectively.

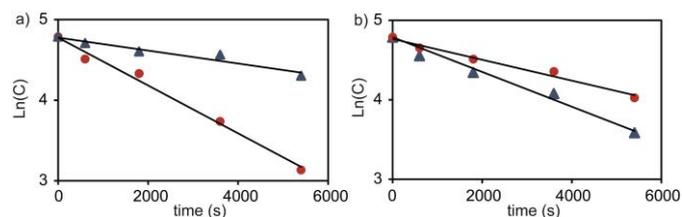


Fig. 5 Plot of guest concentration (C) versus time for a) **3-Cu** and b) **1-Cu** MOFs. L- and D-tryptophan are indicated as circles and triangles, respectively.

In conclusion, two new enantiomerically pure organic tectons **1** and **3** bearing four carboxylate moieties as coordinating sites and two chiral appended chains were designed and prepared. Their reaction, under hydrothermal conditions in DMF, with Zn(II) and Cu(II) cations as metallic nodes leads to the formation of enantiomerically pure porous crystals with their space occupied by the chiral chains. The crystalline materials are robust and exhibit permanent porosity and high thermal stability. In the case of **1**-Cu and **3**-Cu, crystals are stable in water and in organic solvents. The latter solid state architectures were shown to uptake guest molecules. The Copper based porous crystals capture N₂, CO₂ and CH₄ molecules. The sorption of CO₂ takes place at room temperature and under rather low pressure (10 bar). Interestingly, the porous crystals show high affinity for CO₂ with respect to N₂. Furthermore, **1**-Cu and **3**-Cu were shown to adsorb D- and L-tryptophan from water. Interestingly, **3**-Cu preferably adsorbed L-tryptophan: the amount of adsorbed L- versus D-tryptophan resulted in a ratio higher than 3.3 after 30 min. With the aim of exploring selective chiral uptake and separation of other chiral molecules such as alcohols by homochiral porous crystalline architectures, we currently investigate the synthesis of new enantiomerically pure tectons and their combinations with metal centers.

Notes and references

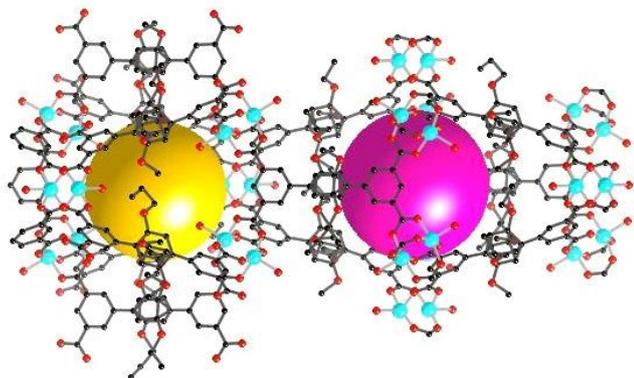
- We thank the Université de Strasbourg, the C.N.R.S, the International centre for Frontier Research in Chemistry (icFRC), the Labex CSC (ANR-10-LABX- 0026 CSC) within the Investissement d'Avenir program ANR-10-IDEX-0002-02, the Institut Universitaire de France, the Ministère de l'Enseignement Supérieur et de la Recherche for financial support. A. C. thanks PRIN n. 2016-CTEBBA, INSTM/Lombardy Region and Cariplo Foundation for financial support.
- (a) H.-C. Zhou and S. Kitagawa, *Chem. Soc. Rev.*, 2014, **43**, 5415; S. Lee, E. Kapustin, O. M. Yaghi, *Science*, 2016, **353**, 808; (b) J.-R. Li, J. Sculley and H.-C. Zhou, *Chem. Rev.*, 2012, **112**, 869; (c) G. Férey, *Chem. Soc. Rev.*, 2008, **37**, 191.
 - N. B. McKeown, *J. Mater. Chem.*, 2010, **20**, 10588; J. R. Holst, A. Trewin and A. I. Cooper, *Nature Chem.*, 2010, **2**, 915; P. Sozzani, S. Bracco, A. Comotti, L. Ferretti and R. Simonutti, *Angew. Chem. Int. Ed.*, 2005, **44**, 1816.
 - (a) B. F. Abrahams, B. F. Hoskins and R. Robson, *J. Am. Chem. Soc.*, 1991, **113**, 3606; (b) S. R. Batten and R. Robson, *Angew. Chem. Int. Ed.*, 1998, **37**, 1460.
 - (a) M. Simard, D. Su, J. D. Wuest, *J. Am. Chem. Soc.*, 1991, **113**, 4696; (b) S. Mann, *Nature*, 1993, **365**, 499; (c) M. W. Hosseini, *Acc. Chem. Res.* 2005, **38**, 313.
 - M. W. Hosseini, *CrystEngComm.*, 2004, **6**, 318.
 - (a) V.N. Yadav, A. Comotti, P. Sozzani, S. Bracco, T. Bonge-Hansen, M. Hennem and C.H. Gorbitz, *Angew. Chem. Int. Ed.*, 2015, **54**, 15684; (b) S.-Y. Zhang, L. Wojtas and M. J. Zaworotko, *J. Am. Chem. Soc.*, 2015, **137**, 12045; (c) A. Comotti, S. Bracco, G. Distefano and P. Sozzani, *Chem. Commun.*, 2009, 284; (d) A. Comotti, A. Fraccarollo, S. Bracco, M. Beretta, G. Distefano, M. Cossi, L. Marchese, C. Riccardi and P. Sozzani, *Cryst. Eng. Comm.*, 2013, **15**, 1503; (e) C. Zhou, Y. Wen and X. Wu, *Cryst. Eng. Commun.*, 2016, **18**, 2792; (f) D. N. Dybtsev, A. L. Nuzhdin, H. Chun, K. P. Bryalnikov, E. P. Talsi, V. P. Fedin and K. Kim, *Angew. Chem. Int. Ed.*, 2006, **45**, 916; (g) Z.-X. Xu, Y.-X. Tan, H.-R. Fu, Y. Kang and J. Zhang, *Chem. Commun.*, 2015, **51**, 2565; (h) Z.-X. Xu, Y.-L. Ma and J. Zhang, *Chem. Commun.*, 2016, **52**, 1923; (i) Z.-G. Gu, C. Zhan, J. Zhang and X. Bu, *Chem. Soc. Rev.*, 2016, **45**, 3122; (l) Z.-X. Xu, H.-R. Fu, X. Wu, Y. Kang and J. Zhang, *Chem. Eur. J.*, 2015, **21**, 10236.
 - (a) D. Bradshaw, T. J. Prior, E. J. Cussen, J. B. Claridge and M. J. Rosseinsky, *J. Am. Chem. Soc.*, 2004, **126**, 6106; (b) Y. Liu, W. Xuan and Y. Cui, *Adv. Mater.*, 2010, **22**, 4112; (c) Y. Peng, T. Gong, K. Zhang, X. Lin, Y. Liu, J. Jiang and Y. Cui, *Nature Commun.*, 2014, **5**, 4406.
 - (a) M. Dolowy and A. Pyka, *Biomed Chromatogr.*, 2014, **28**, 84; (b) W. Pen-Cheng, G. Jun and S.-L. Cheng, *J. Chromatogr. A*, 2002, **942** (1-2), 115.
 - (a) A. Jouaiti, M. W. Hosseini and N. Kyritsakas, *Chem. Commun.*, 2002, 1898; (b) P. Grosshans, A. Jouaiti, V. Bulach, J.-M. Planeix, M. W. Hosseini and J.-F. Nicoud, *Chem. Commun.*, 2003, 1336; (c) M.-J. Lin, A. Jouaiti, P. Grosshans, N. Kyritsakas and M. W. Hosseini, *Chem. Commun.*, 2011, **47**, 7635; (d) P. Larpent, A. Jouaiti, N. Kyritsakas and M. W. Hosseini, *Chem. Commun.*, 2013, **49**, 4468; (e) N. Marets, V. Bulach and M. W. Hosseini, *New J. Chem.*, 2013, **37**, 3549; (f) P. Larpent, A. Jouaiti, N. Kyritsakas and M. W. Hosseini, *Dalton Trans.*, 2014, **43**, 166; (g) C. Xu, A. Guenet, N. Kyritsakas, J.-M. Planeix and M. W. Hosseini, *Inorg. Chem.* 2015, **54**, 10429.
 - (a) X. Duan, Q. Zhang, J. Cai, Y. Cui, C. Wu, Y. Yang and G. Qian, *Micropor. Mesopor. Mater.*, 2014, **190**, 32; (b) S. Lee, E. A. Kapustin and O. M. Yaghi, *Science*, 2016, **353**, 6301; (c) K. J. Hartlieb, J. M. Holcroft, P. Z. Moghadam, N. A. Vermeulen, M. M. Algaradah, M. S. Nassar, Y. Y. Botros, R. Q. Snurr and J. F. Stoddart, *J. Am. Chem. Soc.*, 2016, **138**, 2292.
 - T. A. Makal, X. Wang and H.-C. Zhou, *Cryst. Growth Des.*, 2013, **16**, 4760.
 - Y. He, B. Li, M. O'Keeffe and B. Chen, *Chem. Soc. Rev.*, 2014, **43**, 5618.
 - (a) Z. Guo, H. Wu, G. Srinivas, Y. Zhou, S. Xiang, Z. Chen, Y. Yang, W. Zhou, M. O. Keffe and B. Chen, *Angew. Chem. Int. Ed.*, 2011, **50**, 3178; (b) D. Yuan, D. Zhao, D. Sun and H. C. Zhou, *Angew. Chem. Int. Ed.*, 2010, **49**, 5357.
 - (a) J. R. Li, R. J. Kuppler and H. C. Zhou, *Chem. Soc. Rev.*, 2009, **38**, 1477; (b) H. Zhang, P. Deria, O. K. Farha, J. T. Hupp and R. Q. Snurr, *Energy Environ. Sci.*, 2015, **8**, 1501.
 - (a) Y. Peng, V. Krungleviciute, I. Eryazici, J. T. Hupp, O. K. Farha and T. Yildirim, *J. Am. Chem. Soc.*, 2013, **135**, 11887; (b) H. C. Zhou, J. R. Long and O. M. Yaghi, *Chem. Rev.*, 2012, **112**, 673.
 - J. A. Mason, J. Oktawiec, M. K. Taylor, M. R. Hudson, J. Rodriguez, J. E. Bachman, M. I. Gonzales, A. Cervellino, A. Guagliardi, C. M. Brown, P. L. Llewellyn, N. Masciocchi and J. R. Long, *Nature*, 2015, **527**, 357.
 - S. Gao, C. J. Morris; Z. Lu, Y. Yan, H. G. W. Godfrey, C. Murray, C. C. Tang, K. M. Thomas, S. Yang and M. Schröder, *Chem. Mater.*, 2016, **28**, 2331.
 - L. Chen, P. S. Reiss, S. Y. Chong, D. Holden, K. E. Jelfs, T. Hasell, M. A. Little, A. Kewley, M. E. Briggs, A. Stephenson, K. M. Thomas, J. A. Armstrong, J. Bell, J. Busto, R. Noel, J. Liu, D. M. Strachan, P. K. Thallapally and A. I. Cooper, *Nature Mater.*, 2014, **13**, 954.
 - (a) J. S. Seo, D. Whang, H. Lee, S. I. Jun, J. Oh, Y. J. Jeon and K. Kim, *Nature*, 2000, **404**, 982; (b) Y. Peng, T. Gong, K. Zhang, X. Lin, Y. Liu, J. Jiang and Y. Cui, *Nat. Comm.*, 2014, **5**, 4406; (c) K. Tanaka, N. Hotta, S. Nagasea and K. Yoza, *New J. Chem.*, 2016, **40**, 4891.
 - J. Zhang, Z. Li, W. Gong, X. Han, Y. Liu, and Y. Cui, *Inorg. Chem.*, 2016, **55**, 7229.
 - (a) Z. G. Gu, S. Grosjean, S. Bräse, C. Wölla and L. Heinke, *Chem. Commun.*, 2015, **51**, 8998; (b) J. Zhao, H. Li, Y. Han, R. Li, X. Ding, X. Feng and B. Wang, *J. Mater. Chem. A*, 2015, **3**, 12145; (c) B. Liu, *J. Mater. Chem.*, 2012, **22**, 10094.

Journal Name

COMMUNICATION

22 P. E. Hare and E. Gil-Av, *Science*, 1979, **204**, 1226.

Graphical Abstract



Combination of an enantiomerically pure tecton with Cu(II) cation yields robust porous homochiral crystals displaying preferential adsorption of L-tryptophan.