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Modular Assembly of Metal–Organic Supercontainers Incorporating Sulfonylcalixarenes

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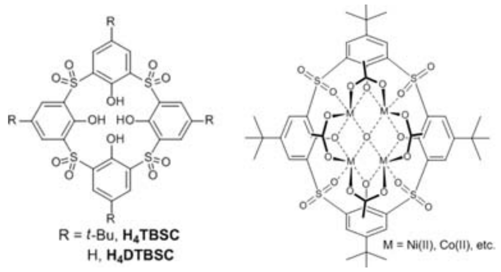
Ⓢ *Supporting Information*

ABSTRACT: A new strategy for the design of container molecules is presented. Sulfonylcalix[4]arenes, which are synthetic macrocyclic containers, are used as building blocks that are combined with various metal ions and tricarboxylate ligands to construct metal–organic "supercontainers" (MOSCs). These MOSCs possess both endo and exo cavities and thus mimic the structure of viruses. The synthesis of MOSCs is highly modular, robust, and predictable. The unique features of MOSCs are expected to provide exciting new opportunities for the exploration of their functional applications.

Container molecules with well-defined hollow structures have attracted significant interest in recent years.[1−11] These intriguing molecular receptors contain concave surfaces suitable for binding a variety of guests and offer unique chemical microenvironments relevant for a number of applications, including encapsulation of otherwise unstable species,[12,13] promotion of chemical transformations,[14−17] storage and separation of gases,[9,18] transportation of small molecules,[19,20] and templated formation of monodisperse nanoparticles.[21] Nature has provided numerous elegant examples of supramolecular containers, such as viruses and other protein assemblies (e.g., ferritin), in which the highly organized structure of the biomolecules is key to their sophisticated function.[22] Several research groups have presented a number of beautiful container systems that are based on covalent,[1,8,9,12] coordination,[3,5−7,10,11] or hydrogen bonding[2,4,23] interactions. However, synthetic tools accessible to chemists for preparing molecular containers remain generally limited. Many artificial receptors have a relatively simple structure, and few synthetic systems can match the function of their biological counterparts. Herein we describe a family of sulfonylcalixarene-incorporated metal–organic "supercontainers" (MOSCs) that mimic the topology of viruses.[24−28] A series of synthetic containers were readily prepared via coordination-driven assembly of metal ions, tricarboxylate ligands, and sulfonylcalix[4]arenes. We show that the synthesis of MOSCs is highly modular, robust, and predictable. We anticipate that the unique synthetic and structural features of MOSCs will provide exciting new opportunities for the exploration of their functional applications.

Calixarenes are a versatile class of macrocyclic containers composed of phenolic units linked by methylene groups.[29,30] Miyano and co-workers pioneered the efforts to synthesize thiacalixarenes, analogues of calixarenes in which the methylene units are replaced by sulfur linkages (Scheme 1).[31−33] More recently, the coordination chemistry of *p*-*tert*-butylsulfonylcalix[4]arene (H_4TBSC) with metal ions and acetate was described.[34] Tetranuclear cluster complexes were obtained via assembly of the quadruply deprotonated $TBSC^{4-}$ ligand, metal cations [e.g., Mn(II), Co(II), and Ni(II)], and acetate anions, where four phenoxo and four sulfonyl oxygen atoms coordinate to four metal ions that are further bound by four acetate groups and one μ_4-hydroxo oxygen (Scheme 1). We reasoned that this tetranuclear moiety contains the desired curvature necessary for constructing molecular containers and could therefore serve as a useful building block for the assembly of nanosized metal–organic capsules if acetate were replaced by a bridging ligand such as 1,3,5-benzenetricarboxylate (BTC^{3-}) (Figure 1). We envisioned this approach to be particularly attractive, as it would offer several unique design features. Most importantly, employing macrocycles such as sulfonylcalixarenes as building blocks and utilizing their lower rim (in contrast to most previous efforts, which have targeted the upper rim of the macrocyclic precursors[2,4,8]) have the potential to provide capsules possessing both endo cavities and exo binding domains.[35] The inherent modularity of MOSCs due to their ternary composition (i.e., metal ions, sulfonylcalixarenes, and carboxylates) can also provide a myriad of possibilities for tuning their structural and functional properties.

Scheme 1. Molecular Structure of (left) Sulfonylcalix[4]arenes and (right) Tetranuclear Complexes



Reaction of nickel(II) nitrate or chloride salt, H_4TBSC,[31,32] and H_3BTC in *N*,*N*-dimethylformamide (DMF) at 100 °C for 24 h indeed afforded the expected container molecule. The compound, designated as **MOSC-1-Ni**, was isolated in a highly

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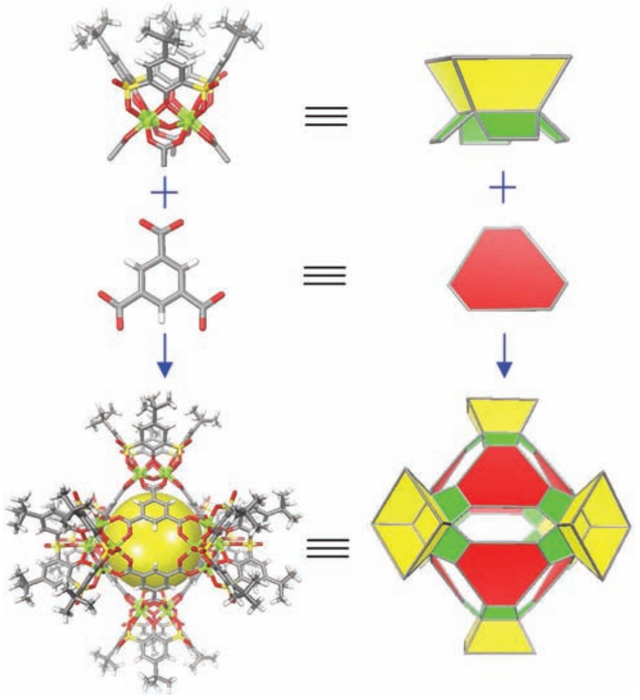

Figure 1. Design principle for the assembly of virus-like metal−organic supercontainers via binding of tetranuclear *p-tert*-butylsulfonylcalix[4]arene complexes with 1,3,5-benzenetricarboxylate. The yellow sphere serves to guide the eyes.

crystalline form and fully characterized by a range of techniques, including X-ray diffraction (XRD), thermogravimetric analysis (TGA), elemental analysis, Fourier transform IR spectroscopy (FTIR), UV−vis spectroscopy, NMR spectroscopy, mass spectrometry (MS), and gas/vapor adsorption.

Single-crystal XRD revealed that **MOSC-1-Ni** has exactly the predicted structure, which consists of six tetranuclear complex units bridged by eight BTC ligands, mimicking the shape of an octahedron (Figure 1). The tetranuclear units in **MOSC-1-Ni** bear a close resemblance to the discrete complexes reported previously.[34] Each Ni(II) center is octahedrally coordinated by one sulfonyl and two phenoxo O atoms from the TBSC^{4-} ligand, two carboxylate O atoms from BTC^{3-} ligands, and one μ_4-O from what appears to be a neutral solvent molecule (likely water) rather than the anionic OH^- species observed in the discrete complex (Figure S1 in the Supporting Information). The exact reason for this subtle difference remains unclear, although it is likely due to a lack of suitable cationic species in our reaction medium. The **MOSC-1-Ni** molecule has an outer diameter of ca. 3 nm, an inner diameter of ca. 1.4 nm, and an estimated internal volume of 0.55 nm^3 (Figure S7).[36] Notably, the capsule has rather small portals (with *static* dimensions of ca. 1.0 Å × 2.3 Å, after taking into account the van der Waals radii of the surface atoms), which can potentially serve as molecular sieves to allow access to its enclosed space only to the smallest guest molecules (e.g., H_2). While **MOSC-1-Ni** should ideally have O_h symmetry, the molecule is slightly distorted in the solid state (with C_{4h} symmetry) and crystallizes in the space group $I4/m$, adopting a pseudo-body-centered cubic (pseudo-bcc) packing mode. Most interestingly, each of the surface sulfonylcalix[4]arene units engages in multiple hydrophobic interactions with five other counterparts from adjacent capsules through their *tert*-butyl groups, forming a noncovalent, elongated octahedron resembling **MOSC-1-Ni** itself (Figure 2, left).[25] Therefore, there exist three separate domains of free volumes in the crystal structure of **MOSC-1-Ni**: the enclosed cavities of the coordination and noncovalent capsules and the interstitial space (Figure 2, right). The total potential solvent-accessible volume is ca. 53%, as calculated using the PLATON program.[37] These volumes are presumably filled with solvent molecules (i.e., DMF and/or H_2O), which are unfortunately highly disordered and could not be located by X-ray crystallography. Nevertheless, on the basis of the TGA and elemental analysis results, the empirical formula of **MOSC-1-Ni** is estimated to be $\{[(\mathrm{Ni}_4(\mu_4\text{-}\mathrm{H_2O})(\mathrm{TBSC})]_6(\mathrm{BTC})_8\}\cdot x\mathrm{DMF}\cdot y\mathrm{H_2O}$ ($x \approx y \approx 60$). **MOSC-1-Ni** appears to be a neutral molecule, as no evidence suggesting the presence of counterionic species could be found.

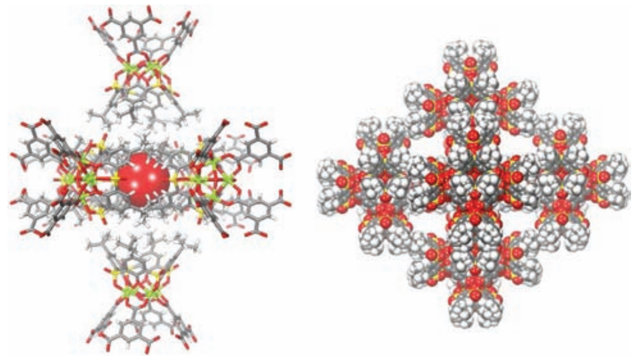

Figure 2. (left) Depiction of the noncovalent octahedral arrangement of six adjacent **MOSC-1-Ni** units. The large red sphere serves to guide the eyes. (right) Crystal packing diagram of **MOSC-1-Ni** showing the interstitial space.

The TGA data (Figure S8) indicate that **MOSC-1-Ni** is thermally stable and does not decompose until 400 °C. The ca. 10% weight loss starting at 200 °C is attributed to the escape of DMF molecules entrapped within the coordination capsule, as the onset temperature significantly exceeds the boiling point of DMF. The crystals of **MOSC-1-Ni** are remarkably robust and remain single-crystalline even when exposed to the atmosphere or soaked in many organic solvents (e.g., acetone) and water (Table S5). This high chemical stability is probably due to the robust coordination backbone of the capsule as well as its favorable crystal packing. While the as-synthesized (i.e., solvated) **MOSC-1-Ni** crystals remain intact in most solvents, the evacuated (i.e., desolvated) sample is moderately soluble in $\mathrm{CHCl_3}$ and $\mathrm{CH_2Cl_2}$, indicating the importance of solvation effects in achieving a higher solubility. Both UV−vis and MS results suggest that **MOSC-1-Ni** molecules remain essentially intact in solution (Figures S11, 12).

With the successful synthesis of **MOSC-1-Ni**, we decided to examine the robustness of our design strategy and the ability to modify the capsule structure. We first attempted the container synthesis with other metal ions. When the Ni(II) salt from the initial reaction was replaced with Co(II) and Mg(II) salts, two isomorphic crystals, designated as **MOSC-1-Co** and **MOSC-1-Mg**, respectively, were obtained. These compounds have identical capsule architectures and similar crystallographic features as **MOSC-1-Ni** (Tables S1 and S3). Variation of the metal ion appears to modify slightly several properties of the capsule, such as its thermal stability (Figure S9). It is also worth noting that **MOSC-1-Mg** should be more suitable for solution

NMR studies than the other isomorphs because of the diamagnetic nature of Mg(II) (Figure S13).

We next evaluated the feasibility of modifying the sulfonylcalix[4]arene unit in our container system. The synthetic chemistry of thiacalixarenes is relatively well established, and functional groups at the para position of the phenol residues can be readily manipulated.[33] We chose de-*p*-*tert*-butylsulfonylcalix[4]arene (H_4DTBSC) as an illustrative example (Scheme 1). When H_4TBSC was replaced with H_4DTBSC in the synthesis of **MOSC-1-Ni**, a new coordination supercontainer, designated as **MOSC-2-Ni**, was obtained. **MOSC-2-Ni** possesses a capsule framework that is rather similar to that of **MOSC-1-Ni** but has S_6 instead of C_{4h} symmetry. The molecule is characterized by a slightly shortened inner diameter (ca. 1.35 nm) and an appreciably reduced outer diameter (ca. 2.5 nm) due to the absence of the *tert*-butyl groups (Figure 3, left). Interestingly, while **MOSC-2-Ni** also forms noncovalent hexameric aggregates in the solid state through recognitions between surface sulfonylcalixarene units from adjacent capsules as in **MOSC-1-Ni**, the noncovalent assemblies have a somewhat distorted shape (Figure S16). **MOSC-2-Ni** crystallizes in the space group $R\bar{3}$ and assumes a pseudo-face-centered cubic (pseudo-fcc) packing mode. The adoption of such a close-packing arrangement in **MOSC-2-Ni**, as compared to the non-close-packed (bcc) arrangement of **MOSC-1-Ni**, is presumably enabled by the absence of the sterically more demanding *p-tert*-butyl groups. The successful assembly of **MOSC-2-Ni** highlights the great potential of functionalizing our container system, as a wide variety of functional groups can in principle be installed at the para position of the phenol residues of sulfonylcalix[4]arenes.[33]

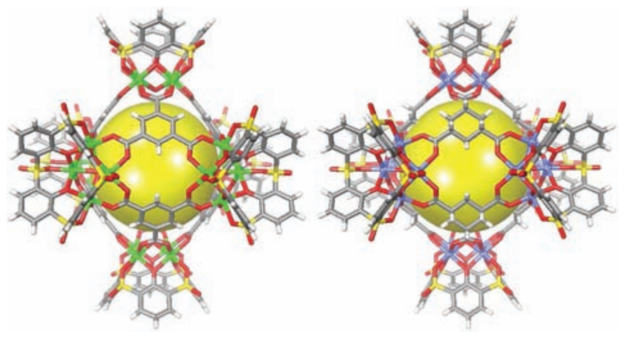

Figure 3. Structural representations of (left) **MOSC-2-Ni** and (right) **MOSC-3-Co**. The yellow spheres serve to guide the eyes.

Finally, we investigated the possibility of varying the carboxylate linker. Attempts to substitute the rigid, planar BTC^{3-} ligand with its more flexible counterpart, *cis*,*cis*-cyclohexane-1,3,5-tricarboxylate (CTC^{3-}), led to the isolation of a new coordination capsule, **MOSC-3-Co**, derived from Co(II), $DTBSC^{4-}$, and CTC^{3-}. **MOSC-3-Co** is isomorphic to **MOSC-2-Ni** (i.e., it has the same S_6 symmetry and crystallizes in the same space group, $R\bar{3}$) despite the obvious conformational differences between BTC^{3-} and CTC^{3-}. This finding is quite notable, as these two carboxylate ligands rarely give rise to isostructural metal–organic assemblies. The inherently flexible nature of CTC^{3-} is nevertheless anticipated to provide more dynamic features to **MOSC-3-Co** and allow easier access to its internal space. The discovery of **MOSC-3-Co** underlines the remarkable modularity of this unique supercontainer system. We further demonstrated that expanded tricarboxylate ligands afford similar MOSC structures with much larger endo cavities and more open portals. Indeed, the reaction of Co(II), $TBSC^{4-}$, and 1,3,5-benzenetribenzoate (BTB^{3-}) generated the enlarged container **MOSC-4-Co**, which has an almost identical molecular and crystal symmetry as **MOSC-1-Ni/Co/Mg** (i.e., C_{4h} point group and $I4/m$ space group, respectively) but significantly increased dimensions (Figures S6 and S19). **MOSC-4-Co** has an outer diameter of ca. 4 nm, an inner diameter of ca. 2.4 nm, and an estimated internal volume of 2.75 nm^3. The windows to its endo cavities have dimensions of ca. 4.8 Å × 5.2 Å, which are notably larger than those of the **MOSC-1** series. We note that during the submission process for our manuscript, a closely related system was reported by Liu et al.[38] This study provides further evidence suggesting that the synthesis of MOSCs is highly robust and can be extended to sulfide-based thiacalix[4]arene precursors.

Preliminary gas/vapor adsorption studies on crystals of MOSCs indicated that the materials are permanently porous, although their sorption profiles do not follow that of a classic type-I isotherm, and some of the MOSCs show interesting CO_2/N_2 selectivity. The Brunauer–Emmett–Teller (BET) surface area of **MOSC-1-Ni** was estimated to be ca. 230 cm^2/g on the basis of the N_2 adsorption isotherm at 77 K, and pronounced hysteresis was observed in all of the isotherms probed (i.e., N_2 at 77 K, CO_2 at 196 K, and benzene and methanol at 293 K; Figure S20). Unexpectedly, **MOSC-4-Co** appeared to have a BET surface area (ca. 250 cm^2/g) and gas/vapor sorption behaviors very similar to those of the **MOSC-1** family (Figure S21), despite its significantly expanded structure. This result implies that the observed sorption properties of MOSCs are likely due to their "extrinsic" porosity (i.e., the empty space formed by crystal packing) rather than the "intrinsic" porosity (i.e., the endo cavities).[39] Most interestingly, **MOSC-2-Ni** exhibited an unusually higher CO_2/N_2 sorption selectivity than the other MOSCs (Figure 4 and Figure S22). The exact origin of this unique selectivity is currently unclear, but further investigation to elucidate its working principle may offer new opportunities for gas separation applications.

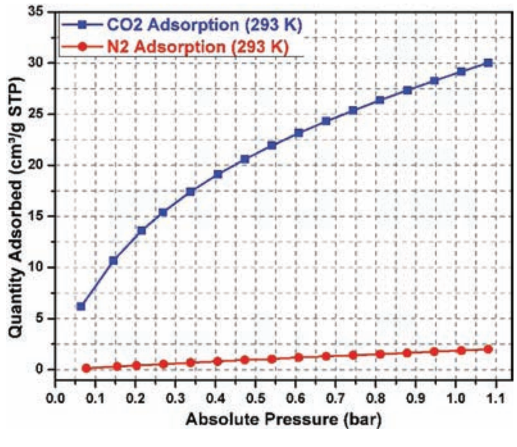

Figure 4. CO_2 and N_2 adsorption isotherms of **MOSC-2-Ni** under ambient conditions.

In summary, we have demonstrated a remarkably modular and robust approach for constructing synthetic receptors via coordination-driven assembling processes. A variety of metal ions, sulfonylcalix[4]arenes, and carboxylates can be employed to afford a new family of metal–organic supercontainer structures. These symmetric and highly unique coordination capsules contain both internal and surface cavities, a trademark feature of viruses, which use the enclosed space to store genetic materials (i.e., DNA or RNA) and the surface binding sites to recognize the specifically targeted hosts.[35] We believe the biomimetic *structural* attributes of our containers bode well for their potential *functional* applications, and we anticipate these intriguing molecules to be particularly promising for allosteric catalysis, biosensing, and controlled drug delivery. Certain aspects of these hypotheses are currently under investigation in our laboratory.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic procedures, characterization of all new compounds, and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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