Host–Guest Systems

Macrocycle Embrace: Encapsulation of Fluoroarenes by \textit{m}-Phenylene Ethynylene Host

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Abstract: We report structural characterization of a new member of \textit{m}-phenylene ethynylene ring family. This shape-persistent macrocycle also co-crystallizes with hexafluoro-, 1,2,4,5-tetrafluoro-, 1,3,5-trifluoro, and 1,4-difluorobenzene. The four complexes are almost isostructural, and all show the fluoroarene included into the central cavity of the macrocycle. Characterized by multiple short C–H···F/C0 contacts, these inclusion complexes further dimerize in the solid state into a 2+2 assembly, in which the two macrocycles embrace each other by their large hydrophobic groups that are rotated by 60° relative to one another.

Shape-persistent macrocycles constructed from arylene and ethynylene structural motifs\textsuperscript{[1]} are characterized by rigid structures and modular synthesis, which make them promising building blocks for the construction of nanoporous solids, liquid crystals, materials for non-linear optics, molecular electronic components, sensors, and microscopic reactors. Well-defined central cavities also suggest that phenylene ethynylene macrocycles (PEMs) should function as versatile supramolecular hosts. Smaller members of this class, in which connections between the rings are \textit{ortho}-positioned, have a cavity, which can typically fit only a single atom. These macrocycles,\textsuperscript{[2]} as well as their metal complexes (in which the metal atom often resides in the center of the cavity),\textsuperscript{[2b, 3]} and complexes with external solvent molecule guests\textsuperscript{[4]} have all been structurally studied. Significantly larger \textit{para}-connected PEMs, often dubbed paraphenyleneacetylenes or “carbon nanorings” on account of their hoop-like nonplanar structures, are less common,\textsuperscript{[5]} but have been shown to include alkylated benzenes\textsuperscript{[5a]} and fullerences\textsuperscript{[5b]} in their central cavities. In contrast, \textit{meta}-connected systems, which are close-to-planar and have a sizable cavity in their center, have been characterized crystallographically\textsuperscript{[6]} including the large shape-persistent systems of Höger\textsuperscript{[7]} and Schlüter\textsuperscript{[8]} but notably in the absence of guests in the central cavity. The only exception are Schlüter’s\textsuperscript{[8]} very large PEMs, which have been shown to crystallize with three ordered molecules of benzene.

Herein, we present a series of four X-ray crystal structures that show that \textit{m}-phenylene ethynylene macrocycle \textit{1} (Figure 1, top) can bind several fluorinated benzenes in an isostructural fashion and 1:1 stoichiometry. These are among the first crystallographically characterized complexes of planar arylene ethynylene macrocycles with included molecular guests.\textsuperscript{[9]}

Compound \textit{1} was synthesized by using a modification of a literature procedure, which is presented in the Supporting Information. Its single crystals were grown by the slow evaporation of a biphasic system, in which the top layer was EtOH and

Figure 1. Macrocyclic \textit{m}-phenylene ethynylene host \textit{1} (top) and its crystal structure (bottom). Thermal ellipsoids are shown at 50% probability.
the bottom layer was a solution of 1 in dichloromethane. Compound 1 crystallizes in P3121 space group, with six molecules of 1 per unit cell. The structure of the macrocycle (Figure 1, bottom) is close to planar, with one of the benzene rings notably distorting from the average plane by 14.7(4)°. Deviations in the triple bonds are minimal: all C=C=C angles are greater than 176.7(3)°. Transannular distances, defined as the distances between the internal hydrogen atoms positioned furthest away from each other across the macrocycle, are 8.63(1), 8.77(1), and 9.02(1) Å.[10] Complex of 1 with 1,4-difluorobenzene (1·C6H4F2) was crystallized by the slow evaporation of a biphasic system, in which the bottom layer contained a solution of 1 in dichloromethane, and the top layer was neat 1,4-difluorobenzene. The two co-crystallize (Figure 2 A, top) in P21/n space group with four molecules of each compound in the unit cell. The structure of the co-crystal shows difluorobenzene included in the central cavity of the macrocycle, with the small but noticeable tilt (13.2(4)°) between the average planes of the guest and the host (excluding the pendant COCEt3 groups). The larger ring does not appear to significantly contract to match difluorobenzene, and the transannular H···H distances in 1 are 8.65(1), 8.83(1), and 8.88(1) Å. Fluorine atoms in trifluorobenzene again establish short contacts with neighboring hydrogens of the macrocycle, characterized by the following H···F distances and C=C···F angles: 2.37(1)Å/147.9(1)°, 2.50(1)Å/146.2(1)°, 2.51(1)Å/138.3(1)°, 2.53(1)Å/145.9(1)°, 2.57(1)Å/148.8(1)°, and 2.77(1)Å/140.0(1)°. Again, and as shown in Figure 2 B, bottom, the two macrocycles interdigitate through their hydrophobic group, encapsulating two molecules of 1,3,5-trifluorobenzene, which are in an antiparallel orientation. Tetrafluorobenzene (1,2,4,5-isomer) co-crystallized with 1 in an isostructural arrangement as its di- and trifluorinated counterparts (Figure 2 C, top). The crystals of this complex grew after seven days from a system in which 1,2,4,5-tetrafluorobenzene was layered onto a solution of 1 in dichloromethane. Once again, 1 essentially does not deform to accommodate C6H2F4, with transannular H···H distances of 8.60(1), 8.80(1), and 8.98(1) Å, and the most distorted benzene ring forming an angle of 12.8(5)° with the average plane of the macrocycle.

Figure 2. Crystal structures of complexes of 1 with 1,2-difluorobenzene (A), 1,3,5-trifluorobenzene (B), and 1,2,4,5-tetrafluorobenzene (C). Top row shows the structure of the complex (thermal ellipsoids presented at 50% probability), whereas the bottom row shows "embraced" dimers of macrocycle 1, in which each macrocycle includes a molecule of fluorinated arene guest into its central cavity.
Average planes of the host and its fluorinated guest are at an angle of 13.0(4). Eight short H-F contacts are observed in the structure of \(1\text{-C}_6\text{H}_2\text{F}_4\); they range in their H-F distances between 2.31(1) and 2.61(1) Å, whereas the corresponding C-H-F angles vary in the 137.5(1)–151.2(1)° region. As with the previous two superstructures, the embraced dimer is observed in the packing diagram (Figure 2C, bottom).

Hexafluorobenzene also co-crystallizes with \(1\) (crystals grown under identical conditions as those of \(1\text{-C}_6\text{H}_2\text{F}_4\)), but this complex has a slightly different structure. The space group here changes to \(P2_1/c\), with four molecules of each compound in the unit cell. Transannular H-H distances in \(1\) are similar to all other complexes (8.74(1), 8.92(1), 8.94(1) Å), but one of the benzene rings of \(1\) now puckers out of the average plane significantly (by 23.8(2)°), resulting in an overall envelope conformation of \(1\). Similar to all other fluoroarenes studied, \(C_6F_6\) is clearly included in the cavity of \(1\) (Figure 3, top), with the tilt angle between the average planes of the host and the guest measuring 8.2(3)°. Short H-F contacts are once again observed, with H-F distances in the 2.39(1)–2.60(1) Å range, and C-H-F angles varying between 135.3(6) and 148.1(6)°. Although the structure of \(1\text{-C}_6\text{F}_6\) resembles its relatives quite closely, its supramolecular organization, shown in Figure 3, bottom, is slightly different: the two macrocycles slip out of the embrace, bringing their bulky alkyl groups into close contact with each other. It should be noted that this crystal structure is of somewhat poorer quality than the preceding four: a problem that persisted even when two separate batches of crystals were used for data collection and refinement.

Despite extensive efforts, we were not able to grow co-crystals of \(1\) with benzene and obtain experimental evidence of the importance of fluorination in this series of self-assembled structures. Therefore, we turned to computation (at the B97-D/TZV(2d,2p) level) to make this comparison.\(^{[13]}\) To simplify the computations, 1 was replaced with analogue 2, in which the three pendant –COOCE\(_3\) groups of 1 were replaced with –COOMe. Supramolecular gas-phase association of 2 was examined with both benzene and hexafluorobenzene. Both cases revealed potential-energy surfaces with numerous, nearly isoenergetic local minima. In both cases, the structures, in which the benzene or perfluorobenzene adopts a planar orientation within the cavity of 2, were saddle points on the energy surfaces, not stable minima. However, for benzene, the energy is lowered by only <0.3 kcal mol\(^{-1}\) if the ring either tilts slightly within the cavity or hovers just outside of the cavity. That is, for benzene, very little energy is required for complete insertion into the cavity. For perfluorobenzene, there is a 2 kcal mol\(^{-1}\) drop in energy going from the fully inserted arrangement to either a tilted arrangement or complex in which the perfluorobenzene hovers 1 Å above the plane of 2. Regardless, this suggests only a moderate cost for \(C_6F_6\) adopting a fully planar orientation inside of 2. Also, for perfluorobenzene, we identified two complexes in which the perfluorobenzene engages in [π−π] stacking interactions with one of the phenyl rings of 2, both of which are approximately 2 kcal mol\(^{-1}\) lower in energy than complexes in which perfluorobenzene resides either within or just outside of the cavity (see the Supporting Information for additional details). Although this is clearly in contrast with the observed crystal structure, we note that the complexes, in which \(C_6F_6\) is positioned outside of the cavity, would be much less amenable to close packing of 1 and would presumably leave a void in the middle of 1. On the other hand, with perfluorobenzene fully inside the cavity of 1, the modest loss in interaction energy could easily be compensated for by the more favorable packing of 1 in the solid state. For benzene, the analogous complexes, in which benzene engages in [C−H−π] interactions with one of the phenyl rings of 2 are of similar energy to complexes featuring benzene in or just outside of the cavity.\(^{[14]}\)

We could observe no evidence of similar interactions between 1 and fluoroarenes in solution. Titration of 1 with \(C_6F_6\) led to no observable changes in its \(^1\)H and \(^19\)F NMR or UV/Vis spectra.\(^{[15]}\) This situation is analogous to the case of hydrocarbon inclusion in the cavities of cyclic paraphenyleneacetylenes, in which no analogous binding was observed in solution.\(^{[5a]}\)

In summary, we have shown that the shape-persistent macrocyclic host 1 can accommodate several fluorinated benzenes in its central cavity, with minimal structural deformations needed. Our results suggest that host–guest chemistry of

![Figure 3. Top: crystal structure of \(1\text{-C}_6\text{F}_6\) (thermal ellipsoids shown at 50% probability). Bottom: the slipped-stack arrangement of the two host–guest complexes within the unit cell.](image-url)
planar m-phenylene ethylene macrocycles may be much richer than previously thought. The observed binding of fluorinated arenes appears to be a combined consequence of crystallographic close packing, an optimal steric match with the host and, possibly, weak [C–H⋯F–C] hydrogen bonds. It would be intriguing to examine whether other guests could be included in the cavity of 1, possibly using other intramolecular binding interactions. For example, Flood and co-workers have demonstrated that anions can be bound in macrocyclic cavities through the exclusive use of C–H hydrogen bond donors. In that respect, azo-derivatized analogues of [12,17] may sufficiently alter its electronic properties to allow observation of anion binding, perhaps even in solution. Another area of interest is looking at fluorinated arenes too large to fit snugly within the cavity of 1, whether they will instead thread through it, offering a route to a new class of rigid rotaxanes. We hope that future work in our laboratories may provide answers to these questions.

**Experimental Section**

Crystallographic information for compound 1: C₇₉H₆₈F₁₂O₆·C₆F₆, Mᵣ = 1129.29 g mol⁻¹; crystal dimensions 0.30 × 0.25 × 0.25 mm³; trigonal crystal system; space group P3,21; unit-cell dimensions: a = 23.6003(3) Å, β = 90.00°, c = 19.7136(3) Å, γ = 120.00°, V = 9508.92(1) Å³; Z = 6; ρｃｄｃｌ = 1.838 Mgm⁻³; μ = 1.338 mm⁻¹; radiation wavelength 1.54178 Å; θ = 123(2)°; θｃｍａｘ = 66.62°; 65393 measured reflections (out of which 5543 independent); Rₑ = 0.045; Rω = 0.313; largest diff. peak and hole: 1.371 and −0.611 e Å⁻³.

Crystallographic information for complex 1·C₆H₄F₂: C₆H₄F₂O₃, Mᵣ = 1141.34 g mol⁻¹; crystal dimensions 0.40 × 0.06 × 0.06 mm³; monoclinic crystal system; space group P2₁/n; unit-cell dimensions: a = 7.5333(1) Å, β = 90.00°, c = 22.7598(4) Å, β = 93.686(1)°, V = 36.8754(7) Å³, γ = 90.00°, V = 6309. 44(18) Å³; Z = 4; ρｃｄｃｌ = 1.202 Mgm⁻³; μ = 0.626 mm⁻¹; radiation wavelength 1.54178 Å; θ = 113(2)°; θｃｍａｘ = 66.53°; 43 173 measured reflections (out of which 10 995 independent); Rₑ = 0.0324; Rω = 0.1145; largest diff. peak and hole: 0.366 and −0.408 e Å⁻³.

Crystallographic information for complex 1·C₆H₄F₂: C₆H₄F₂O₃·C₆F₆, Mᵣ = 1159.33 g mol⁻¹; crystal dimensions 0.40 × 0.10 × 0.08 mm³; monoclinic crystal system; space group P2₁/n; unit-cell dimensions: a = 6.7640(4) Å, β = 90.00°, c = 22.7572(3) Å, β = 94.2461(1)°, V = 36.5575(5) Å³, γ = 90.00°, V = 6345.26(15) Å³; Z = 4; ρｃｄｃ𝑙 = 1.214 Mgm⁻³; μ = 0.654 mm⁻¹; radiation wavelength 1.54178 Å; θ = 113(2)°; θｃｍａ𝑥 = 62.42°; 41 749 measured reflections (out of which 10 379 independent); Rₑ = 0.1301; Rω = 0.2172; largest diff. peak and hole: 0.433 and −0.409 e Å⁻³.

Crystallographic information for complex 1·C₆H₄F₂: C₆H₄ClF₂O₄·C₆F₆, Mᵣ = 1177.32 g mol⁻¹; crystal dimensions 0.40 × 0.12 × 0.10 mm³; monoclinic crystal system; space group P2₁/n; unit-cell dimensions: a = 7.6495(4) Å, β = 90.00°, c = 22.7639(10) Å, β = 94.466(2)°, V = 36.5143(16) Å³, γ = 90.00°, V = 6339.03(5) Å³; Z = 4; ρｃｄｃℓ = 1.234 Mgm⁻³; μ = 0.866 mm⁻¹; radiation wavelength 1.54178 Å; θ = 123(2)°; θｃｍａｘ = 66.62°; 43 547 measured reflections (out of which 11 027 independent); Rₑ = 0.0237; Rω = 0.0541; wR₂ = 0.1532; largest diff. peak and hole: 0.456 and −0.621 e Å⁻³.

Crystallographic information for complex 1·C₆H₄F₂: C₆H₄ClF₂O₄·C₆F₆, Mᵣ = 1298.23 g mol⁻¹; crystal dimensions 0.38 × 0.03 × 0.02 mm³; monoclinic crystal system; space group P2₁/c; unit-cell dimensions: a = 10.8228(3) Å, β = 90.00°, b = 28.4588(7) Å, γ = 98.1522(13)°, c = 21.9360(6) Å, γ = 90.00°, V = 6688.13(1) Å³; Z = 4; ρｃｄｃℓ = 1.299 Mgm⁻³; μ = 0.166 mm⁻¹; radiation wavelength 0.71073 Å; θ = 173(2)°; θｃｍａ𝑥 = 27.5°; 35 099 measured reflections (out of which 25 453 independent); Rₑ = 0.045; Rω = 0.366; largest diff. peak and hole: 1.371 and −0.611 e Å⁻³.

**CCDC**

The Cambridge Crystallographic Data Centre contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Additional experimental data can be found in the Supporting Information.

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