Communication

Constructing Crystalline Covalent Organic Frameworks from Chiral Building Blocks

Hai-Sen Xu, San-Yuan Ding, Wan-Kai An, Han Wu, and Wei Wang

J. Am. Chem. Soc., **Just Accepted Manuscript** • Publication Date (Web): 01 Sep 2016

Constructing Crystalline Covalent Organic Frameworks from Chiral Building Blocks

Hai-Sen Xu,[†] San-Yuan Ding,*[,†] Wan-Kai An,[†] Han Wu,[†] and Wei Wang*[,†,‡]

[†]State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou, Gansu 730000, China

[‡]Collaborative Innovation Center of Chemical Science and Engineering, Tianjin 300071, China

Supporting Information Placeholder

ABSTRACT: Covalent organic frameworks (COFs) represent a new type of crystalline porous materials which are covalently assembled from organic building blocks. Construction of functional COFs is however a difficult task because it has to simultaneously meet the requirements for crystallinity and functionality. We report herein a facile strategy for the direct construction of chiral-functionalized COFs from chiral building blocks. The key design is to use the rigid scaffold 4,4'-(1*H*-benzo[*d*]imidazole-4,7-diyl)dianiline (**2**) for attaching a variety of chiral moieties. As a first example, the chiral pyrrolidine-embedded building block (*S*)-4,4'-(2-(pyrrolidin-2-yl)-1*H*-benzo[*d*]imidazole-4,7-diyl)dianiline (**3**) was accordingly synthesized and applied for the successful construction of two chiral COFs, **LZU-72** and **LZU-76**. Our experimental results further showed that these chiral COFs are structurally robust and highly active as heterogeneous organocatalysts.

Chiral compounds are of great importance in pharmaceutics, agriculture, and other chemical industries.[1] In recent years, chiral materials have attracted intensive research interest because they combine the advantages of chiral functionality and facile reusability.[2] Particularly, chiral porous materials have emerged as a new research area towards the promising applications in catalysis,[3] separation,[4] and recognition.[5] To date, most of the chiral porous materials are synthesized via post-modification of achiral porous supports with chiral moieties (Figure 1a).[6] This strategy, however, leads to uneven distribution and less loading of chiral functionalities.[7] In this context, the direct construction of porous materials from chiral building blocks represents an alternative but challenging approach (Figure 1b).[3b,8] In 2009, we initiated a project focusing on the "bottom-up" construction of porous organic materials.[9] Two chiral porous polymers (CPP), JH-CPP and TADDOL-CPP were accordingly synthesized from chiral building blocks.[10] Due to fast and irreversible formation of strong covalent bonds, these CPP materials were unfortunately amorphous in nature. Accordingly, the reproducibility of their synthesis and function was less controlled.[11] In this regard, crystalline porous materials with well-defined structures are highly desired for chiral applications. In this contribution, we achieved the direct construction of crystalline covalent organic frameworks from chiral building blocks.

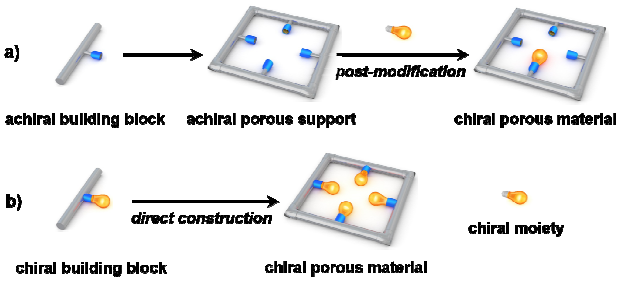


Figure 1. General strategies for constructing chiral porous materials: a) post-modification of achiral porous supports with chiral moieties, and, b) direct construction from chiral building blocks. The latter strategy intrinsically guarantees the homogeneous dispersion of chiral functionalities with the highest content.

Introduced by the seminal work of Yaghi,[12] covalent organic frameworks (COFs) represent an emerging class of crystalline porous materials which are covalently constructed from organic components.[13] In comparison with amorphous polymers, COFs possess well-defined crystalline structures with regular pore channels, which could potentially work as "organic zeolite".[14] However, functional COFs remain difficult to synthesize because crystallinity, porosity, and functionality have to be simultaneously taken into account. In this context, construction of chiral COFs is, if not possible, extremely challenging. The key bottleneck is the intrinsic mismatch between the symmetry for crystalline structure and asymmetry for chiral functionality. Very recently, Jiang pioneered the research by a successful post-modification (Figure 1a) of achiral COFs with chiral moieties.[3f,g] However, the direct construction of chiral COFs from chiral building blocks (Figure 1b) remains unexploited.

We tackled this challenge by the judicious design of chiral building blocks (Figure 2). Firstly, the linear-structured 4,4'-diamino-*p*-terphenyl (**1**) was chosen as the basic backbone because the rigid and symmetric terphenyl group is ideal for constructing COFs with large open channels.[15] Base on this backbone, the imidazole group[16] was incorporated into the middle phenyl ring to afford the scaffold 4,4'-(1*H*-benzo[*d*]imidazole-4,7-diyl)dianiline (**2**). Note that the scaffold **2** is very versatile for attaching a variety of functional moieties.[17] For example, the chiral pyrrolidine moiety could be further incorporated to afford the chiral building block (*S*)-4,4'-(2-(pyrrolidin-2-yl)-1*H*-benzo[*d*]imidazole-4,7-diyl)dianiline (**3**). It is worth to

mention that, **3** is very facile to synthesize with 99% enantiomeric excess (*ee*) from commercially available *N*-Boc-*L*-proline (see Supporting Information for details) and, it perfectly integrates the asymmetric chirality with the symmetric backbone.

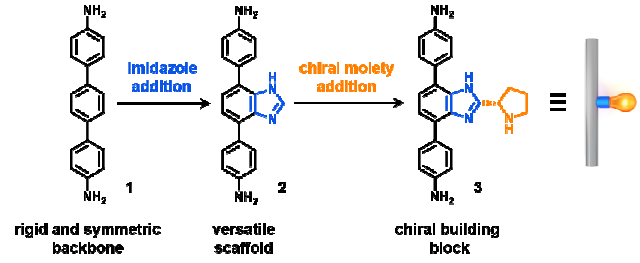


Figure 2. Our design for the chiral building block **3**, which integrates the rigid and symmetric backbone with the chiral-pyrrolidine moiety.

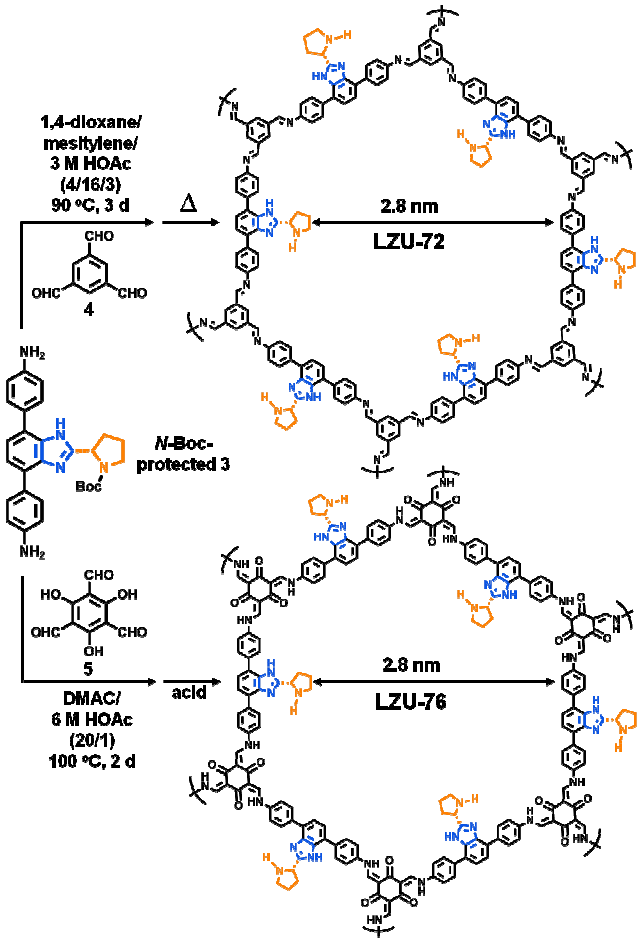


Figure 3. Schematic representation for the direct construction of chiral COFs, **LZU-72** and **LZU-76**.

As a primary test, we used the achiral diamine **2** and 1,3,5-triformylbenzene (**4**) to explore the possibility of synthesizing crystalline COFs. To our delight, a highly-crystalline COF, **LZU-70**, was successfully obtained with permanent porosity (see Supporting Information for details). It therefore encouraged us to construct chiral COFs directly from the chiral building block **3** under similar conditions. As shown in Figure 3, two chiral COFs, **LZU-72** and **LZU-76,** were eventually synthesized from the direct condensation of *N*-Boc-protected **3**[18] with **4** or triformylphloroglucinol (**5**), respectively (see Supporting Information for details). The synthetic condition is quite mild and the synthetic route is well reproducible. Therefore, these chiral crystalline COFs could be easily synthesized for chiral applications.

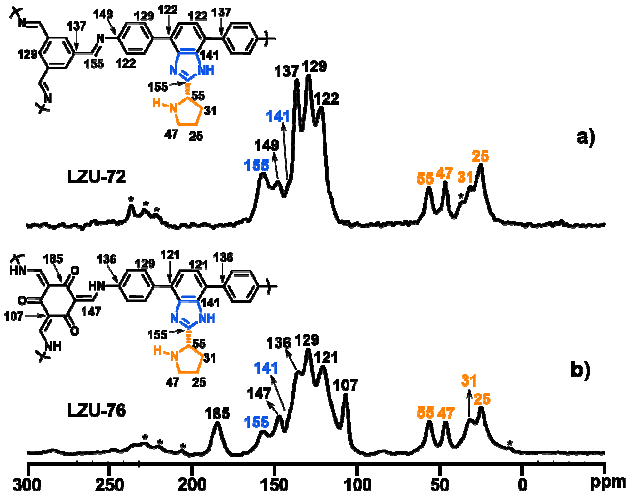


Figure 4. ^{13}C CP/MAS NMR spectra of **LZU-72** (a) and **LZU-76** (b). The asterisks denote the spinning sidebands. Assignments of ^{13}C chemical shifts were indicated in the chemical structures of **LZU-72** and **LZU-76**, respectively.

The atomic-level construction of **LZU-72** and **LZU-76** was assessed by Fourier transform infrared (FT-IR) and solid-state NMR spectroscopy. The FT-IR spectrum of **LZU-72** showed an intense –C=N– stretch at 1621 cm^{-1}, indicating the formation of imine bonds (Figure S16). **LZU-76** displayed a strong –C–N– stretch at 1256 cm^{-1} and a –C=C– stretch at 1592 cm^{-1}, which are characteristic of *β*–ketoenamine linkages (Figure S39).[14d,19] More detailed information was given by ^{13}C cross-polarization magic-angle spinning (CP/MAS) NMR analysis (Figure 4). The ^{13}C CP/MAS NMR spectra of both COFs exhibited signals at 25, 31, 47, and 55 ppm, which are assigned to the chiral pyrrolidine moieties. The detailed assignments of ^{13}C chemical shifts were depicted in Figure 4.

The crystalline structures of **LZU-72** and **LZU-76** were determined by powder X-ray diffraction (PXRD) analysis with Cu K*α* radiaction. The observed PXRD patterns of **LZU-72** (Figure 5a, black) showed an intense peak with the *d* spacing of 32.42 Å and two other peaks with *d* spacings of 16.21 and 10.81 Å, which correspond to the 100, 200, and 300 reflections, respectively. Similarly, the observed PXRD patterns of **LZU-76** (Figure 5b, black) exhibited three peaks with the *d* spacings of 32.40, 16.20, and 10.80 Å, respectively. Structural modeling was then conducted with the software of Materials Studio (ver. 7.0). The Pawley-refined PXRD profiles matched the experimental PXRD patterns very well (R_{wp} of 6.73% and R_p = 4.86% for **LZU-72**; R_{wp} of 4.59% and R_p of 2.90% for **LZU-76**). Comparison of the experimental and the calculated PXRD patterns (Figures S37 and S56) indicated that the stacking structures of **LZU-72** and **LZU-76** were both the eclipsed arrangements. Notably, both COFs possess the chiral space group of *P*3, which should be originated from the existence of chiral building blocks. In addition, the transmission electron micrographs (TEM) image (Figure S36) showed long-ordered channels in **LZU-72** with a distinct pore size

of 2.0 nm. Meanwhile, the scanning electron microscopy (SEM) images revealed that **LZU-72** exhibited a sphere morphology (Figure 5c), while **LZU-76** showed a thread-like morphology (Figure 5d).

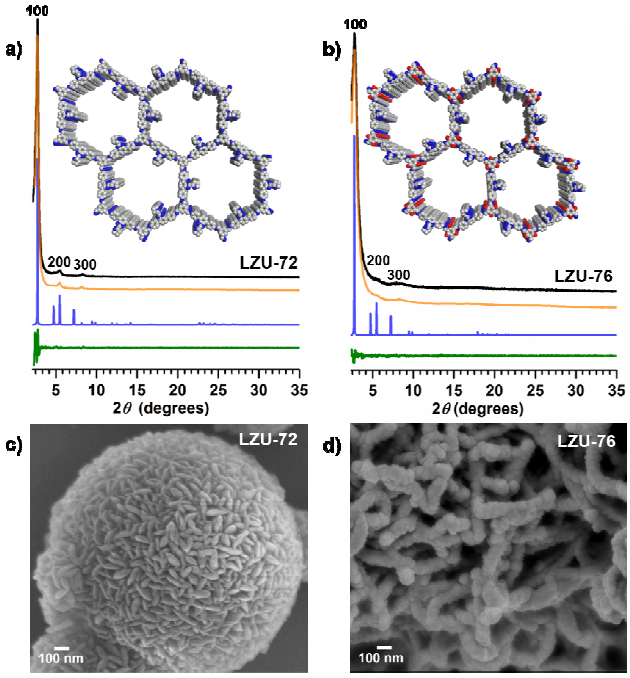
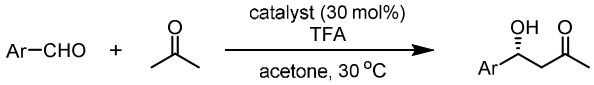


Figure 5. Experimental (black), Pawley refined (orange), and simulated (blue) PXRD patterns of **LZU-72** (a) and **LZU-76** (b). The difference plots between the experimental and the refined PXRD patterns are presented in green. Insets: The extended structures based on the eclipsed arrangements. C, grey; O, red; N, blue. H atoms are omitted for clarity. SEM images of **LZU-72** (c) and **LZU-76** (d).

The permanent porosity of **LZU-72** and **LZU-76** was confirmed by nitrogen adsorption-desorption experiments at 77 K (Figures S25 and S48). The Brunauer-Emmett-Teller (BET) surface areas of **LZU-72** (Figure S26) and **LZU-76** (Figure S49) were calculated to be 1114 and 758 $m^2\ g^{-1}$, respectively. The difference in the experimental BET surface areas of **LZU-72** and **LZU-76** could be attributed to the different crystallinity.[20] Meanwhile, the theoretical BET surface areas were calculated as 1521 $m^2\ g^{-1}$ for **LZU-72** (Figure S32) and 1189 $m^2\ g^{-1}$ for **LZU-76** (Figure S53), respectively. These theoretical values are higher than the experimental values, the case of which was also previously reported for other 2D COFs.[21] The pore volumes were evaluated (at P/P_0 = 0.99) to be 0.98 $cm^3\ g^{-1}$ for **LZU-72** and 0.66 $cm^3\ g^{-1}$ for **LZU-76**. Calculated by nonlocal density functional theory (NLDFT) method, both COFs exhibited a narrow pore size distribution between 1.2 and 2.2 nm (Figures S28 and S51). The difference in the pore size data derived from the model structure and gas adsorption isotherms may be attributed to the microcrystalline nature of the synthesized COFs.[14d,22]

One of the most value-add applications of chiral materials is as heterogeneous asymmetric catalysts. In this aspect, the straight channels within these two crystalline COFs could provide efficient access to the chiral-pyrrolidine sites and thus facilitate the transport of reactants and products. In particular, **LZU-76** is more stable under acidic conditions (Figure S42) due to the robust β–ketoenamine linkages.[14d] Accordingly, we chose **LZU-76** to test its catalytic activity.

Table 1. Catalytic Activity Test of LZU-76 in Asymmetric Aldol Reaction[a]



Entry	Ar	Catalyst	Time [h]	Yield [%][b]	e.r.[c]
1	4-NO_2Ph	**LZU-76**	18	73	94.0:6.0
2	2-NO_2Ph	**LZU-76**	18	84	93.7:6.3
3	4-CNPh	**LZU-76**	48	71	93.5:6.5
4	4-BrPh	**LZU-76**	96	46	88.4:11.6
5	2-naphthyl	**LZU-76**	80	25	91.4:8.6
6	4-NO_2Ph	DPBIP[d]	6	82	93.1:6.9

[a]General conditions: aromatic aldehydes (0.20 mmol), **LZU-76** (0.06 mmol), trifluoroacetic acid (TFA) (0.06 mmol), and acetone (1.0 mL). [b]Isolated yield. [c]Enantiomeric ratios (e.r.) were determined by chiral HPLC. [d]For the purpose of comparison, (*S*)-4,7-diphenyl-2-(pyrrolidin-2-yl)-1*H*-benzo[*d*] imidazole (DPBIP) was synthesized as the homogeneous counterpart of **LZU-76**.

The catalytic activity of **LZU-76** was evaluated in the asymmetric aldol reaction, which is one of the most important routes for asymmetric C–C bond formation.[23] As shown in Table 1, catalyzed by **LZU-76**, the reaction afforded the desired aldol products with excellent enantioselectivity (88.4:11.6-94.0:6.0 e.r., entries 1-5). For the purpose of comparison, a model catalyst, (*S*)-4,7-diphenyl-2-(pyrrolidin-2-yl)-1*H*-benzo[*d*]imidazole (DPBIP) was synthesized as the homogeneous counterpart of **LZU-76** and its catalytic activity was investigated under the same conditions. The result indicates that **LZU-76** (entry 1) showed comparable enantioselectivity to DPBIP (entry 6). In addition, **LZU-76** could be easily recovered by centrifugation and reused at least for 3 times without loss of enantioselectivity (Table S4). The PXRD patterns (Figure S57) and ^{13}C CP/MAS NMR spectra (Figure S58) of the recycled **LZU-76** demonstrated that the crystallinity and covalent-bonding were maintained.

In conclusion, we develop herein a straightforward strategy for constructing chiral COFs directly from chiral building blocks. The key design for the functional building blocks is the use of rigid **2** as the scaffold for attaching the chiral moieties. As a first example, two chiral COFs, **LZU-72** and **LZU-76**, were successfully constructed from the chiral-pyrrolidine-containing building block **3**. Given that the versatile scaffold **2** could attach different chiral moieties, various chiral COFs are expected to facilely construct via this strategy. It, therefore, paves a new way for the construction of functional COFs for high value-added applications.

ASSOCIATED CONTENT

Supporting Information

Detailed synthetic procedures, FT-IR spectra, ^{13}C CP/MAS NMR spectra, TGA traces, gas adsorption, SEM images, TEM images, PXRD patterns, modeling details and atomic coordinates, catalytic activity test, liquid NMR spectra, and

HPLC spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

wang_wei@lzu.edu.cn; dingsy@lzu.edu.cn

ACKNOWLEDGMENT

This work was financially supported by the National Natural Science Foundation of China (Nos. 21425206 and 21502081).

REFERENCES

(1) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley and Sons: New York, 1994.

(2) (a) Liu, M.; Zhang, L.; Wang, T. *Chem. Rev.* **2015**, *115*, 7304. (b) Ye, Y.; Cook, T. R.; Wang, S.-P.; Wu, J.; Li, S.; Stang, P. J. *J. Am. Chem. Soc.* **2015**, *137*, 11896. (c) Rojas, A.; Arteaga, O.; Kahr, B.; Camblor, M. A. *J. Am. Chem. Soc.* **2013**, *135*, 11975. (d) Kaushik, M.; Basu, K.; Benoit, C.; Cirtiu, C. M.; Vali, H.; Moores, A. *J. Am. Chem. Soc.* **2015**, *137*, 6124. (e) Yu, J.; Xu, R. *J. Mater. Chem.* **2008**, *18*, 4021. (f) MacLean, M. W. A.; Reid, L. M.; Wu, X.; Crudden, C. M. *Chem. - Asian. J.* **2015**, *10*, 70. (g) Qiu, H.; Che, S. *Chem. Soc. Rev.* **2011**, *40*, 1259. (h) Yashima, E.; Maeda, K. *Macromolecules* **2008**, *41*, 3. (i) Schröder, M. *Functional Metal-Organic Frameworks: Gas Storage, Separation and Catalysis;* Springer: Berlin, 2010. (j) Morris, R. E.; Bu, X. *Nat. Chem.* **2010**, *2*, 353. (k) Kelly, J. A.; Giese, M.; Shopsowitz, K. E.; Hamad, W. Y.; MacLachlan, M. J. *Acc. Chem. Res.* **2014**, *47*, 1088.

(3) (a) Gross, E.; Liu, J. H.; Alayoglu, S.; Marcus, M. A.; Fakra, S. C.; Toste, F. D.; Somorjai, G. A. *J. Am. Chem. Soc.* **2013**, *135*, 3881. (b) Kundu, D. S.; Schmidt, J.; Bleschke, C.; Thomas, A.; Blechert, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 5456. (c) Dang, D.; Wu, P.; He, C.; Xie, Z.; Duan, C. *J. Am. Chem. Soc.* **2010**, *132*, 14321. (d) Yoon, M.; Srirambalaji, R.; Kim, K. *Chem. Rev.* **2012**, *112*, 1196. (e) Bonnefoy, J.; Legrand, A.; Quadrelli, E. A.; Canivet, J.; Farrusseng, D. *J. Am. Chem. Soc.* **2015**, *137*, 9409. (f) Xu, H.; Chen, X.; Gao, J.; Lin, J.; Addicoat, M.; Irle, S.; Jiang, D. *Chem. Commun.* **2014**, *50*, 1292. (g) Xu, H.; Gao, J.; Jiang, D. *Nat. Chem.* **2015**, *7*, 905.

(4) (a) Shen, J.; Okamoto, Y. *Chem. Rev.* **2016**, *116*, 1094. (b) Liu, Y.; Xuan, W. M.; Cui, Y. *Adv. Mater.* **2010**, *22*, 4112. (c) Weng, X.; Baez, J. E.; Khiterer, M.; Hoe, M. Y.; Bao, Z.; Shea, K. J. *Angew. Chem., Int. Ed.* **2015**, *54*, 11214. (d) Li, P.; He, Y.; Guang, J.; Weng, L.; Zhao, J. C.-G.; Xiang, S.; Chen, B. *J. Am. Chem. Soc.* **2014**, *136*, 547. (e) Wu, K.; Li, K.; Hou, Y.-J.; Pan, M.; Zhang, L.-Y.; Chen, L.; Su, C.-Y. *Nat. Commun.* **2016**, *7*. 10487.

(5) (a) Wanderley, M. M.; Wang, C.; Wu, C.-D.; Lin, W. *J. Am. Chem. Soc.* **2012**, *134*, 9050. (b) Xuan, W.; Zhang, M.; Liu, Y.; Chen, Z.; Cui, Y. *J. Am. Chem. Soc.* **2012**, *134*, 6904.

(6) (a) Trindade, A. F.; Gois, P. M. P.; Afonso, C. A. M. *Chem. Rev.* **2009**, *109*, 418. (b) Heitbaum, M.; Glorius, F.; Escher, I. *Angew. Chem., Int. Ed.* **2006**, *45*, 4732. (c) Van Der Voort, P.; Esquivel, D.; De Canck, E.; Goethals, F.; Van Driessche, I.; Romero-Salguero, F. J. *Chem. Soc. Rev.* **2013**, *42*, 3913.

(7) (a) Gruttadauria, M.; Giacalone, F.; Noto, R. *Chem. Soc. Rev.* **2008**, *37*, 1666. (b) Hoffmann, F.; Cornelius, M.; Morell, J.; Fröba, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 3216.

(8) (a) Kuschel, A.; Sievers, H.; Polarz, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 9513. (b) Ma, L.; Falkowski, J. M.; Abney, C.; Lin, W. *Nat. Chem.* **2010**, *2*, 838.

(9) Du, X.; Sun, Y.; Tan, B.; Teng, Q.; Yao, X.; Su, C.; Wang, W. *Chem. Commun.* **2010**, *46*, 970.

(10) (a) Wang, C. A.; Zhang, Z. K.; Yue, T.; Sun, Y. L.; Wang, L.; Wang, W. D.; Zhang, Y.; Liu, C.; Wang, W. *Chem. - Eur. J.* **2012**, *18*, 6718. (b) An, W.-K.; Han, M.-Y.; Wang, C.-A.; Yu, S.-M.; Zhang, Y.; Bai, S.; Wang, W. *Chem. - Eur. J.* **2014**, *20*, 11019.

(11) (a) Wu, D.; Xu, F.; Sun, B.; Fu, R.; He, H.; Matyjaszewski, K. *Chem. Rev.* **2012**, *112*, 3959. (b) Kaur, P.; Hupp, J. T.; Nguyen, S. T. *Acs Catal.* **2011**, *1*, 819.

(12) Côté, A. P.; Benin, A. I.; Ockwig, N. W.; O'Keeffe, M.; Matzger, A. J.; Yaghi, O. M. *Science* **2005**, *310*, 1166.

(13) (a) Waller, P. J.; Gándara, F.; Yaghi, O. M. *Acc. Chem. Res.* **2015**, *48*, 3053. (b) Ding, S.-Y.; Wang, W. *Chem. Soc. Rev.* **2013**, *42*, 548. (c) Feng, X.; Ding, X.; Jiang, D. *Chem. Soc. Rev.* **2012**, *41*, 6010. (d) Slater, A. G.; Cooper, A. I. *Science* **2015**, *348*, 6238. (e) Colson, J. W.; Dichtel, W. R. *Nat. Chem.* **2013**, *5*, 453.

(14) For selected examples, see : (a) Uribe-Romo, F. J.; Hunt, J. R.; Furukawa, H.; Klock, C.; O'Keeffe, M.; Yaghi, O. M. *J. Am. Chem. Soc.* **2009**, *131*, 4570. (b) Uribe-Romo, F. J.; Doonan, C. J.; Furukawa, H.; Oisaki, K.; Yaghi, O. M. *J. Am. Chem. Soc.* **2011**, *133*, 11478. (c) Lin, S.; Diercks, C. S.; Zhang, Y.-B.; Kornienko, N.; Nichols, E. M.; Zhao, Y.; Paris, A. R.; Kim, D.; Yang, P.; Yaghi, O. M.; Chang, C. J. *Science* **2015**, *349*, 1208. (d) Kandambeth, S.; Mallick, A.; Lukose, B.; Mane, M. V.; Heine, T.; Banerjee, R. *J. Am. Chem. Soc.* **2012**, *134*, 19524. (e) Fang, Q.; Zhuang, Z.; Gu, S.; Kaspar, R. B.; Zheng, J.; Wang, J.; Qiu, S.; Yan, Y. *Nat. Commun.* **2014**, *5*, 4503. (f) Ascherl, L.; Sick, T.; Margraf, J. T.; Lapidus, S. H.; Calik, M.; Hettstedt, C.; Karaghiosoff, K.; Döblinger, M.; Clark, T.; Chapman, K. W.; Auras, F.; Bein, T. *Nat. Chem.* **2016**, *8*, 310. (g) Zhou, T.-Y.; Xu, S.-Q.; Wen, Q.; Pang, Z.-F.; Zhao, X. *J. Am. Chem. Soc.* **2014**, *136*, 15885. (h) Zeng, Y.; Zou, R.; Luo, Z.; Zhang, H.; Yao, X.; Ma, X.; Zou, R.; Zhao, Y. *J. Am. Chem. Soc.* **2015**, *137*, 1020. (i) Zhu, Y.; Wan, S.; Jin, Y.; Zhang, W. *J. Am. Chem. Soc.* **2015**, *137*, 13772. (j) Vyas, V. S.; Haase, F.; Stegbauer, L.; Savasci, G.; Podjaski, F.; Ochsenfeld, C.; Lotsch, B. V. *Nat. Commun.* **2015**, *6*, 8508. (k) Lin, G.; Ding, H.; Yuan, D.; Wang, B.; Wang, C. *J. Am. Chem. Soc.* **2016**, *138*, 3302. (l) Ding, S.-Y.; Dong, M.; Wang, Y.-W.; Chen, Y.-T.; Wang, H.-Z.; Su, C.-Y.; Wang, W. *J. Am. Chem. Soc.* **2016**, *138*, 3031. (m) Song, J.-R.; Sun, J.; Liu, J.; Huang, Z.-T.; Zheng, Q.-Y. *Chem. Commun.* **2014**, *50*, 788. (n) H. Wei; S. Chai; N. Hu; Z. Yang; L. Wei; L. Wang, *Chem. Commun.* **2015**, *51*, 12178. (o) Ma, H.; Liu, B.; Li, B.; Zhang, L.; Li, Y.-G.; Tan, H.-Q.; Zang, H.-Y.; Zhu, G. *J. Am. Chem. Soc.* **2016**, *138*, 5897. (p) Kuhn, P.; Antonietti, M.; Thomas, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 3450.

(15) Zhu, Y.; Zhang, W. *Chem. Sci.* **2014**, *5*, 4957.

(16) (a) Hofmann, K. *Imidazole and its derivatives*; Interscience Publishers: New York, NY, 1953; Vol. 6. (b)Preedy, V. R. *Imidazole Dipeptides: Chemistry, Analysis, Function and Effects*; RSC Publishing: Cambridge, U.K., 2015.

(17) (a) Zhang, Z.; Xie, F.; Jia, J.; Zhang, W. *J. Am. Chem. Soc.* **2010**, *132*, 15939. (b) Li, Y.; Ding, K.; Sandoval, C. A. *Org. Lett.* **2009**, *11*, 907. (c) Lacoste, E.; Vaique, E.; Berlande, M.; Pianet, I.; Vincent, J. M.; Landais, Y. *Eur. J. Org. Chem.* **2007**, 167. (d) Zhang, B.; Jiang, Z.; Zhou, X.; Lu, S.; Li, J.; Liu, Y.; Li, C. *Angew. Chem., Int. Ed.* **2012**, *51*, 13159.

(18) As pyrrolidine groups could react with acetic acid (HOAc) under solvothermal conditions, the pyrrolidine moiety of chiral building block **3** was protected with a Boc group. Similar strategies have been found in other materials systems. For selected examples see: (a) Lun, D. J.; Waterhouse, G. I. N.; Telfer, S. G. *J. Am. Chem. Soc.* **2011**, *133*, 5806. (b) Wu, P.; He, C.; Wang, J.; Peng, X.; Li, X.; An, Y.; Duan, C. *J. Am. Chem. Soc.* **2012**, *134*, 14991. (c) Bass, J. D.; Solovyov, A.; Pascall, A. J.; Katz, A. *J. Am. Chem. Soc.* **2006**, *128*, 3737. (d) Tanabe, K. K.; Allen, C. A.; Cohen, S. M. *Angew. Chem., Int. Ed.* **2010**, *49*, 9730. (e) Fracaroli, A. M.; Siman, P.; Nagib, D. A.; Suzuki, M.; Furukawa, H.; Toste, F. D.; Yaghi, O. M. *J. Am. Chem. Soc.* **2016**, *138*, 8352.

(19) (a) DeBlase, C. R.; Silberstein, K. E.; Truong, T.-T.; Abruña, H. D.; Dichtel, W. R. *J. Am. Chem. Soc.* **2013**, *135*, 16821. (b) Fang, Q.; Gu, S.; Zheng, J.; Zhuang, Z.; Qiu, S.; Yan, Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 2878.

(20) Chandra, S.; Kundu, T.; Kandambeth, S.; BabaRao, R.; Marathe, Y.; Kunjir, S. M.; Banerjee, R. *J. Am. Chem. Soc.* **2014**, *136*, 6570.

(21) Spitler, E. L.; Koo, B. T.; Novotney, J. L.; Colson, J. W.; Uribe-Romo, F. J.; Gutierrez, G. D.; Clancy, P.; Dichtel, W. R. *J. Am. Chem. Soc.* **2011**, *133*, 19416.

(22) (a) Calik, M.; Sick, T.; Dogru, M.; Döblinger, M.; Datz, S.; Budde, H.; Hartschuh, A.; Auras, F.; Bein, T., *J. Am. Chem. Soc.* **2016**, *138*, 1234. (b) Smith, B. J.; Overholts, A. C.; Hwang, N.; Dichtel, W. R., *Chem. Commun.* **2016**, *52*, 3690.

(23) *Modern Aldol Reactions*; Mahrwald, R., Ed.; Wiley-VCH: Weinheim, 2004.

TOC