Host–Guest Complexes

DOI: 10.1002/ange.201408400

Modulating the Binding of Polycyclic Aromatic Hydrocarbons Inside a Hexacationic Cage by Anion–π Interactions**

*Nema Hafezi, James M. Holcroft, Karel J. Hartlieb, Edward J. Dale, Nicolaas A. Vermeulen, Charlotte L. Stern, Amy A. Sarjeant, and J. Fraser Stoddart**

Dedicated to Professor Jean-Marie Lehn on the occasion of his 75th birthday

Abstract: *We report the template-directed synthesis of BlueCage^{6+}, a macrobicyclic cyclophane composed of six pyridinium rings fused with two central triazines and bridged by three paraxylylene units. These moieties endow the cage with a remarkably electron-poor cavity, which makes it a powerful receptor for polycyclic aromatic hydrocarbons (PAHs). Upon forming a 1:1 complex with pyrene in acetonitrile, however, BlueCage·6 PF_6 exhibits a lower association constant K_a than its progenitor ExCage·6 PF_6. A close inspection reveals that the six PF_6^- counterions of BlueCage^{6+} occupy the cavity in a fleeting manner as a consequence of anion–π interactions and, as a result, compete with the PAH guests. This conclusion is supported by a one order of magnitude increase in the K_a value for pyrene in BlueCage^{6+} when the PF_6^- counterions are replaced by much bulkier anions. The presence of anion–π interactions is supported by X-ray crystallography, and confirms the presence of a PF_6^- counterion inside its cavity.*

The advent[1] of supramolecular chemistry marked a departure from the near-to-sole preoccupation of chemists with the covalent bond and more towards an understanding of emergent properties which are the prerogative of weak coordinative and noncovalent bonding interactions. The pioneering research by Lehn,[2] Cram,[3] and Pedersen[4] instilled a deep sense of appreciation for these interactions, which are part and parcel of all biological systems, and continue to inspire[5] chemists in their design of adaptive functional materials. Supramolecular chemistry also laid the foundations for the emergence of the mechanical bond,[6] effectively opening up a new domain in molecular chemistry under the mantle of mechanically interlocked molecules[7] (MIMs), for example, catenanes and rotaxanes. As a consequence of their electrostatic and redox properties,[8] polycationic macrocycles such as cyclobis(paraquat-*p*-phenylene)[9] (CBPQT^{4+}) have played a crucial role in establishing the functional aspect (e.g., switching) of MIMs. Recently, we described[10] the evolution (Figure 1) of CBPQT^{4+} into its extended homologue Ex^{n}Box^{4+} ($n = 1$–3), which displays high affinities for sequestering polycyclic aromatic hydrocarbons (PAHs), and subsequently to the three-dimensional analogue[11] ExCage^{6+}.

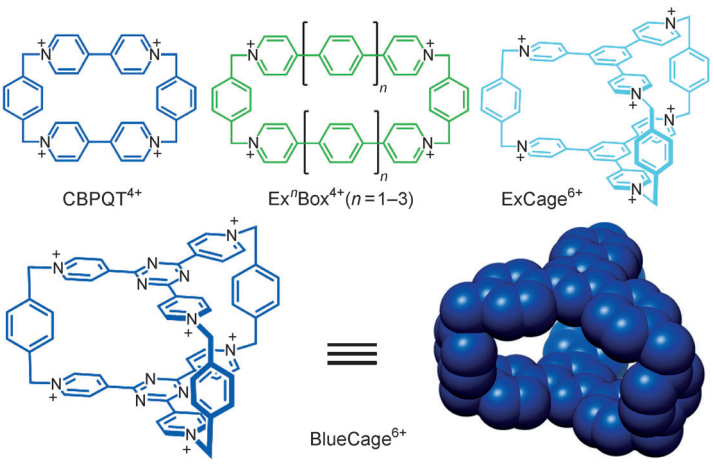


Figure 1. Structural formulas of CBPQT^{4+}, Ex^{n}Box^{4+}, ExCage^{6+}, and BlueCage^{6+} along with a space-filling representation of BlueCage^{6+}.

ExCage^{6+}, which possesses averaged D_{3h} symmetry, is composed (Figure 1) of three pyridinium units that are fused to the central benzenoid rings with 1,3,5-substitution patterns and paired together by three bridging paraxylylene units. As a consequence of its macrobicyclic nature, the larger cavity permits[11] increased orbital overlap between ExCage^{6+} and PAHs, thereby leading to higher complexation strengths in solution. The 1:1 complexes formed between ExCage^{6+} and the smaller PAHs give some insights into the nature of molecular recognition, as evidenced by the solid-state superstructure of naphthalene⊂ExCage·6 PF_6, where the PAH guest is situated with a relative geometry that ensures maximum orbital overlap with two of the three pyridinium units in each platform and minimal contribution from the central benzenoid ring. Moreover, a closer inspection of the

[*] Dr. N. Hafezi, Dr. J. M. Holcroft, Dr. K. J. Hartlieb, E. J. Dale, Dr. N. A. Vermeulen, C. L. Stern, Dr. A. A. Sarjeant, Prof. J. F. Stoddart
Center for the Chemistry of Integrated Systems
Department of Chemistry, Northwestern University
2145 Sheridan Road, Evanston, IL 60208 (USA)
E-mail: stoddart@northwestern.edu

[**] We thank Dr. Saman Shafaie for collecting the high-resolution mass spectrometric data. This research is part of the Joint Center of Excellence in Integrated Nano-Systems (JCIN) at King Abdul-Aziz City for Science and Technology (KACST) (Project 94-938) and Northwestern University (NU). We would like to thank both KACST and NU for their continued support of this research.

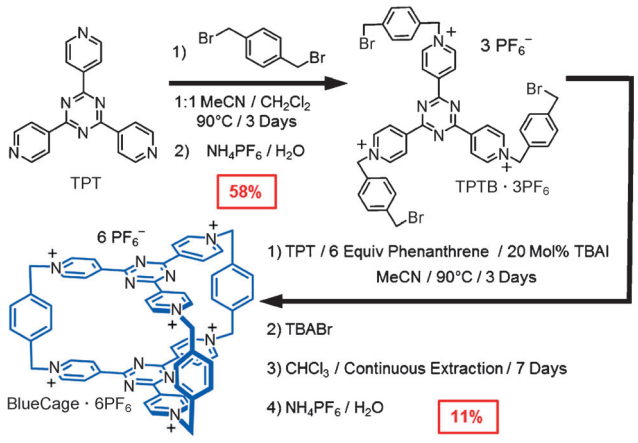
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201408400.

solid-state structure of ExCage^{6+} reveals that the pyridinium rings assume slightly staggered conformations, resulting from steric interactions with the hydrogen atoms of the central benzenoid rings, hence impairing π–π stacking between the tritopic platforms and the bound PAHs.

Herein, we report the template-directed synthesis[12] and characterization of a near relative of ExCage^{6+} we have called[13] (Figure 1) BlueCage^{6+}, which possesses two centrally located, electron-poor triazine rings designed to impart more favorable stereoelectronic interactions with PAHs on account of the increased torsional freedom accorded to the bonded six pyridinium rings. We also draw attention to an unexpected observation—namely, the fact that the K_a values of 1:1 complexes formed between BlueCage·6 PF_6 and PAHs are smaller than those of ExCage·6 PF_6. We present experimental evidence that allows us to attribute this modulation in complex stabilities to competing anion–π interactions between PF_6^- counterions and BlueCage^{6+}, which is shown by X-ray crystallography to form a 1:1 complex in the solid state with one of the PF_6^- counterions. Finally, we demonstrate that if we replace the PF_6^- counterions with the much larger tetrakis(3,5-bis(trifluoromethylphenyl))borate ($BArF^-$) anions, then the binding efficiency of BlueCage^{6+} towards PAHs is restored.

The template-directed synthesis[12] of BlueCage·6 PF_6 was achieved by a procedure (Scheme 1) similar to that described[11] for ExCage·6 PF_6. Treatment of 2,4,6-tris(4-pyridyl)-1,3,5-triazine[14] (TPT) with 10 equiv of 1,4-bis(bromomethyl)benzene in MeCN/CH_2Cl_2 (1:1) heated at 90 °C for 3 days afforded TPTB in 58 % yield following counterion exchange. The reaction of TPTB·3 PF_6 with TPT in the presence of 6 equiv of phenanthrene as a template and 20 mol % of tetrabutylammonium iodide (TBAI) in MeCN at 90 °C for 3 days furnished phenanthrene⊂BlueCage·6 Br, following precipitation of the crude product with tetrabutylammonium bromide (TBABr). Continuous extraction with $CHCl_3$ for 7 days, followed by preparative reverse-phase HPLC and anion exchange with aqueous NH_4PF_6, afforded BlueCage·6 PF_6 as a white solid in 11 % yield.[15]

Single crystals, suitable for X-ray crystallography, were grown by vapor diffusion of Et_2O into a solution of BlueCage·6 PF_6 in MeCN. Aside from one of the PF_6^- counterions,



Scheme 1. Template-directed synthesis of BlueCage·6 PF_6.

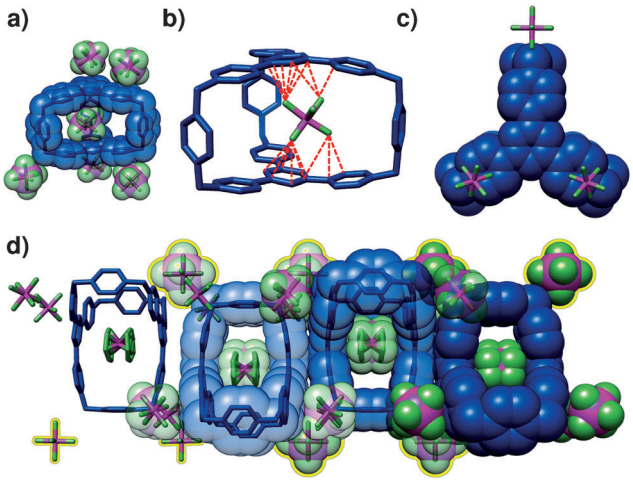


Figure 2. a) Space-filling/tubular representation showing the encapsulation of one of the six PF_6^- counterions inside the cage and the fact that five of the six counterions are involved in anion-π interactions with BlueCage^{6+}, which is displayed in different tones of blue (P = magenta, F = green). b) Side-on view employing a tubular representation where the dashed red lines draw attention to anion-π interactions ranging from 2.74 to 3.05 Å including the encapsulated PF_6^- counterion. c) Top view, employing a tubular and space-filling representation, showing how the counterions located external to the cavity of the cage enter into anion-π interactions. The four symmetry-equivalent external PF_6^- counterions possess anion-π contacts ranging from 2.99 to 3.22 Å. d) Tubular, merging into a space-filling, representation of the long-range packing along the *b* axis of BlueCage^{6+} and their associated PF_6^- counterions. PF_6^- counterions highlighted in yellow display 50% occupancy, whereas the PF_6^- counterions inside the cavity are disordered between two sites, but exhibit 100% occupancy at their given locations.

which participates exclusively through C–H···F hydrogen bonding with one of the CH_2 units in BlueCage^{6+}, the solid-state superstructure[16] reveals (Figure 2) the existence of anion–π interactions[17] between the cage and the other five PF_6^- counterions.[18] Four of these five anion–π interactions occur on the exterior of the cage between single PF_6^- ions and the π systems of some of the pyridinium rings, with distances between 3.08 and 3.43 Å, which are well within the 3.00–3.50 Å range that typically embody anion–π interactions. These interactions are augmented further by one C–H···F hydrogen bond (ca. 3.63 Å) between each of these symmetry-equivalent PF_6^- ions and their proximal CH_2 groups on BlueCage^{6+}. Furthermore, there is a notable absence of any bifurcated C–H hydrogen bonding, which is typically observed between anions and the hydrogen atoms of the pyridinium and the CH_2 units of other polycationic receptors. The fifth source of anion–π interactions arises from the PF_6^- ion situated in a slightly disordered fashion between two equal occupancy sites inside the cavity of the cage interacting with the triazine units, more so than the six pyridinium rings. The distances between the PF_6^- ion and the two central triazines are shorter than typical anion–π interactions, with distances[16b] as low as 2.75 Å. This observation is further exemplified by the fact that the included PF_6^- ion causes[19] each of the trigonal platforms to bow outward from planarity by almost 1 Å in each case.

The question arises regarding the existence[17] of anion–π interactions between BlueCage^{6+} and its anions in solution. Anion–π interactions—as reported in seminal investigations by Mascal,[20] Frontera,[21] and Alkorta[22]—describe the favorable electrostatic complementarity between a negatively charged entity and an electron-deficient π system. Our interest here in this interaction stems from comparing the K_a values of 1:1 complexes formed by BlueCage·6 PF_6 and ExCage·6 PF_6 in MeCN. We expected that BlueCage·6 PF_6 would possess a higher affinity for PAHs than would ExCage·6 PF_6 on account of the electron-poor triazine rings in the former, which render it capable of forming stronger π–π stacking interactions than the benzenoid rings in ExCage^{6+}. ITC experiments on the binding of pyrene by BlueCage·6 PF_6 in MeCN at 25 °C gave (Figure 3) a K_a value of $4.93 \times 10^5\ M^{-1}$,

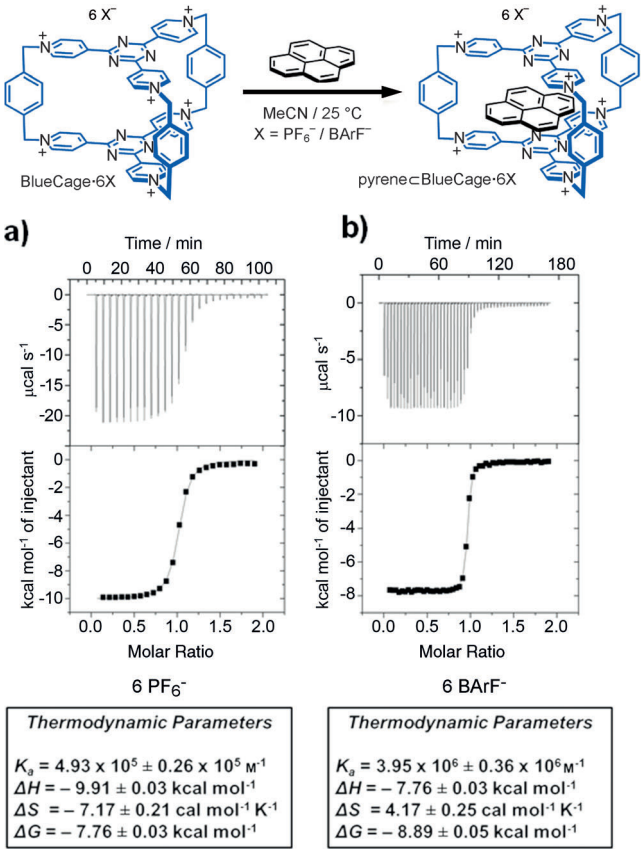


Figure 3. Isothermal titration calorimetry (ITC) traces of a) BlueCage·6 PF_6 and b) BlueCage·6 BArF, with corrections made for the heat of dilution of pyrene. Detailed experimental procedures, as well as the ITC titration of ExCage·6 BArF, are outlined in the Supporting Information.

in contrast with an association constant of $6.77 \times 10^5\ M^{-1}$ for the pyrene⊂ExCage·6 PF_6 complex formed under the same conditions. A detailed examination of the enthalpic and entropic contributions of these two 1:1 complexes sheds some light on this somewhat counterintuitive finding. The ΔH values for the association of BlueCage·6 PF_6 and ExCage·6 PF_6 with pyrene are −9.91 and −10.82 kcal mol^{-1}, respectively. This difference in exothermicity suggests that a small energy penalty was imposed upon the complexation of pyrene by BlueCage·6 PF_6, compared to that by ExCage·6 PF_6. We propose that this energy penalty of nearly 1 kcal mol^{-1} originates from the displacement of a PF_6^- counterion residing inside the cage in the case of BlueCage^{6+}. Further support for this rationalization comes from the difference in the entropy changes of the two cages on binding pyrene. In the case of BlueCage·6 PF_6, the ΔS value is −7.17 cal $mol^{-1}\,K^{-1}$, whereas in the case of ExCage·6 PF_6, it is −9.10 cal $mol^{-1}\,K^{-1}$. Whereas the complexation of ExCage·6 PF_6 with pyrene can be considered to be two entities forming one complex, the analogous transformation involving BlueCage·6 PF_6 can be interpreted[23] as guest exchange between pyrene and the resident PF_6^- counterion.

If the PF_6^- counterions enter the cage in a transient manner and mitigate the binding ability of BlueCage^{6+}, then replacing them with larger anions should conceivably enhance the affinity of this host towards PAHs, as they would be incapable of entering the cavity. The $BArF^-$ ion suits this purpose. The preparation of BlueCage·6 BArF was accomplished by two successive anion exchanges, first by converting the corresponding PF_6^- salt into the water-soluble Cl^- salt using TBACl in MeCN, and subsequently exchanging the halides for the $BArF^-$ ion using Na[BArF]. With the $BArF^-$ salt in hand, we examined its binding interaction with pyrene using ITC. Upon titration (Figure 3) of a 5 mM solution of pyrene in MeCN into a 0.5 mM solution of BlueCage·6 BArF charged inside an ITC cell, a K_a value of $3.95 \times 10^6\ M^{-1}$ was observed,[24] which is one order of magnitude greater than those for the PF_6^- salts of both cages. For comparison, the $BArF^-$ salt of ExCage^{6+} was prepared in a similar manner and shown to have an association constant of $6.0 \times 10^5\ M^{-1}$ (see Figure S1 in the Supporting Information). The origin of this increase was determined to be largely entropic, with $\Delta S =$ 4.17 cal $mol^{-1}\,K^{-1}$, whereas the enthalpy of complexation was found to be less exothermic, with $\Delta H = -7.76$ kcal mol^{-1}. We attribute these changes in thermodynamic parameters to the lack of anions which would otherwise occupy the cavity, thus permitting solvent molecules to reside inside it. The increase in entropy most likely corresponds to the expulsion of these solvent molecules by pyrene. On the other hand, the decrease in exothermicity may be interpreted[25] by the energy cost required to desolvate the cavity to facilitate entry of the guest.

Single crystals of coronene⊂BlueCage·6 PF_6 suitable for X-ray crystallography[26] were obtained (Figure 4) by vapor diffusion of iPr_2O into a solution of MeCN. Whereas coronene⊂ExCage·6 PF_6 displays a C_s-symmetric conformation in the solid state as a consequence of the 9.5–12° change in dihedral angles incurred in two of the pyridinium panels by the benzenoid ring, a negligible change is found in the dihedral angles (ca. 2.5–3.1°) of the pyridinium units and the triazine ring in the solid-state superstructure of coronene⊂BlueCage·6 PF_6, thus permitting retention of its averaged C_{3h} symmetry. The absence of torsional strain in the platforms of coronene⊂BlueCage·6 PF_6 permits optimal π–π stacking with the PAH and is evident by the deep purple color of the crystals. This contrast may also be attributed to the formation of three off-centered η-6 C–H···π interactions between the protons of coronene and the paraxylylene panels in coron-

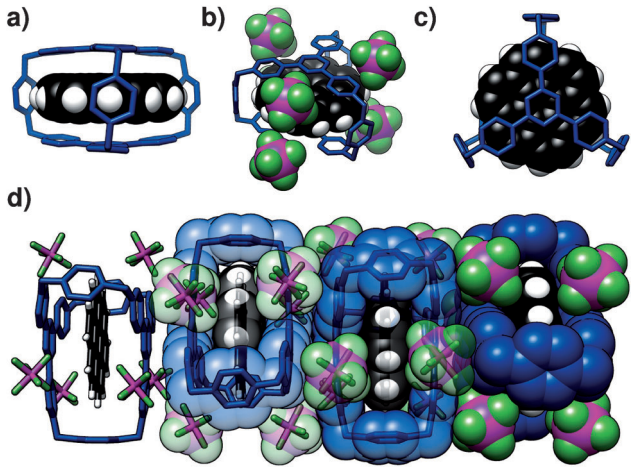


Figure 4. a) Side-on view of the 1:1 complex between BlueCage^{6+} and coronene (black), employing a space-filling/tubular representation depicting the π···π stacking interactions and also the C–H···π interactions (3.43 Å) of selected protons on the coronene with respect to the centroids on the bridging paraxylylene units. b) Space-filling/tubular representation of the 1:1 complex interacting by means of C–H···F hydrogen bonds displayed in perspective with some PF_6^- counterions (P = magenta, F = green). c) Top view employing a space-filling/tubular representation of coronene⊂BlueCage^{6+}, showing how the PAH is located precisely about the principal axis of the cage, such that it interacts in a π···π stacking manner with all three pyridinium units. d) Progression from a tubular to space-filling superstructure showing anions participating in hydrogen bonding (ca. 3.19–3.45 Å) and anion-π interactions (ca. 2.85–2.86 Å).

ene⊂BlueCage·6PF_6, each with a distance of 3.43 Å between the proton and the arene centroid. We also observe C–H···F hydrogen bonding between the PF_6^- ions and the β protons of the pyridinium rings, with distances ranging between 3.19 and 3.45 Å.

The redox behavior of BlueCage^{6+} and its half-cage analogue[27a] TBPT^{3+} were examined (Figure 5) by cyclic voltammetry (CV) in Me_2SO solution. The potentials for successive two-electron reductions of BlueCage^{6+} are less

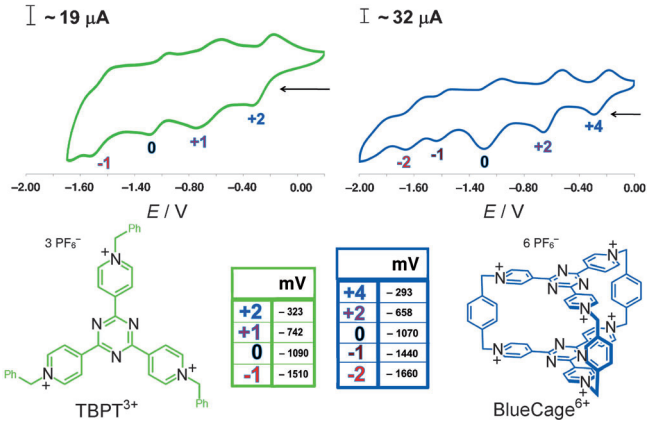


Figure 5. Cyclic voltammetry of 0.5 mM BlueCage·6PF_6 in Ar-purged Me_2SO at 298 K, with oxidation states indicated for each reduction wave. Detailed experimental procedures can be found in the Supporting Information.

negative (−293/−658/−1070/−1440 mV) than those[11] of ExCage^{6+}, an observation which can be attributed to resonance stabilization of successive radical cations by the triazine rings. BlueCage^{6+} and TBPT^{3+} register similar potentials for the first three reductions, thus indicating a lack of electronic communication between the two tritopic platforms of the cage when undergoing reduction from its hexacationic state to its neutral state (see Figure S2 in the Supporting Information). The introduction of the triazine units into BlueCage^{6+} also extends its redox behavior down into the anionic regime, where communication[27b] between the two platforms is finally observed, namely, upon reduction to the dianionic state.

In summary, we report herein the synthesis of BlueCage^{6+}, a hexacationic macrobicyclic receptor comprised of pyridinium units fused together by electron-poor triazine rings. Despite being inherently more electron-poor than its progenitor ExCage^{6+}, the PF_6^- salt of BlueCage^{6+} displayed a comparably inferior association constant with PAHs. Closer scrutiny of this counterintuitive result reveals that the PF_6^- counterions of the host are not mere spectators, but in fact occupy the cavity of BlueCage^{6+} in a fleeting fashion through anion–π interactions. This observation is supported by the one order of magnitude increase in the association constant observed for the corresponding $BArF^-$ salt with respect to the PF_6^- salt, and is evident in the X-ray crystal structure, which confirms the presence of PF_6^- residing[28] inside the cavity.

Experimental Section

BlueCage·6PF_6: A mixture of TPTB·3PF_6 (1.70 g, 1.31 mmol), 2,4,6-tris(4-pyridyl)-1,3,5-triazine (408 mg, 1.31 mmol), TBAI (97 mg, 0.26 mmol), and phenanthrene (2.10 g, 11.8 mmol) in MeCN (500 mL) was heated under reflux in an atmosphere of argon for 3 days. The reaction mixture was cooled to room temperature and treated with an excess of TBABr to precipitate the remaining solid, which was collected by filtration. The filter cake was triturated with a minimum amount of H_2O and the combined aqueous fractions were subjected to continuous extraction with $CHCl_3$ for 7 days to remove the phenanthrene template. The aqueous phase was concentrated under vacuum and purified by preparative reverse-phase HPLC (C_{18} column), starting with H_2O containing 0.1% TFA as eluant, and increasing to 25% of MeCN/0.1% TFA. The combined fractions were concentrated under vacuum and treated with saturated aqueous NH_4PF_6 to furnish pure BlueCage·6PF_6 (257 mg, 143 μmol, 11%) as a white solid. ^{1}H NMR (500 MHz, CD_3CN): $\delta = 9.06$ (d, $J = 6.5$ Hz, 12H), 9.05 (d, $J = 6.5$ Hz, 12H), 7.63 (s, 12H), 5.82 ppm (s, 12H). ^{13}C NMR (125 MHz, CD_3CN): $\delta = 169.4$, 150.4, 146.1, 136.8, 130.8, 128.7, 65.7 ppm. ^{19}F NMR (470 MHz, CD_3CN): $\delta = -71.0$ ppm (d, $J = 706.9$ Hz). ^{31}P NMR (162 MHz, CD_3CN): $\delta = -143.59$ ppm (sept, $J = 708.6$ Hz). HRMS (ESI) calcd for $C_{60}H_{48}F_{24}N_{12}P_4$: $m/z = 758.1341$ $[M-2PF_6]^{2+}$; found: 758.1346.

Received: August 20, 2014
Published online: November 19, 2014

Keywords: cage compounds · cyclophanes · host–guest complexes · supramolecular chemistry

[1] a) J.-M. Lehn, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 89–112; *Angew. Chem.* **1988**, *100*, 91–116; b) J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, Wiley-VCH, Wein-

heim, **1995**; c) J.-M. Lehn, *Science* **2002**, *295*, 2400 – 2403; d) J.-M. Lehn, *Angew. Chem. Int. Ed.* **2013**, *52*, 2836 – 2850; *Angew. Chem.* **2013**, *125*, 2906 – 2921.

[2] a) B. Dietrich, J.-M. Lehn, J.-P. Sauvage, *Tetrahedron Lett.* **1969**, *10*, 2885 – 2888; b) B. Dietrich, J.-M. Lehn, J.-P. Sauvage, *Tetrahedron Lett.* **1969**, *10*, 2889 – 2892; c) B. Dietrich, J.-M. Lehn, J.-P. Sauvage, J. Blanzat, *Tetrahedron* **1973**, *29*, 1629 – 1645; d) B. Dietrich, J.-M. Lehn, J.-P. Sauvage, *Tetrahedron* **1973**, *29*, 1647 – 1658; e) J.-M. Lehn, *Acc. Chem. Res.* **1978**, *11*, 49 – 57, and references therein; f) J.-M. Lehn, *Pure Appl. Chem.* **1978**, *50*, 871 – 892.

[3] a) E. P. Kyba, R. C. Helgeson, K. Madan, G. W. Gokel, T. L. Tarnowski, S. S. Moore, D. J. Cram, *J. Am. Chem. Soc.* **1977**, *99*, 2564 – 2571; b) D. J. Cram, *Nature* **1992**, *356*, 29 – 36; c) D. J. Cram, J. M. Cram, *Container Molecules and their Guests*, Royal Society of Chemistry, Cambridge, **1994**, and references therein.

[4] a) C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 2495 – 2496; b) C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 7017 – 7036; c) C. J. Pedersen, *J. Am. Chem. Soc.* **1970**, *92*, 386 – 391; d) C. J. Pedersen, *J. Am. Chem. Soc.* **1970**, *92*, 391 – 394; e) C. J. Pedersen, *Aldrichimica Acta* **1971**, *4*, 1 – 4; f) C. J. Pedersen, H. Frensdorff, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 16 – 25; *Angew. Chem.* **1972**, *84*, 16 – 26; g) C. J. Pedersen, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1021 – 1027; *Angew. Chem.* **1988**, *100*, 1053 – 1059; h) C. J. Pedersen, *Science* **1988**, *241*, 536 – 540, and references therein.

[5] a) J.-M. Lehn, *Makromol. Chem. Macromol. Symp.* **1993**, *69*, 1 – 17; b) O. Ikkala, G. ten Brinke, *Science* **2002**, *295*, 2407 – 2409; c) N. M. Sangeetha, U. Maitra, *Chem. Soc. Rev.* **2005**, *34*, 821 – 836; d) J. A. A. W. Elemans, A. E. Rowan, R. J. M. Nolte, *J. Mater. Chem.* **2003**, *13*, 2661 – 2670; e) D. M. Vriezema, M. C. Aragones, J. A. A. W. Elemans, J. J. L. M. Cornelissen, A. E. Rowan, R. J. M. Nolte, *Chem. Rev.* **2005**, *105*, 1445 – 1489; f) T. Aida, E. W. Meijer, S. I. Stupp, *Science* **2012**, *335*, 813 – 817; g) S. I. Stupp, L. C. Palmer, *Chem. Mater.* **2014**, *26*, 507 – 518; h) J. Boekhoven, S. I. Stupp, *Adv. Mater.* **2014**, *26*, 1642 – 1659.

[6] J. F. Stoddart, *Angew. Chem. Int. Ed.* **2012**, *51*, 12902 – 12903; *Angew. Chem.* **2012**, *124*, 13076 – 13077.

[7] a) C. O. Dietrich-Buchecker, J.-P. Sauvage, J.-M. Kern, *J. Am. Chem. Soc.* **1984**, *106*, 3043 – 3045; b) C. O. Dietrich-Buchecker, J.-P. Sauvage, *Chem. Rev.* **1987**, *87*, 795 – 810; c) J.-P. Sauvage, *Acc. Chem. Res.* **1990**, *23*, 319 – 327; d) D. B. Amabilino, J. F. Stoddart, *Chem. Rev.* **1995**, *95*, 2725 – 2829; e) M. J. Blanco, M. Consuelo-Jimenez, J.-C. Chambron, V. Heitz, M. Linke, J.-P. Sauvage, *Chem. Soc. Rev.* **1999**, *28*, 293 – 305; f) E. R. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem. Int. Ed.* **2007**, *46*, 72 – 191; *Angew. Chem.* **2007**, *119*, 72 – 196; g) J. F. Stoddart, *Chem. Soc. Rev.* **2009**, *38*, 1521 – 1529; h) S. F. M. van Dongen, S. Cantekin, J. A. A. W. Elemans, A. E. Rowan, R. J. M. Nolte, *Chem. Soc. Rev.* **2014**, *43*, 99 – 122; i) N. H. Evans, P. D. Beer, *Chem. Soc. Rev.* **2014**, *43*, 4658 – 4683.

[8] a) A. Coskun, D. C. Friedman, H. Li, K. Patel, H. A. Khatib, J. F. Stoddart, *J. Am. Chem. Soc.* **2009**, *131*, 2493 – 2495; b) H. Li, Z. Zhu, A. C. Fahrenbach, B. M. Savoie, C. Ke, J. C. Barnes, J. Li, Y. Zhao, L. M. Lilley, T. J. Marks, M. A. Ratner, J. F. Stoddart, *J. Am. Chem. Soc.* **2013**, *135*, 456 – 467.

[9] a) C. Seel, F. Vögtle, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 528 – 549; *Angew. Chem.* **1992**, *104*, 542 – 563; b) M. Asakawa, W. Dehaen, G. L'abbe, S. Menzer, J. Nouwen, F. Raymo, J. F. Stoddart, D. J. Williams, *J. Org. Chem.* **1996**, *61*, 9591 – 9595; c) W. R. Dichtel, O. Š. Miljanić, W. Zhang, J. M. Spruell, K. Patel, I. Aprahamian, J. R. Heath, J. F. Stoddart, *Acc. Chem. Res.* **2008**, *41*, 1750 – 1761, and references therein.

[10] a) J. C. Barnes, M. Juríček, N. L. Strutt, M. Frasconi, S. Sampath, M. A. Giesener, P. L. McGrier, C. J. Bruns, C. L. Stern, A. A. Sarjeant, J. F. Stoddart, *J. Am. Chem. Soc.* **2013**, *135*, 183 – 192; b) M. Juríček, J. C. Barnes, E. J. Dale, W. Liu, N. L. Strutt, C. J. Bruns, N. A. Vermeulen, K. C. Ghooray, A. A. Sarjeant, C. L. Stern, Y. Y. Botros, W. A. Goddard III, J. F. Stoddart, *J. Am. Chem. Soc.* **2013**, *135*, 12736 – 12746; c) J. C. Barnes, M. Juríček, N. A. Vermeulen, E. J. Dale, J. F. Stoddart, *J. Org. Chem.* **2013**, *78*, 11962 – 11969; d) M. Juríček, N. L. Strutt, J. C. Barnes, A. N. Butterfield, E. J. Dale, K. K. Baldridge, J. F. Stoddart, J. S. Siegel, *Nat. Chem.* **2014**, *6*, 222 – 228.

[11] E. J. Dale, N. A. Vermeulen, A. A. Thomas, J. C. Barnes, M. Juríček, A. K. Blackburn, N. L. Strutt, A. A. Sarjeant, C. L. Stern, S. E. Denmark, J. F. Stoddart, *J. Am. Chem. Soc.* **2014**, *136*, 10669 – 10682.

[12] a) S. Anderson, H. L. Anderson, J. K. M. Sanders, *Acc. Chem. Res.* **1993**, *26*, 469 – 475; b) R. Cacciapaglia, L. Mandolini, *Chem. Soc. Rev.* **1993**, *22*, 221 – 231; c) R. Hoss, F. Vögtle, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 375 – 384; *Angew. Chem.* **1994**, *106*, 389 – 398; d) T. J. Hubin, D. H. Busch, *Coord. Chem. Rev.* **2000**, *200*, 5 – 52; e) C. D. Meyer, C. S. Joiner, J. F. Stoddart, *Chem. Soc. Rev.* **2007**, *36*, 1705 – 1723; f) J. D. Crowley, S. M. Goldup, A. L. Lee, D. A. Leigh, R. T. McBurney, *Chem. Soc. Rev.* **2009**, *38*, 1530 – 1541.

[13] We have named this compound BlueCage^{6+} in deference to CBPQT^{4+}, which is often referred to colloquially as "BlueBox^{4+}".

[14] a) H. L. Anderson, S. Anderson, J. K. M. Sanders, *J. Chem. Soc. Perkin Trans. 1* **1995**, 2231 – 2245; b) for comprehensive reviews on the supramolecular chemistry of 2,4,6-tris(4-pyridyl)-1,3,5-triazine and isomers thereof, see M. Fujita, K. Umemoto, M. Yoshizawa, N. Fujita, T. Kusukawa, K. Biradha, *Chem. Commun.* **2001**, 509 – 518; M. Yoshizawa, J. K. Klosterman, M. Fujita, *Angew. Chem. Int. Ed.* **2009**, *48*, 3418 – 3438; *Angew. Chem.* **2009**, *121*, 3470 – 3490; J. K. Klosterman, Y. Yamauchi, M. Fujita, *Chem. Soc. Rev.* **2009**, *38*, 1714 – 1725; B. Therrien, *J. Organomet. Chem.* **2011**, *696*, 637 – 651.

[15] The lower yields observed for the preparation of BlueCage·6 PF_6 with respect to those reported (Ref. [11]) for ExCage·6 PF_6 could be the consequence of the electron-withdrawing effects of the triazine core suppressing the nucleophilicity of the pyridyl nitrogen atoms. In the absence of either phenanthrene or TBAI, only trace amounts of BlueCage·6 PF_6 were isolated.

[16] a) Crystal data for BlueCage·6 PF_6 (M_r = 1806.92): orthorhombic, space group *Cmcm* (no. 63), a = 26.8415(10), b = 14.9670(6), c = 22.0219(10) Å, V = 8847.0(6) Å^3, Z = 4, T = 250.01 K, μ(CuKα) = 2.202 mm^{-1}, ρ_{calcd} = 1.357 g cm^{-3}, out of the 39287 reflections measured, 2832 were unique (R_{int} = 0.1254, $R\sigma$ = 0.0710) and were used in all calculations. The final $R1$ was 0.0622 ($I > 2\sigma(I)$) and $wR2$ was 0.1724 (all data); b) the anion-π distances reported herein are measured between fluoride atoms of the PF_6^- counterions and the proximal centroid (for η-2 complexes) or plane (η-3 ≤ η-6 complexes) defined by the sp^2 atoms composing either the pyridinium or triazine rings; c) during the refinement process, a region of electron density was identified outside the cavity that appeared to correspond to an MeCN molecule in proximity to the counterion residing in the cage, perhaps as a result of C–H hydrogen bonding. The structure, however, was too disordered to be characterized with any accuracy, and was thus removed using the SQUEEZE function in PLATON (Spek, 2003); d) CCDC 1011900 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.

[17] a) H.-J. Schneider, *Angew. Chem.* **1991**, *103*, 1419 – 1439; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1417 – 1436; b) H.-J. Schneider, T. Blatter, B. Palm, U. Pfingstag, V. Rüdiger, I. Theis, *J. Am. Chem. Soc.* **1992**, *114*, 7704 – 7708; c) H.-J. Schneider, F. Werner, T. Blatter, *J. Phys. Org. Chem.* **1993**, *6*, 590 – 594; d) B. L. Schottel, H. T. Chiftodes, K. R. Dunbar, *Chem. Soc. Rev.* **2008**, *37*, 68 – 83;

e) A. Frontera, P. Gamez, M. Mascal, T. J. Mooibroek, J. Reedijk, *Angew. Chem. Int. Ed.* **2011**, *50*, 9564 – 9583; *Angew. Chem.* **2011**, *123*, 9736 – 9756; f) H. T. Chiftodes, K. R. Dunbar, *Acc. Chem. Res.* **2012**, *47*, 894 – 906, and references therein; g) S. T. Schneebeli, M. Frasconi, Z. Liu, Y. Wu, D. M. Gardner, N. L. Strutt, C. Cheng, R. Carmieli, M. R. Wasielewski, J. F. Stoddart, *Angew. Chem.* **2013**, *125*, 13338 – 13342; *Angew. Chem. Int. Ed.* **2013**, *52*, 13100 – 13104.

[18] The solid-state superstructure of BlueCage·6 PF_6 is distinguished from its progenitor ExCage·6 PF_6 by the presence of bifurcated C–H hydrogen bonding between the PF_6^- counterions and the α protons of the pyridinium ring and CH_2 protons in the latter case. While there are anion–π interactions between $ExCage^{6+}$ and its counterions in the solid state, albeit only a couple, these interactions are heavily reinforced by hydrogen bonding with the cage and residual MeCN molecules.

[19] For an example of anion – π induced self-assembly on the part of a dynamic host, see H. T. Chifotides, I. D. Giles, K. R. Dunbar, *J. Am. Chem. Soc.* **2013**, *135*, 3039 – 3055.

[20] M. Mascal, A. Armstrong, M. D. Bartberger, *J. Am. Chem. Soc.* **2002**, *124*, 6274 – 6276.

[21] D. Quiñonero, C. Garau, C. Rotger, A. Frontera, P. Ballester, A. Costa, P. Deyà, *Angew. Chem. Int. Ed.* **2002**, *41*, 3389 – 3392; *Angew. Chem.* **2002**, *114*, 3539 – 3542.

[22] I. Alkorta, I. Rozas, J. Elguero, *J. Am. Chem. Soc.* **2002**, *124*, 8593 – 8598.

[23] The substantial charge density inherent in polycationic cyclophanes, such as $CBPQT^{4+}$, Ex^nBox^{4+}, and $ExCage^{6+}$, precludes the complete dissolution of their corresponding anions, even at low concentrations, and results in exceptionally high concentrations in the immediate vicinity of the receptor. In the case of BlueCage·6 PF_6, this effect inflates the association constant between the receptor and the PF_6^- ions to such an extent that it renders them competitive towards conventional guests.

[24] For a similar observation made when comparing the PF_6^- salt of $CBPQT^{4+}$ with the tris(tetrachlorocatecholate)salt, see a) B. W. Laursen, S. Nygaard, J. O. Jeppesen, J. F. Stoddart, *Org. Lett.* **2004**, *6*, 4167 – 4170; b) S. S. Andersen, M. Jensen, A. Sørensen, E. Miyazaki, K. Takimiya, B. W. Laursen, A. H. Flood, J. O. Jeppesen, *Chem. Commun.* **2012**, *48*, 5157 – 5159.

[25] Although the existence of a PF_6^- anion-π complex has been unambiguously demonstrated in the solid state and strongly suggested by ITC data, we were unable to distinguish the PF_6^- counterion residing inside the cage from ones outside using ^{19}F and ^{31}P NMR spectroscopy, an observation that is indicative of rapid exchange between the anions in each environment. For an example in which NMR spectroscopy is unable to corroborate the presence of an anionic guest unambiguously found in the solid state, see C. R. K. Glasson, G. V. Meehan, J. K. Clegg, L. F. Lindoy, P. Turner, M. B. Duriska, R. Willis, *Chem. Commun.* **2008**, 1190 – 1192.

[26] a) Crystal data for coronene⊂BlueCage·6 PF_6 ($M_r = 2107.26$): trigonal, space group $R\bar{3}c$ (no. 167), $a = 30.1019(10)$, $b = 30.1019(10)$, $c = 41.3504(18)$ Å, $V = 32449(3)$ Å^3, $Z = 12$, $T = 100(2)$ K, $\mu(CuK\alpha) = 1.881$ mm^{-1}, $\rho_{calcd} = 1.294$ g cm^{-3}, out of the 33456 reflections measured, 5197 were unique ($R_{int} = 0.1011$, $R\sigma = 0.0729$) and were used in all calculations. The final $R1$ was 0.0931 ($I > 2\sigma(I)$) and $wR2$ was 0.3099 (all data); b) for the criteria used to define anion-π distances in coronene⊂BlueCage·6 PF_6, see Ref. [16b]; c) CCDC 1011901 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.

[27] a) W.-K. Gries, E. Günther, S. Hünig, *Liebigs Ann. Chem.* **1991**, 1021 – 1028; b) we attribute the 150 mV shift in the reduction potential for producing $BlueCage^{2-}$ to Coulombic repulsion between the incoming free electron and the anionic platform composing $BlueCage^-$.

[28] For an example of a self-assembled supramolecular receptor for a PF_6^- counterion, see M. C. Fyfe, P. T. Glink, S. Menzer, J. F. Stoddart, A. J. P. White, D. J. Williams, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2068 – 2070; *Angew. Chem.* **1997**, *109*, 2158 – 2160.

