The 1990s saw a quest towards synthesizing modular porous materials from metal-containing linker groups and organic molecule struts. The idea, perhaps in analogy to the spools and sticks of the popular “Tinkertoy” sets, was to use molecular linkers with multiple chelating sites and molecular struts of different lengths to generate porous solid materials with custom-designed pore sizes and shapes. In 1998 Omar M. Yaghi, currently at UCLA, succeeded in developing a systematic route towards synthesizing metal-organic framework (MOF) materials. Since then, MOFs with many metal ion/metal oxide based linkers and a wide variety of bidentate (or multidentate) organic struts have been synthesized. The MOFs are structurally robust, withstanding relatively high temperatures and pressures. They have found many applications in gas-phase separations and gas storage, prominently in H₂ storage and CO₂ separation from flue gases. MOF-5 (or IRMOF-1) is the prototype MOF phase with a cubic unit cell, Zn₆O metal oxide linkers (with a formal +6 charge) bound to p-benzenedicarboxylate organic struts in three perpendicular directions.

Most MOFs show some degree of selectivity towards guest adsorption from the gas or solution phase. The simplest mechanism of guest separation in MOF materials is based on pore aperture size where large gas or solute molecules are excluded from the solid phase and smaller gas molecules diffuse through the pores to get to the other side of the MOF barrier, much like the action of a sieve. This type of separation is based on considerations of the van der Waals radii of the guests and MOF molecules lining the pore apertures. Geometric selectivity operates in the so-called “sorting domain” and is effective when the pore aperture diameter is close to the molecular diameters of the molecules in the mixture.

MOFs with large pore apertures cannot separate components of a mixture based on geometric factors alone. However, many MOFs have organic struts with electron-rich functional groups such as aromatic rings. In these cases the MOFs can separate mixture components based on the different van der Waals interaction strengths between guests and the framework. Guests with greater numbers of electrons overall and stronger total van der Waals interactions, such as CO₂, are selectively attracted to electron-rich parts of the framework over smaller guests like CO, N₂, CH₄, or H₂. A similar mechanism can apply to cases where the metal ion linker in the MOF has unsaturated (open) coordinate sites. The representative example of this class of MOF is HKUST-1 where the unsaturated Cu coordination site can act as a centre of H₂ or acetylene guest binding. The mechanism of guest adsorption and separation based on different guest–host interaction strengths is called the “coverage domain”. The selectivity in these cases is based on the electron density of the guest molecules and will have limited chemical specificity when gas-phase molecules of the same type are used. The coverage domain mechanism is operative at low and medium external guest pressures. An example of the preferential binding of CO₂ molecules to specific electron-rich sites in the ZIF-68 structure at low pressure is shown in Figure 1.

Achieving better chemical specificity for guest molecule binding requires custom-designed sites which geometrically and chemically bind to specific adsorbates but at the same time do not disrupt the MOF framework topology. Designing such a system is the important advance achieved by Li, Yahgi, Stoddart and coworkers, who have incorporated large macrocyclic polyether moieties into a cubic isoreticular MOF lattice. Li et al. use a modified form of the electron-rich bis-p-phenylene-34-crown-10 (BPP34C10) molecule shown in Figure 2. A 1,5-naphtho-p-phenylene-36-crown-10 analogue was also synthesized but is not further discussed. The electron-rich cyclic BPP34C10 forms a pseudodortaxane complex with the electron-deficient N,N'-dimethyl-4,4'-bipyridinium dication (paraquat, PQT²⁺, Figure 2) where the two pyridinium rings of PQT²⁺ are aligned parallel to the two aromatic rings in BPP34C10 by π-π stacking interactions. Hydrogen bonding by the macrocycle ether oxygen atoms with the α-CH atoms of paraquat and electrostatic interactions between the hydroquinone ring oxygen atoms and the para-
Figure 2. a) A schematic representation of the BPP34C10 molecule. b) The PQT$^{2+}$ ion. Oxygen atoms are shown by black, carbon atoms by dark grey, nitrogen atoms by light grey, and hydrogen atoms by white spheres.

quat N atoms also stabilize the complex,\(^\text{[13]}\)

Li et al. incorporated a phenylene ring of BPP34C10 as the central rung in the alternating sequence of phenylene and ethynyl groups of a strut that is capped by carboxylic acid groups and is called BPP34C10DA. With Zn$_4$O linkers, these struts form a cubic analogue of MOF-5 called MOF-1001, see Figure 3. The framework of MOF 1001 is well determined in the X-ray crystal structure, but the ring components of BPP34C10DA are highly disordered and not easily resolved.

Figure 3. The framework structure of the cubic MOF-1001 unit cell. The BPP34C10DA struts have disordered macrocycle rings which are not shown. A sample configuration for the strut with the polyether ring is shown on the right.

Similar to BPP34C10, the BPP34C10DA molecule forms a stable complex with PQT$^{2+}$, shown in Figure 4.\(^\text{12}\) Li et al. observe rapid and partially reversible change of colour associated with the appearance of a charge transfer interaction upon adding PQT·2PF$_6$ (from a saturated acetone solution) to MOF-1001. This is evidence of PQT$^{2+}$ binding to BPP34C10DA sites of MOF-1001 similar to PQT$^{2+}$ binding to free BPP34C10DA. The rapid color change upon mixing shows that the MOF-1001 structure is open enough to allow for the free diffusion of PQT$^{2+}$ from the solution.

When incorporating a macrocycle or enzyme (as will inevitably happen in the future) into a MOF, it is important that the nature of the binding site does not change. To retain the concept of modularity, the MOF should act primarily as a support. The conformation of the free BPP34C10 macrocycle in the pure solid state is almost identical to that of the macrocycle in the solid phase of the [BPP34C10·PQT][PF$_6$]$_2$ complex, with the aromatic rings of the crown ether parallel to each other and to those of the PQT$^{2+}$ guest. This shows that guest insertion does not require extensive rearrangement of the host structure and will occur rapidly. It is not clear whether there are large conformational changes in the BPP34C10DA moieties of MOF 1001 upon complexation with PQT$^{2+}$, but the immediate colour change upon mixing of the solutions indicates that the confirmation of BPP34C10DA in the empty MOF is similar to that of the pseudorotaxane [BPP34C10DA-PQT]$^{2+}$ in the MOF. The shift in the $^{15}$N solid-state NMR peak of PQT$^{2+}$ upon complexation in the in the BPP34C10DA strut of MOF-1001 is also very similar to the shift of the PQT$^{2+}$ peak in the free strut. These observations are indications that the MOF framework acts as a support for the host moiety without changing its configuration. This guarantees the transferability of the properties of the binding site from the free strut to the binding site incorporated into the MOF.

If, as expected, the aromatic rings of the PQT$^{2+}$ in the MOF-1001 unit cell are aligned parallel to the phenylene rings of BPP34C10DA, there will be three sets of PQT$^{2+}$ molecules aligned parallel to the three unit cell vectors and this could give the MOF/strut/substrate crystals interesting optical properties that can differ from the solid strut/substrate crystals where all PQT$^{2+}$ groups are aligned in the same crystallographic direction. This may lead to differing optical properties of charge transfer complexes in the MOF and free strut.

The synthesis of MOF-1001 shows that isoreticular frameworks with Zn$_4$O linkers and struts terminated with p-benzene-carboxylate-based moieties are robust enough to withstand the inclusion of bulky binding groups attached strategically to the strut. The struts are long enough that MOFs incorporating other catenane- and rotaxane-forming groups or even small biological enzymes can likely be synthesized.

Catenanes and rotaxanes have been suggested as the basis for molecular machines\(^\text{[14]}\) and logic units for data storage.\(^\text{[15]}\) The hybrid MOF/macrocyle structures can act as scaffolds for these components, opening up a new series of applications for MOF materials. Rotaxanes and catenanes are usually placed on surfaces and incorporating them into the three-dimensional structure of MOFs will give the possibility of much higher component densities. These molecular machines can be activated by light or electrical current. The conjugated $\pi$-systems of the struts in MOF-1001 makes them electrical conducting\(^\text{[16]}\) and photochemical manipulation of the MOF–substrate complexes is also feasible. Given these potentialities, many exciting and ingenious applications of MOFs incorporating macrocycles will undoubtedly be suggested in the near future.

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Selective Guest Docking in MOFs

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