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Host–Guest Systems

Macrocycle Embrace: Encapsulation of Fluoroarenes by *m*-Phenylene Ethynylene Host

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Abstract: We report structural characterization of a new member of *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–C 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[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 *ortho*-positioned, have a cavity, which can typically fit only a single atom. These macrocycles,[2] as well as their metal complexes (in which the metal atom often resides in the center of the cavity),[2b,3] and complexes with external solvent molecule guests[4] have all been structurally studied. Significantly larger *para*-connected PEMs, often dubbed para-phenyleneacetylenes or "carbon nanorings" on account of their hoop-like nonplanar structures, are less common,[5] but have been shown to include alkylated benzenes[5a] and fullerenes[5b] in their central cavities. In contrast, *meta*-connected systems, which are close-to-planar and have a sizable cavity in their center, have been characterized crystallographically,[6] including the large shape-persistent systems of Höger[7] and Schlüter,[8] but notably in the absence of guests in the central cavity. The only exception are Schlüter's[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 *m*-phenylene ethynylene macrocycle **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.[9]

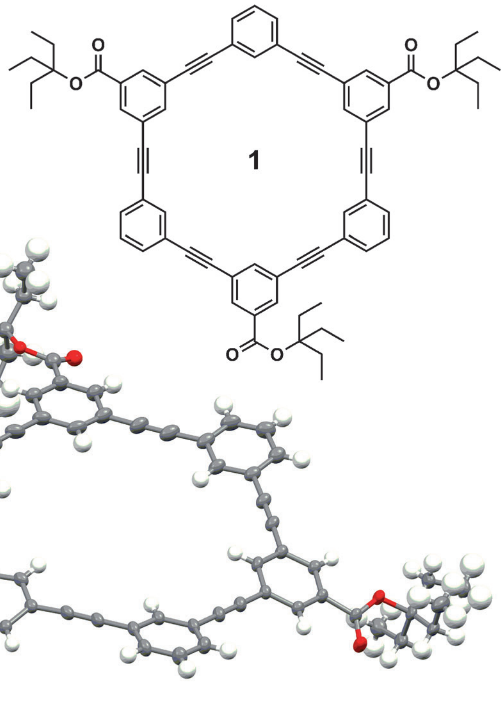

Figure 1. Macrocyclic *m*-phenylene ethynylene host **1** (top) and its crystal structure (bottom). Thermal ellipsoids are shown at 50% probability.

Compound **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

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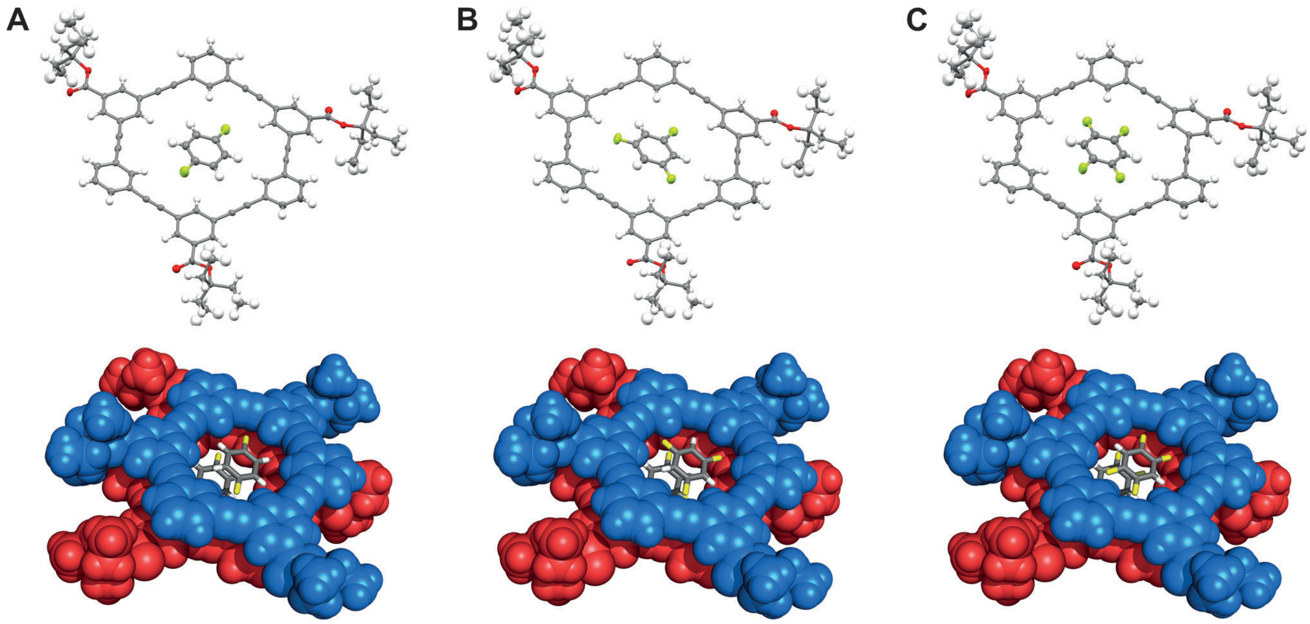

Figure 2. Crystal structures of complexes of **1** with 1,2-difluorobenzene (A), 1,3,5-trifluorobenzene (B), and 1,2,4,5,-tetrafluorobenzene (C). Top row shows the structure of the complex (thermal ellipsoids presented at 50 % probability), whereas the bottom row shows "embraced" dimers of macrocycle **1**, in which each macrocycle includes a molecule of fluorinated arene guest into its central cavity.

the bottom layer was a solution of **1** in dichloromethane. Compound **1** crystallizes in $P3_121$ 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 ($\mathbf{1}\cdot C_6H_4F_2$) 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 $P2_1/n$ 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 $COOCEt_3$ groups). The larger ring does not appear to significantly contract to match difluorobenzene, and the transannular H–H distances are rather similar to those observed in the crystal structure of "empty" **1**: 8.44(1), 8.93(1), and 8.98(1) Å. Each of the two fluorine atoms of difluorobenzene establishes short contacts with two internal hydrogens from the benzene rings of **1**. These contacts are characterized by H···F distances of 2.36(1), 2.44(1), 2.57(1), and 2.65(1) Å, and C–H···F angles of 155.4(1), 142.7(1), 152.0(1), and 149.6(1)° (given in the same order as the distances). Thus, some of them could be interpreted as weak C–H···F–C hydrogen bonds,[11] as they are generally shorter than the sum of van der Waals radii for hydrogen and fluorine (2.67 Å).

This inclusion complex dimerizes in the solid state; as shown in Figure 2 A, bottom, two molecules of **1** stack on top of each other, but rotated by 60° relative to one another. This rotation allows their bulky $COOCEt_3$ pendant groups to avoid steric hindrance; in effect, the two macrocycles "embrace" each other,[12] and each one of them includes a 1,4-difluorobenzene guest molecule.

A very similar structure is observed for the complex of **1** and 1,3,5-trifluorobenzene ($\mathbf{1}\cdot C_6H_3F_3$, shown in Figure 2 B), which was crystallized under identical conditions. This couple also crystallizes in the $P2_1/n$ space group with four molecules of each compound in the unit cell. Tilt angle between the averaged planes of the macrocyclic host and the trifluorobenzene guest is 14.8(4)°, whereas 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–H···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 $C_6H_2F_4$, 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.

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**·$C_6H_2F_4$; 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**·$C_6H_2F_4$), 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**·C_6F_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.

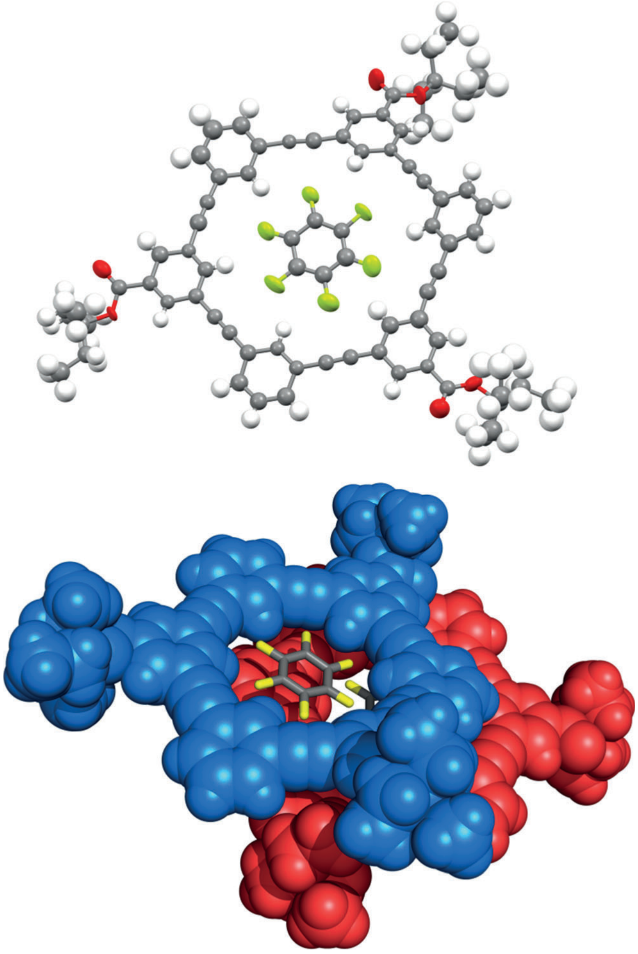

Figure 3. Top: crystal structure of **1**·C_6F_6 (thermal ellipsoids shown at 50% probability). Bottom: the slipped-stack arrangement of the two host–guest complexes within the unit cell.

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 –COOCEt$_3$ 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 $<0.3\ \mathrm{kcal\,mol^{-1}}$ 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 $2\ \mathrm{kcal\,mol^{-1}}$ 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 $2\ \mathrm{kcal\,mol^{-1}}$ 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 ^1H 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 planar *m*-phenylene ethynylene 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 amply demonstrated[16] that anions can be bound in macrocyclic cavities through the exclusive use of C–H hydrogen bond donors. In that respect, aza-derivatized analogues of **1**[9,12,17] 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**: $C_{73}H_{69.90}Cl_2O_{6.95}$, $M_r=1129.29\ g\,mol^{-1}$; crystal dimensions $0.30\times0.25\times0.25\ mm^3$; trigonal crystal system; space group $P3_121$; unit-cell dimensions: $a=23.6003(3)$ Å, $\alpha=90.00^\circ$, $b=23.6003(3)$ Å, $\beta=90.00^\circ$, $c=19.7136(3)$ Å, $\gamma=120.00^\circ$, $V=9508.9(2)$ Å^3; $Z=6$; $\rho_{calcd}=1.183\,Mg\,m^{-3}$; $\mu=1.338\ mm^{-1}$; radiation wavelength 1.54178 Å; $T=123(2)$ K; $\theta_{max}=66.62^\circ$; 65395 measured reflections (out of which 11107 independent); $R_{int}=0.0242$; $R_1=0.0464$; $wR_2=0.1296$; largest diff. peak and hole: 0.483 and -0.362 e Å^{-3}.

Crystallographic information for complex $\mathbf{1}\cdot C_6H_4F_2$: $C_{78}H_{70}F_2O_6$, $M_r=1141.34\ g\,mol^{-1}$; crystal dimensions $0.40\times0.08\times0.06\ mm^3$; monoclinic crystal system; space group $P2_1/n$; unit-cell dimensions: $a=7.5333(1)$ Å, $\alpha=90.00^\circ$, $b=22.7598(4)$ Å, $\beta=93.686(1)^\circ$, $c=36.8754(7)$ Å, $\gamma=90.00^\circ$, $V=6309.\ 44(18)$ Å^3; $Z=4$; $\rho_{calcd}=1.202\,Mg\,m^{-3}$; $\mu=0.626\ mm^{-1}$; radiation wavelength 1.54178 Å; $T=113(2)$ K; $\theta_{max}=66.53^\circ$; 43173 measured reflections (out of which 10995 independent); $R_{int}=0.0234$; $R_1=0.0438$; $wR_2=0.1145$; largest diff. peak and hole: 0.366 and -0.408 e Å^{-3}.

Crystallographic information for complex $\mathbf{1}\cdot C_6H_3F_3$: $C_{78}H_{69}F_3O_6$, $M_r=1159.33\ g\,mol^{-1}$; crystal dimensions $0.40\times0.10\times0.08\ mm^3$; monoclinic crystal system; space group $P2_1/n$; unit-cell dimensions: $a=7.6480(41)$ Å, $\alpha=90.00^\circ$, $b=22.7572(3)$ Å, $\beta=94.246(1)^\circ$, $c=36.5575(5)$ Å, $\gamma=90.00^\circ$, $V=6345.26(15)$ Å^3; $Z=4$; $\rho_{calcd}=1.214\,Mg\,m^{-3}$; $\mu=0.654\ mm^{-1}$; radiation wavelength 1.54178 Å; $T=113(2)$ K; $\theta_{max}=62.42^\circ$; 41749 measured reflections (out of which 10379 independent); $R_{int}=0.1301$; $R_1=0.0628$; $wR_2=0.1712$; largest diff. peak and hole: 0.433 and -0.409 e Å^{-3}.

Crystallographic information for complex $\mathbf{1}\cdot C_6H_2F_4$: $C_{78}H_{68}F_4O_6$, $M_r=1177.32\ g\,mol^{-1}$; crystal dimensions $0.40\times0.12\times0.10\ mm^3$; monoclinic crystal system; space group $P2_1/n$; unit-cell dimensions: $a=7.6495(4)$ Å, $\alpha=90.00^\circ$, $b=22.7639(10)$ Å, $\beta=94.466(2)^\circ$, $c=36.5143(16)$ Å, $\gamma=90.00^\circ$, $V=6339.0(5)$ Å^3; $Z=4$; $\rho_{calcd}=1.234\,Mg\,m^{-3}$; $\mu=0.686\ mm^{-1}$; radiation wavelength 1.54178 Å; $T=123(2)$ K; $\theta_{max}=66.62^\circ$; 43547 measured reflections (out of which 11027 independent); $R_{int}=0.0237$; $R_1=0.0541$; $wR_2=0.1532$; largest diff. peak and hole: 0.456 and -0.621 e Å^{-3}.

Crystallographic information for complex $\mathbf{1}\cdot C_6F_6$: $C_{79}H_{68}Cl_2F_6O_6$, $M_r=1298.23\ g\,mol^{-1}$; crystal dimensions $0.38\times0.03\times0.02\ mm^3$; monoclinic crystal system; space group $P2_1/c$; unit-cell dimensions: $a=10.8228(3)$ Å, $\alpha=90.00^\circ$, $b=28.4588(7)$ Å, $\beta=98.1522(13)^\circ$, $c=21.9360(6)$ Å, $\gamma=90.00^\circ$, $V=6688.1(3)$ Å^3; $Z=4$; $\rho_{calcd}=1.289\,Mg\,m^{-3}$; $\mu=0.168\ mm^{-1}$; radiation wavelength 0.71073 Å; $T=173(2)$ K; $\theta_{max}=27.5^\circ$; 15099 measured reflections (out of which 5453 independent); $R_{int}=0.045$; $R_1=0.144$; $wR_2=0.366$; largest diff. peak and hole: 1.371 and -0.611 e Å^{-3}.

CCDC-1015944 (**1**), CCDC-1015943 ($\mathbf{1}\cdot C_6H_4F_2$), CCDC-1015946 ($\mathbf{1}\cdot C_6H_3F_3$), CCDC-1015945 ($\mathbf{1}\cdot C_6H_2F_4$), and CCDC-1015947 ($\mathbf{1}\cdot C_6F_6$) contain 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.

All computations utilized Gaussian 09[18] and were carried out at the B97-D/TZV(2d,2p) level of theory.[13] All structures were fully optimized and harmonic vibrational frequencies computed to confirm that the structures located were energy minima.

Additional experimental data can be found in the Supporting Information.

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Keywords: fluoroarenes · inclusion complexes · macrocycles · shape persistency · X-ray diffraction

[1] For reviews, see: a) W. Zhang, J. S. Moore, *Angew. Chem. Int. Ed.* **2006**, *45*, 4416–4439; *Angew. Chem.* **2006**, *118*, 4524–4548; b) D. Zhao, J. S. Moore, *Chem. Commun.* **2003**, 807–818; c) D. E. Gross, L. Zang, J. S. Moore, *Pure Appl. Chem.* **2012**, *84*, 869–878; d) K. Campbell, R. R. Tykwinski in *Carbon-Rich Compounds: From Molecules to Materials* (Eds.: M. M. Haley, R. R. Tykwinski), Wiley-VCH, Weinheim, **2006**, pp. 229–294.

[2] a) M. Dudič, I. Císařová, J. Michl, *J. Org. Chem.* **2012**, *77*, 68–74; b) D. Solooki, J. D. Bradshaw, C. A. Tessier, W. J. Youngs, R. F. See, M. Churchill, J. D. Ferrara, *J. Organomet. Chem.* **1994**, *470*, 231–236; c) K. P. Baldwin, R. S. Simons, J. Rose, P. Zimmerman, D. M. Hercules, C. A. Tessier, W. J. Youngs, *Chem. Commun.* **1994**, 1257–1258; d) S. Nobusue, Y. Mukai, Y. Fukumoto, R. Umeda, K. Tahara, M. Sonoda, Y. Tobe, *Chem. Eur. J.* **2012**, *18*, 12814–12824; e) H. M. Cho, H. Weissman, J. S. Moore, *J. Org. Chem.* **2008**, *73*, 4256–4258; f) M. Kiguchi, K. Tahara, Y. Takahashi, K. Hasui, Y. Tobe, *Chem. Lett.* **2010**, *39*, 788–789; g) N. Fuentes, A. Martin-Lasanta, L. Alvarez de Cienfuegos, R. Robles, D. Choquesillo-Lazarte, J. M. García-Ruiz, L. Martínez-Fernández, I. Corral, M. Ribagorda, A. J. Mota, D. J. Cárdenas, M. C. Carreño, J. M. Cuerva, *Angew. Chem. Int. Ed.* **2012**, *51*, 13036–13040; *Angew. Chem.* **2012**, *124*, 13213–13217; h) H. Hinrichs, A. K. Fischer, P. G. Jones, H. Hopf, M. M. Haley, *Org. Lett.* **2005**, *7*, 3793–3795; i) C. Eickmeier, H. Junga, A. J. Matzger, F. Scherhag, M. Shim, K. P. C. Vollhardt, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2103–2108; *Angew. Chem.* **1997**, *109*, 2194–2199; j) K. Tahara, T. Fujita, M. Sonoda, M. Shiro, Y. Tobe, *J. Am. Chem. Soc.* **2008**, *130*, 14339–14345; k) I. Hisaki, E. Kometani, H. Shigemitsu, A. Saeki, S. Seki, N. Tohnai, M. Miyata, *Cryst.*

Growth Des. **2011**, *11*, 5488–5497; l) H. Irngartinger, L. Leiserowitz, G. M. J. Schmidt, *J. Chem. Soc. B* **1970**, 497–504; m) H. Shigemitsu, I. Hisaki, E. Kometani, D. Yasumiya, Y. Sakamoto, K. Osaka, T. S. Thakur, A. Saeki, S. Seki, F. Kimura, T. Kimura, N. Tohnai, M. Miyata, *Chem. Eur. J.* **2013**, *19*, 15366–15377; n) M. M. Haley, M. L. Bell, J. J. English, C. A. Johnson, T. J. R. Weakley, *J. Am. Chem. Soc.* **1997**, *119*, 2956–2957; o) K. P. Baldwin, A. J. Matzger, D. A. Scheiman, C. A. Tessier, K. P. C. Vollhardt, W. J. Youngs, *Synlett* **1995**, 1215–1218; p) O. Š. Miljanić, K. P. C. Vollhardt, G. D. Whitener, *Synlett* **2003**, 29–34; q) I. Hisaki, N. Manabe, K. Osaka, A. Saeki, S. Seki, N. Tohnai, M. Miyata, *Bull. Chem. Soc. Jpn.* **2013**, *86*, 322–333; r) J. J. Pak, T. J. R. Weakley, M. M. Haley, D. Y. K. Lau, J. F. Stoddart, *Synthesis* **2002**, 1256–1260; s) J. J. Pak, T. J. R. Weakley, M. M. Haley, *J. Am. Chem. Soc.* **1999**, *121*, 8182–8192; t) T. Nishinaga, Y. Miyata, N. Nodera, K. Komatsu, *Tetrahedron* **2004**, *60*, 3375–3382; u) L. Guo, J. D. Bradshaw, C. A. Tessier, W. J. Youngs, *J. Chem. Soc. Chem. Commun.* **1994**, 243–244.

[3] a) J. D. Ferrara, C. Tessier-Young, W. J. Youngs, *J. Am. Chem. Soc.* **1985**, *107*, 6719–6721; b) J. D. Ferrara, C. Tessier-Youngs, W. J. Youngs, *Organometallics* **1987**, *6*, 676–678; c) J. D. Ferrara, A. Djebli, C. Tessier-Youngs, W. J. Youngs, *J. Am. Chem. Soc.* **1988**, *110*, 647–649; d) A. Djebli, J. D. Ferrara, C. Tessier-Youngs, W. J. Youngs, *Chem. Commun.* **1988**, 548–549; e) J. D. Ferrara, C. Tessier-Youngs, W. J. Youngs, *Inorg. Chem.* **1988**, *27*, 2201–2202; f) M. Iyoda, T. Horino, F. Takahashi, M. Hasegawa, M. Yoshida, Y. Kuwatani, *Tetrahedron Lett.* **2001**, *42*, 6883–6886; g) W. J. Youngs, J. D. Kinder, J. D. Bradshaw, C. A. Tessier, *Organometallics* **1993**, *12*, 2406–2407.

[4] a) I. Hisaki, H. Senga, Y. Sakamoto, S. Tsuzuki, N. Tohnai, M. Miyata, *Chem. Eur. J.* **2009**, *15*, 13336–13340; b) A. J. Matzger, M. Shim, K. P. C. Vollhardt, *Chem. Commun.* **1999**, 1871–1872; c) I. Hisaki, Y. Sakamoto, H. Shigemitsu, N. Tohnai, M. Miyata, S. Seki, A. Saeki, S. Tagawa, *Chem. Eur. J.* **2008**, *14*, 4178–4187; d) I. Hisaki, H. Senga, H. Shigemitsu, N. Tohnai, M. Miyata, *Chem. Eur. J.* **2011**, *17*, 14348–14353; e) H. Shigemitsu, I. Hisaki, E. Kometani, N. Tohnai, M. Miyata, *Chem. Lett.* **2012**, *41*, 1535–1537.

[5] a) T. Kawase, Y. Seirai, H. R. Darabi, M. Oda, Y. Sarakai, K. Tashiro, *Angew. Chem. Int. Ed.* **2003**, *42*, 1621–1624; *Angew. Chem.* **2003**, *115*, 1659–1662; b) T. Kawase, K. Tanaka, N. Fujiwara, H. R. Darabi, M. Oda, *Angew. Chem. Int. Ed.* **2003**, *42*, 1624–1628; *Angew. Chem.* **2003**, *115*, 1662–1666. For an example of a system with both *ortho*- and *para*-linkages, see: c) J. Luo, Q. Yan, Y. Zhou, T. Li, N. Zhu, C. Bai, Y. Cao, J. Wang, J. Pei, D. Zhao, *Chem. Commun.* **2010**, *46*, 5725–5727.

[6] For phenylene ethynylene macrocycles with one or more *meta*-linkages and with three benzene rings, see: a) T. Kawase, N. Ueda, M. Oda, *Tetrahedron Lett.* **1997**, *38*, 6681–6684; b) Y. Tobe, J.-y. Kishi, I. Ohki, M. Sonoda, *J. Org. Chem.* **2003**, *68*, 3330–3332. For those with four benzene rings, see: c) T. Kawase, N. Ueda, H. R. Darabi, M. Oda, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1556–1558; *Angew. Chem.* **1996**, *108*, 1658–1660; d) T. Kawase, Y. Hosokawa, H. Kurata, M. Oda, *Chem. Lett.* **1999**, 745–746. Five benzene rings: e) J. Yamakawa, M. Ohkoshi, F. Takahashi, T. Nishiuchi, Y. Kuwatami, T. Nishinaga, M. Yoshida, M. Iyoda, *Chem. Lett.* **2008**, *37*, 784–785; f) A. Blaszczyk, M. Chadim, C. von Hänisch, M. Mayor, *Eur. J. Org. Chem.* **2006**, 3809–3825; g) N. Weibel, A. Mishchenko, T. Wandlowski, M. Neuburger, Y. Leroux, M. Mayor, *Eur. J. Org. Chem.* **2009**, 6140–6150. Six benzene rings: h) B. Traber, T. Oeser, R. Gleiter, *Eur. J. Org. Chem.* **2005**, 1283–1292; i) P.-H. Ge, W. Fu, W. A. Herrmann, E. Herdtweck, C. Campana, R. D. Adams, U. H. F. Bunz, *Angew. Chem. Int. Ed.* **2000**, *39*, 3607–3610; *Angew. Chem.* **2000**, *112*, 3753–3756; j) Y. Hosokawa, T. Kawase, M. Oda, *Chem. Commun.* **2001**, 1948–1949; k) D. Venkataraman, S. Lee, J. Zhang, J. S. Moore, *Nature* **1994**, *371*, 591–593.

[7] a) S. Höger, X. H. Cheng, A.-D. Ramminger, V. Enkelmann, A. Rapp, M. Mondeshki, I. Schnell, *Angew. Chem. Int. Ed.* **2005**, *44*, 2801–2805; *Angew. Chem.* **2005**, *117*, 2862–2866; b) S. Höger, D. L. Morrison, V. Enkelmann, *J. Am. Chem. Soc.* **2002**, *124*, 6734–6736; c) S. Höger, V. Enkelmann, K. Bonrad, C. Tschierske, *Angew. Chem. Int. Ed.* **2000**, *39*, 2267–2270; *Angew. Chem.* **2000**, *112*, 2355–2358; d) S. Höger, V. Enkelmann, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2713–2716; *Angew. Chem.* **1995**, *107*, 2917–2919.

[8] C. Grave, D. Lentz, A. Schäfer, P. Samorì, J. P. Rabe, P. Franke, A. D. Schlüter, *J. Am. Chem. Soc.* **2003**, *125*, 6907–6918.

[9] Solution-phase binding of aza-derivatized analog of **1** to maltoside was observed, see: a) H. Abe, Y. Chida, H. Kurokawa, M. Inouye, *J. Org. Chem.* **2011**, *76*, 3366–3371. For binding of fluoroarenes to nonplanar hosts and metal–organic frameworks (MOFs), see: b) G. D. Enright, K. A. Udachin, J. A. Ripmeester, *Chem. Commun.* **2004**, 1360–1361; c) S. Shimomura, M. Higuchi, R. Matsuda, K. Yoneda, Y. Hijikata, Y. Kubota, Y. Mita, J. Kim, M. Takata, S. Kitagawa, *Nat. Chem.* **2010**, *2*, 633–637; d) M. du Plessis, V. J. Smith, L. J. Barbour, *CrystEngComm* **2014**, *16*, 4126–4132.

[10] Lengths of C–H bonds have been normalized to values obtained from neutron diffraction, see: T. Steiner, *Angew. Chem. Int. Ed.* **2002**, *41*, 48–76; *Angew. Chem.* **2002**, *114*, 50–80.

[11] a) J. L. Alonso, S. Antolínez, S. Blanco, A. Lesarri, J. C. López, W. Caminati, *J. Am. Chem. Soc.* **2004**, *126*, 3244–3249; b) V. R. Thalladi, H.-C. Weiss, D. Bläser, R. Boese, A. Nangia, G. R. Desiraju, *J. Am. Chem. Soc.* **1998**, *120*, 8702–8710; c) J. A. K. Howard, V. J. Hoy, D. O'Hagan, G. T. Smith, *Tetrahedron* **1996**, *52*, 12613–12622.

[12] Similar dimerization has been previously observed in the crystal structure of an aza-derivatized *m*-phenylene ethynylene macrocycle, see: H. Abe, K. Ohtani, D. Suzuki, Y. Chida, Y. Shimada, S. Matsumoto, M. Inouye, *Org. Lett.* **2014**, *16*, 828–831.

[13] a) A. Schäfer, C. Huber, R. Ahlrichs, *J. Chem. Phys.* **1994**, *100*, 5829–5835; b) S. Grimme, *J. Comput. Chem.* **2006**, *27*, 1787–1799.

[14] We have also performed an analogous computation on compound **3**, in which the entire –COOEt$_3$ group has been replaced with a hydrogen atom. Relative energy differences in this case are remarkably similar to those observed for various con-conformations of **2**$\cdot C_6H_6$ and **2**$\cdot C_6F_6$, with the highest discrepancy being 0.57 kcal mol^{-1}. This is perhaps a further indication of importance of crystal packing in the formation of observed structures.

[15] H. Takezawa, T. Murase, G. Resnati, P. Metrangolo, M. Fujita, *J. Am. Chem. Soc.* **2014**, *136*, 1786–1788.

[16] a) S. Lee, C.-H. Chen, A. H. Flood, *Nat. Chem.* **2013**, *5*, 704–710; b) Y. Hua, A. H. Flood, *Chem. Soc. Rev.* **2010**, *39*, 1262–1271; c) Y. Li, A. H. Flood, *J. Am. Chem. Soc.* **2008**, *130*, 12111–12122; d) Y. Li, A. H. Flood, *Angew. Chem. Int. Ed.* **2008**, *47*, 2649–2652; *Angew. Chem.* **2008**, *120*, 2689–2692.

[17] H. Abe, H. Kurokawa, Y. Chida, M. Inouye, *J. Org. Chem.* **2011**, *76*, 309–311.

[18] Gaussian 09, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2009**.

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COMMUNICATION

Host–Guest Systems

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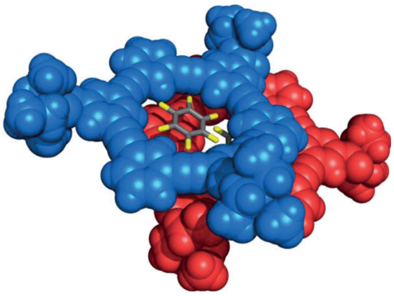
■■ – ■■

Macrocycle Embrace: Encapsulation of Fluoroarenes by *m*-Phenylene Ethynylene Host



Planar and shape-persistent *m*-phenylene ethynylene macrocyclic host crystallizes in 1:1 complexes with a series of fluoroarene guests, including 1,3,5-trifluorobenzene. The combination of (pseudo)sixfold symmetry of the host and threefold symmetry of the guest is reminiscent of the combination of symmetries observed in the arabesques of Alhmabra (see figure).

A shape-persistent macrocycle…
…from the *m*-phenylene ethynylene family is capable of encapsulating 1,2-difluorobenzene, 1,3,5-trifluorobenzene, 1,2,4,5-tetrafluorobenzene, and hexafluorobenzene, in an almost isostructural arrangement, which places the fluoroarene into the cavity of the macrocycle. Curiously, symmetries of the (pseudo)hexagonal host and its guests do not have to be matched; this combination of various symmetries is reminiscent of the arabesques of Alhambra, as shown in the artist's rendition. For more details, see the Full Paper by O. Š. Miljanić et al. on page ■■ ff.