# Metal–organic frameworks with designed chiral recognition sites†

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**Linking struts containing Cram-like bisbinaphthyl[22]crown-6 with $Zn_4O(CO_2)_6$ joints affords metal–organic frameworks with chiral recognition sites that are highly designed, ordered and placed in a precise manner throughout the entire crystal.**

The modular assembly of metal–organic frameworks (MOFs)[1] from organic struts and inorganic joints[2] lends itself to the preparation of a virtually unlimited collection of these three-dimensional structures based on the seemingly endless combinations and permutations of commercially available precursors.[3] The vast majority of MOFs prepared using this approach (Fig. 1a) contain (i) a *sorting domain*,[4] whereby the pore apertures act as sieves based on size- and shape-selectivity and/or (ii) a *coverage domain*[5] wherein the internal pore surfaces interact non-specifically with guest molecules as a consequence of noncovalent binding forces. Recently, we described[6] the synthesis of a linear organic strut (*rac*-**1**, Fig. 1b) possessing a bisparaphenylene[34]crown-10 (BPP34C10) recognition site and its subsequent incorporation into MOF-1001. Such 'designer struts' constitute[6,7] multi-step synthetic targets, which allow the incorporation of specific features and functions into MOFs. This designer approach has led to a new type of distribution domain—the *active domain*[6]—wherein an ordered distribution of guests throughout the MOF is maintained by highly specific stereoelectronic control in addition to the size and shape selectivity inherent to the MOF itself. For example, MOF-1001 crystals were shown to uptake quantitatively—by virtue of the formation of strong charge-transfer complexes—the π-electron-deficient paraquat (methyl viologen) dication ($PQT^{2+}$) into each of the π-electron-rich BPP34C10 host sites which are repeated periodically in three dimensions throughout the extended framework. The BPP34C10-functionalized struts possess a plane of chirality and so lend themselves to the preparation of MOFs with chirally active domains that are akin—albeit in a greatly simplified form—to enzyme active-sites

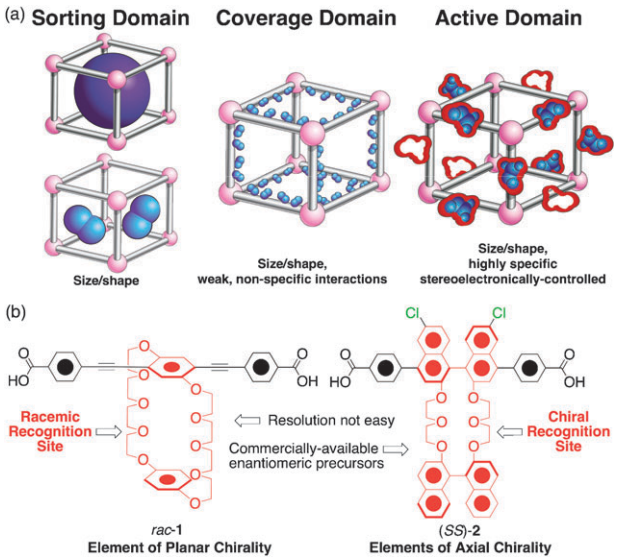


**Fig. 1** (a) A graphical representation of the three distribution domains for guests in metal–organic frameworks (MOFs). The *sorting domain* separates guest molecules primarily by means of a sieve-like action based on size and shape. The *coverage domain* packs guest molecules as a result of non-specific interactions arising from weak noncovalent bonding forces occurring with the framework of the MOF. The *active domain* relies on the high specificity of the incorporated host recognition sites for complementary guests. (b) Strut *rac*-**1** with a plane of chirality—but yet not resolvable at room temperature—used to prepare MOF-1001, and strut (*SS*)-**2** with two axes of chirality.

capable of stereoselective molecular recognition. Challenges, however, have arisen in the preparation and isolation of the pure enantiomers of *rac*-**1** as a consequence of racemization—a process which could be arrested by extending the length of the strut to prevent passage of the crown ether over the terminal carboxylic acid functions. Struts possessing axial chirality are an attractive and potentially more practical alternative since axially-chiral crown ether-containing struts can be prepared from commercially available enantiopure synthetic precursors. We report, herein, the design, synthesis and incorporation of the dilocular (two chiral elements) struts (*SS*)-**2** and (*RR*)-**2** into (*SS*)-MOF-1020 and (*RR*)-MOF-1020, respectively. The design of (*SS*)-**2** and (*RR*)-**2** is based on the seminal work of Cram and co-workers[8] in the 1970s and 1980s, wherein dilocular bisbinaphthyl crown ether hosts were found to bind enantiomers of primary alkylammonium ions selectively. Modification of these chiral hosts by extending out from the 4 and 4′ positions[9] of one of the two binaphthyl units with *p*-carboxylic acid-functionalized phenylene rings provides a dilocular strut for incorporation into MOFs.

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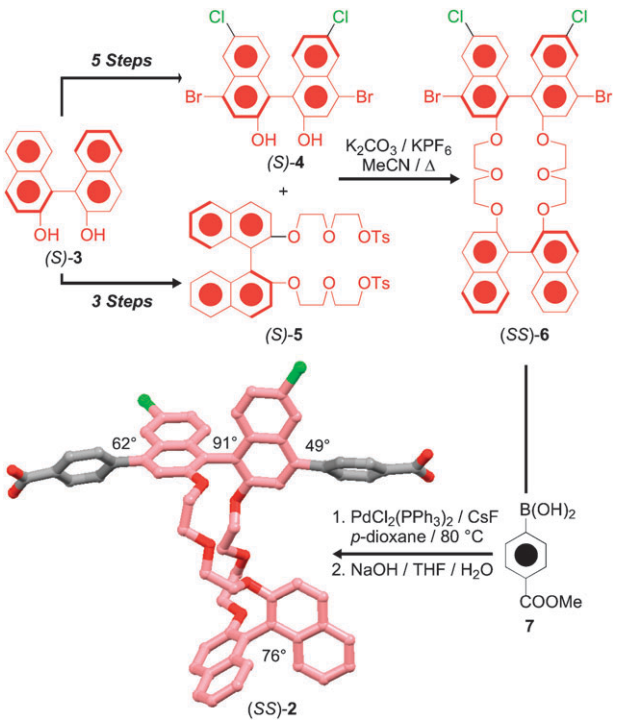
The synthesis of (*SS*)-**2** is outlined in Scheme 1. The intermediate (*S*)-**4** was prepared from commercially available (*S*)-1,1′-binaphthalene-2,2′-diol (*S*)-**3** in five steps (see the ESI†) according to a modified procedure adapted from that of Lin and co-workers.[10] Macrocyclization of (*S*)-**4** with (*S*)-**5**, which was prepared (see the ESI†) in three steps from (*S*)-**3**, proceeded in high yield on account of the template-assisted ring closure to give the dilocular macrocyclic intermediate (*SS*)-**6**. Chemoselective Suzuki–Miyaura cross-coupling of (*SS*)-**6** with 4-(methoxycarbonyl)phenylboronic acid (**7**), followed by saponification, provided the diacid (*SS*)-**2**. The overall synthesis, in which chromatography is avoided in all but two of the 11 steps, is high yielding, convergent, and scalable. Single crystals of (*SS*)-**2**, suitable for X-ray crystallography, were obtained by slow vapour diffusion of pentane into a solution of (*SS*)-**2** in THF (see the ESI†). The solid-state structure (Scheme 1) confirms the absolute chirality of the dicarboxylic acid (*SS*)-**2**. The distance between the two carboxylic acid carbon atoms is 18.6 Å, and the $CO_2H$ groups form typical hydrogen bonded carboxylic acid dimers with the $CO_2H$ functions in adjacent molecules.

In order to verify that (*SS*)-**2** acts as an active domain that is capable of binding guests, $^1$H NMR spectra (see Fig. S1 and S2 in the ESI†) were recorded for a range of different ratios of the diester derivative of (*SS*)-**2**—the dimethyl ester was used in place of the diacid for solubility reasons—and (*S*)-α-methylbenzylammonium perchlorate in $CD_2Cl_2$ at 298 K. A combination




**Scheme 1** Partial synthetic route leading to the production of the dicarboxylic acid-terminated strut (*SS*)-**2**. The corresponding enantiomer, (*RR*)-**2**, was prepared in a similar fashion. The structural representation is of a single-crystal X-ray structure of (*SS*)-**2**. C, grey/pink; O, red; Cl, green. Hydrogen atoms have been omitted for clarity. There are dihedral angles of 91° and 76° between the average mean planes of the two naphthyl ring systems and 62° and 49° between the average mean planes of the *p*-carboxyphenyl and the associated naphthyl ring systems.

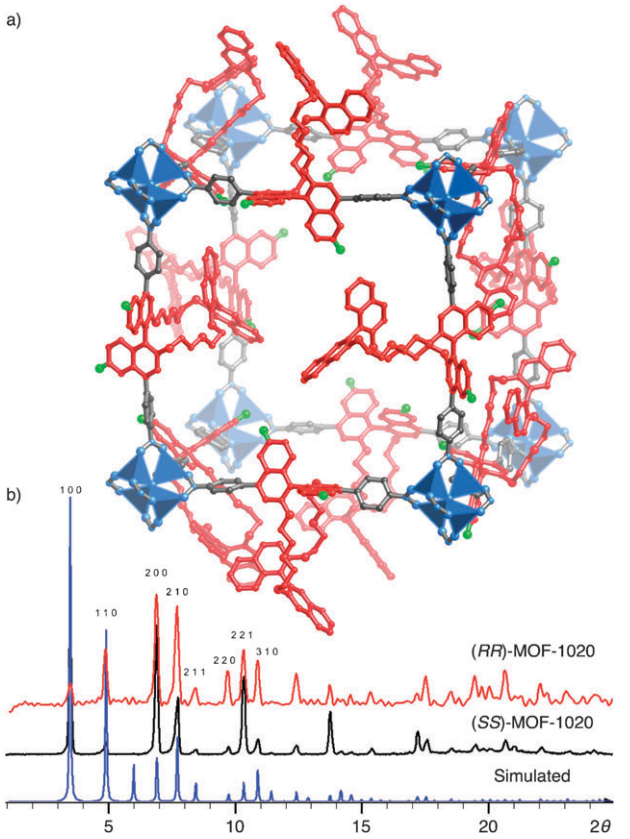



**Fig. 2** (a) A ball-and-stick representation of the unit cell present in (*SS*)-MOF-1020. The inorganic secondary building unit (SBU), $Zn_4O(CO_2)_6$, is represented by blue polyhedra. The dilocular organic struts (black) each possess axially chiral recognition sites in the form of (*SS*)-bisbinaphthyl [22]crown-6 receptors (red). H atoms have been omitted for clarity. The flexibility of the bisbinaphthyl[22]crown-6 host sites prevented the assignment for the precise positions of the atoms in the organic link. Nevertheless, the positions of the atoms belonging to the SBU were accurately determined using single-crystal X-ray crystallography (see the ESI†) and were used to model (b) the powder X-ray diffraction (PXRD) patterns: simulated [blue, (*SS*)-MOF-1020] and experimental [black, (*SS*)-MOF-1020 and red, (*RR*)-MOF-1020] PXRD patterns.

of upfield and downfield shifts of several $^1$H resonances is indicative of inclusion complex formation. More specifically, as the concentration of the guest [(*S*)-α-methylbenzylammonium perchlorate] is decreased relative to the host [the dimethyl ester derivative of (*SS*)-**2**], the resonances corresponding to the benzylic methine and homobenzylic methyl protons shift upfield by approximately 0.27 and 0.36 ppm, respectively. Concomitant downfield shifts are observed for the crown ether methylene resonances closest to the two binaphthyl moieties in the host, ranging from 0.07 to 0.17 ppm in magnitude.

Homochiral (*SS*)-MOF-1020 was prepared‡ using a solvothermal procedure wherein an *N*,*N*-dimethylformamide (DMF) solution of (*SS*)-**2** and $Zn(NO_3)_2{\cdot}4H_2O$ was heated in an oven with a temperature step program of 65, 75 and 85 °C each for a 24 h period [similarly, (*RR*)-MOF-1020 was obtained from (*RR*)-**2**]. The cubic crystals of (*SS*)-MOF-1020 were analyzed by single-crystal X-ray crystallography which revealed a structure (Fig. 2a) isoreticular with MOF-1001.

Chiral struts emanate from each secondary building unit (SBU)—single $Zn_4O(CO_2)_6$ clusters—in an octahedral array to form an extended cubic net belonging to the *P*23 space group. The positions of the atoms belonging to the SBU were accurately determined. The precise positions of the atoms in the organic link, however, were highly disordered because of the flexibility of the bisbinaphthyl[22]crown-6 host sites. Nevertheless, the positions of the atoms were modeled along with the assigned atomic positions of the SBU using *Cerius*[2] software, and the computed powder X-ray diffraction (PXRD) pattern was compared with experimental data (Fig. 2b). The simulated diffraction pattern matches the experimentally recorded ones for (*SS*)- and (*RR*)-MOF-1020.[11]

Thermal gravimetric analysis (TGA) was performed (see Fig. S5 in the ESI†) in order to evaluate the thermal stability of (*SS*)-MOF-1020. The percentage weight-loss patterns for as-synthesized, acetone-exchanged and activated (supercritical $CO_2$)[12] (*SS*)-MOF-1020 revealed nearly identical MOF decomposition temperatures at approximately 325 °C. A sharp one-step TGA profile—as is commonly observed upon MOF decomposition—gives way to a stepwise weight-loss pattern between 350–600 °C for (*SS*)-MOF-1020. This characteristic is attributed to the subsequent decomposition of the organic strut, as the TGA of (*SS*)-**2** reveals a similar decomposition profile. A PXRD was recorded for an activated sample of (*SS*)-MOF-1020 in order to probe the integrity of the framework (see Fig. S4 in the ESI†). Although the activated sample provided a significantly different PXRD pattern, crystallinity was partially restored upon re-solvation with fresh DMF. This phenomenon suggests that the activated MOF goes through a structural distortion that is recoverable *via* re-solvation. Phenomena of this kind are observed[13] with highly porous MOFs wherein guest molecules sustain and stabilize the open structure, but upon their removal, the crystalline framework distorts in an effort to maintain the integrity of the framework by forming weak noncovalent bonds.

The precise placement of organic struts containing optically-active dilocular bisbinaphthyl[22]crown-6 hosts inside metal–organic frameworks augurs well for the development of a range of exquisitely engineered chiral stationary phases for carrying out the separation of enantiomers by high-performance liquid chromatography.

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## Notes and references

‡ MOF synthesis: DMF (10 mL, Fisher) was added to a solid mixture of (*SS*)-**2** (20 mg, 0.0196 mmol) and $Zn(NO_3)_2{\cdot}4H_2O$ (20 mg, 0.0672 mmol) in a 20 mL scintillation vial. The vial was capped tightly and the mixture was sonicated for 3 min to dissolve all solid material. The resulting homogeneous solution was placed in a programmable oven, with a temperature step program of 65, 75 and 85 °C for 24 h each. The reaction mixture was cooled to rt and then the block-shaped crystals were washed with fresh DMF (3 × 1 mL). Elemental analysis (evacuated): calcd: C 66.94%, H 3.99%, Cl 6.37%; found: C 65.63%, H 3.96%, Cl 5.96%. Crystal data for MOF-1020: cubic, space group *P*23, $a$ = 25.7527(6) Å, $V$ = 17079.2(7) Å$^3$, $\lambda$ = 1.54178 Å$^3$, $Z$ = 1. Atoms of the ligand were highly disordered and therefore could not be located. The framework was modeled based on the locations of the heavy atoms that were found.

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