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A Heptagon-Containing HBC-Based Macrocycle

Vicente G. Jiménez, Arthur H. G. David, Juan M. Cuerva, Victor Blanco* and Araceli G. Campaña*

Abstract: A cyclophane incorporating two units of a heptagon-containing extended polycyclic aromatic hydrocarbon (PAH), analogue of the hexa-*peri*-hexabenzocoronene (HBC) moiety (hept-HBC), is reported. This cyclophane represents a new class of macrocyclic structures that incorporate for the first time seven-membered rings within extended PAH frameworks. The saddle curvature of the hept-HBC macrocycle units induced by the presence of the non-hexagonal ring along with the flexible alkyl linkers generate a cavity with shape complementarity and appropriate size to enable π interactions with fullerenes. Therefore, the cyclophane forms host-guest complexes with C_{60} and C_{70} with estimated binding constants of $K_a = 420 \pm 2$ M^{-1} and $K_a = (6.49 \pm 0.23) \times 10^3$ M^{-1} respectively. As a result, the macrocycle can selectively bind C_{70} in the presence of an excess of a mixture of C_{60} and C_{70}.

Many examples have been reported of organic macrocycles and metallacycles with different size and shape that incorporate polycyclic aromatic hydrocarbons (PAHs) in their structures.[1] However, most of those examples, with the exception of some of the recent carbon nanobelts,[2] are restricted to PAHs with a small number of fused rings. Thus, the examples of macrocycles that exhibit extended aromatic systems such as the hexa-*peri*-hexabenzocoronene (HBC) unit are much scarcer. In fact, only a few examples of HBC-containing cyclophanes or strained macrocycles and cages derived from [*n*]cycloparaphenylenes (CPP) have been reported. Among the cyclophanes, we can highlight the seminal work of Watson, Rabe, Müllen and co-workers describing a macrocycle with two HBC units linked by aliphatic chains[3] and a more recent similar structure differing in the spacer units (Figure 1a).[4] As part of the increasing interest on the development of strained nanohoops,[1g,h, 5] which started with the synthesis of the first CPPs, a variety of derivatives of different size incorporating up to eight HBC units have been prepared in the last few years (Figure 1a).[6] Interestingly, the strained nature of the structures formed resulted in the distortion of the planarity of the HBC units giving rise to curved surfaces.

On the other hand, it has recently emerged a growing interest in the development of extended PAHs incorporating seven-membered rings, resulting in nonplanar structures with a negative saddle curvature.[7,8] These compounds are relevant due to the properties they exhibit as their usual higher solubility in comparison with their purely hexagonal counterparts, which enhances their processability and characterization, but also their interesting (chiro)optical or non-linear optical properties, mainly in combination with other structural defects such as helicenes.[9]

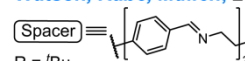Moreover, relevant magnetic or electronic properties have also been predicted for these structures.[10]

a) **Previous work:** HBC-based macrocycles and cages
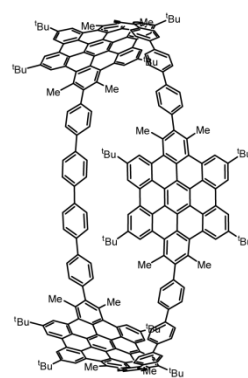
- HBC-containing cyclophanes
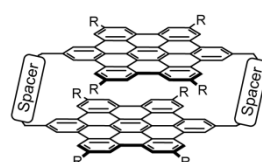
Spacer ≡ ─(CH₂)₈─
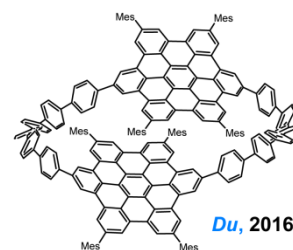R = 3,7-dimethyloctanyl
Watson, Rabe, Müllen, **2004**

R = *t*Bu
Akine, Nabeshima, **2018**

- Strained HBC-based macrocycles

Nishiuchi, Müllen, **2015**

Du, **2016**

Du, **2018**

n = 1; R = -
n = 1; R = 4-4'-biphenyl   *Ito,* **2019**
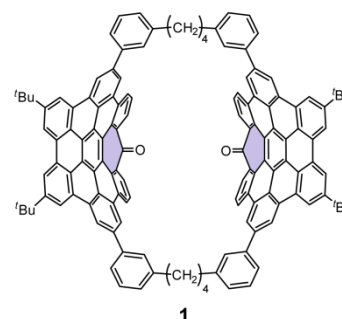n = 3, 5; R = -   *Du,* **2020**
Du, **2017**
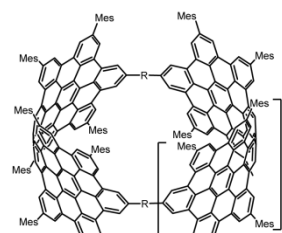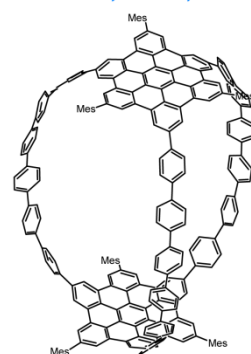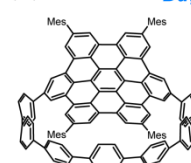
Yang, Du, **2019**

b) **This work:** First heptagon-containing HBC-based macrocycle

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Figure 1. a) Previous HBC-based cyclophanes and strained nanohoops. b) Macrocycle incorporating two saddle-shaped heptagon-containing hexabenzocoronene analogues (hept-HBC) described in this work. (Mes = 4-(1,3,5-trimethylphenyl)).

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Nevertheless, despite this increasing interest in the design and development of a variety of extended PAHs or nanographenes incorporating heptagons, their inclusion in macrocyclic structures and the study of the resulting properties, especially the possible supramolecular interactions with curved guests, has remained, to the best of our knowledge, completely unexplored. This is somewhat surprising, taking into account that the curvature induced by the presence of the seven membered ring could facilitate the formation of less strained macrocyclic structures or increase the shape complementarity with curved π systems in comparison with their planar purely hexagonal counterparts.

Here we report the synthesis, characterization and supramolecular behaviour as host for fullerenes of a novel macrocycle constituted by two units of heptagon-containing HBC analogues (hept-HBC) (**1**) (Figure 1b).
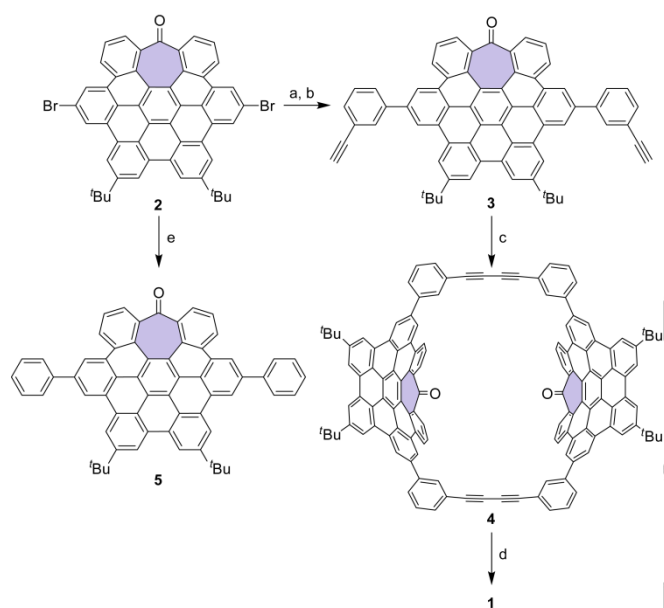
Scheme 1. Synthesis of hept-HBC-based macrocycle **1** and model **5**. Reagents and conditions: a) 3-[(trimethylsilyl)ethynyl]phenylboronic acid pinacol ester, Pd(PPh$_3$)$_4$, K$_2$CO$_3$, toluene/H$_2$O, reflux, 16 h, 38%; b) tetrabutylammonium fluoride (TBAF), THF/H$_2$O, RT, 2 h, 99%; c) CuCl, CuCl$_2$, pyridine, 27 h, RT, 28%; d) H$_2$, PtO$_2$, THF/MeOH, RT, 18 h, 72%; e) phenylboronic acid, Pd(PPh$_3$)$_4$, K$_2$CO$_3$, toluene/H$_2$O/EtOH, reflux, 20 h, 70%.

The key intermediate for the synthesis of cyclophane **1** is the saddle hept-HBC analogue **2**,[11] functionalized with two Br atoms in the adequate positions to enable the introduction of the linker moieties and the formation of a macrocycle (Scheme 1). We prepared this dibromide derivative following our reported synthetic strategy that gives access to distorted heptagon-containing HBC analogues with different functionalization patterns.[12] This strategy involved subsequent Sonogashira couplings starting from 2,2'-dibromobenzophenone, a Co-catalyzed alkyne cyclotrimerization and a final Scholl-type oxidative cyclodehidrogenation (see the Supporting Information for further details). Suzuki coupling between **2** and 3-[(trimethylsilyl)ethynyl]phenylboronic acid pinacol ester followed by cleavage of the trimethylsilyl protecting group yielded diyne **3**.

Glaser alkyne homocoupling of **3** in dilute conditions afforded macrocycle **4** which underwent selective hydrogenation of the butadiyne groups using PtO$_2$ as catalyst to yield the target cyclophane **1** (Scheme 1).
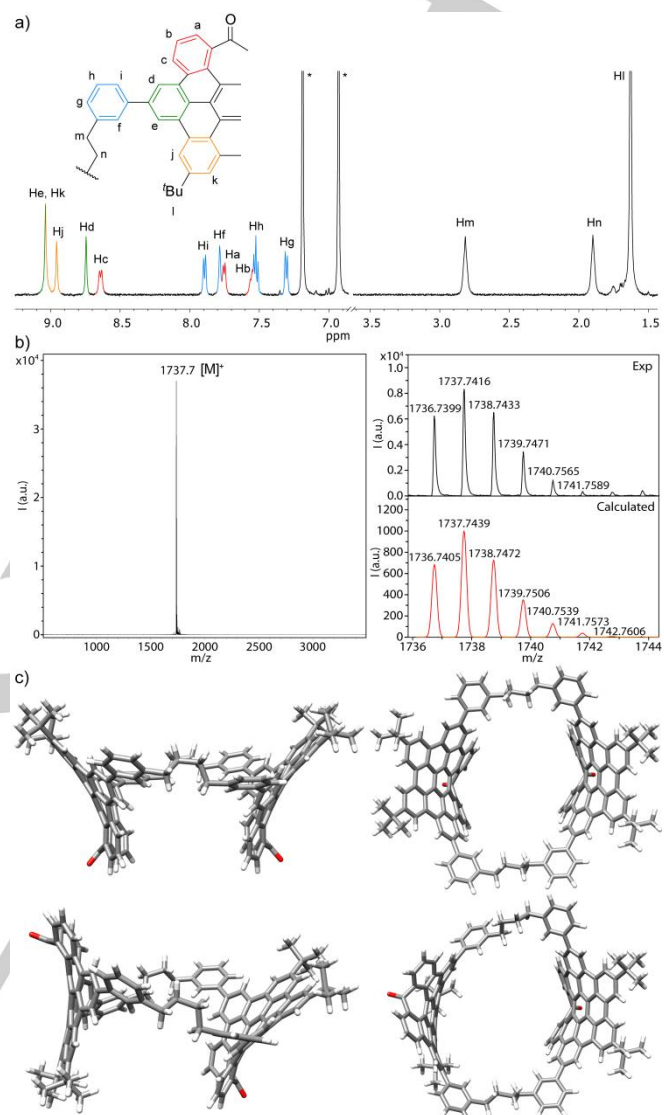
Figure 2. a) Partial ^{1}H NMR (400 MHz, [D$_4$]-o-DCB, 25 ºC) spectra of **1**. b) MALDI-TOF mass spectra of **1** (left) and experimental (top right) and calculated (bottom right) HR-MS isotopic distribution for the [M]$^+$ ion. c) Side (left) and top (right) views of the DFT (ωB97XD/def2SVP in o-DCB) optimized structure of *syn*-**1** (top) and *anti*-**1** (bottom). Colour coding: C, grey; H, white; O, red.

The good solubility of hept-HBC-based macrocycle **1** in chlorinated organic solvents such as dichloromethane, tetrachloroethane or o-dichlorobenzene (o-DCB) allowed its characterization by NMR spectroscopy. In principle, two main possible conformers could be considered depending on whether the ketone moieties have the same (*syn*) or opposite (*anti*) orientation. Thus, broad resonances could be observed in the ^{1}H NMR spectrum in C$_2$D$_2$Cl$_4$ at room temperature, which resolved into well-defined signals at 358 K (Figure S18).[13] This could be

explained by a coalescence situation that results in fast exchange in the NMR timescale upon heating. On the contrary, the ^{1}H NMR spectrum in [D$_4$]-o-DCB showed only one set of well-defined signals at room temperature (Figure 2a and Figure S16), which could be assigned with the aid of 2D NMR experiments, confirming the proposed structure. Moreover, the identity of the compound was further confirmed by MALDI-TOF mass spectrometry. The spectrum showed a single signal corresponding to the [M]$^+$ ion with a HRMS exact mass and isotopic distribution in excellent agreement with the calculated ones (Figure 2b). The UV-Vis spectrum of **1** in o-DCB shows an absorption band between 320 and 420 nm (λ_{max} = 365 nm, ε = 1.4 × 10^6 L mol^{-1}) with a shoulder at 395 nm (ε = 4.9 × 10^5 L mol^{-1}). Upon irradiation at 365 nm, the macrocycle shows luminescence, with an emission band in the 450-570 region, with its maximum at 490 nm (Figure S31).

The structure of the two different conformers of **1** was also investigated by means of DFT calculations at the ωB97XD/def2SVP level. The optimized structure of syn-**1** displays a basket or calix-like shape defined by the saddled curvature induced by the seven-membered rings of the hept-HBC units. The distance between the central part of the hept-HBC units ranges $ca.$ 12.8-18.0 Å, while the distance between the side aliphatic chains is $ca.$ 15.6 Å (Figures 2c and S53), giving a cavity effective size of $ca.$ 9.4−14.6 Å × 12.2 Å (see the Supporting Information for further details).[14] $Anti$-**1** also exhibits a basket-like structure, although more distorted than the syn conformer (Figures 2c and S54).

The presence of an internal cavity demarcated by the curved hept-HBC units could enable macrocycle to act as a supramolecular receptor of aromatic compounds by means of π interactions between the distorted π-extended PAH derivatives and the guest. Although it has been suggested that heptagon-containing extended PAHs can interact with fullerene,[15] the supramolecular behaviour of these saddle systems has remained essentially unexplored. For this reason, we decided to study their ability to form supramolecular entities with fullerenes.

We first investigated the self-association of hept-HBC model **5**,[16] prepared from dibromide **2** by Suzuki coupling with phenylboronic acid (Scheme 1). The ^{1}H NMR spectra of **5** in the 1-100 mM range showed important changes in the chemical shift of the aromatic signals (Figures S35-S36). The fitting of the δ values at the different concentrations gave us the value of the monomer-dimer equilibrium constant (K_d = 24 ± 4 M^{-1}) (Figure S37).[17] We then studied the recognition of C$_{60}$ and C$_{70}$ by **5**. ^{13}C NMR experiments showed that addition of model derivative **5** to a solution of C$_{60}$ or C$_{70}$ resulted in changes in the chemical shift of the fullerene signals, indicating the presence of supramolecular interactions between the hept-HBC unit and the fullerene molecules (Figures S30, S40 and S42). ^{13}C NMR titrations allowed us to estimate the binding constants as K_a = 18.2 ± 0.1 M^{-1} (in C$_2$D$_2$Cl$_4$) or 20.0 ± 0.1 M^{-1} (in [D$_4$]-o-DCB) with C$_{60}$ and K_a = 3.75 ± 0.02 M^{-1} (in [D$_4$]-o-DCB) with C$_{70}$ using a 1:1 fitting model (see the Supporting Information for details).[18,19] These are relevant results as they evidence that simple hept-HBC derivatives can play an interesting role in supramolecular chemistry, demonstrating that, although weakly, they can form

supramolecular aggregates with curved π systems. The extended π surface together with the curvature induced by the presence of the seven-membered ring, which favours the geometrical complementarity are factors that can account for this molecular recognition.

Having demonstrated that simple hept-HBC derivatives can participate in supramolecular interactions, we studied the host-guest chemistry of cyclophane **1**. Again, we chose C$_{60}$ and C$_{70}$ as potential guests for our macrocycle as the curvature on the aromatic surface would enhance the shape complementarity with curved aromatic guests.[1h,20] In addition, the C$_{60}$ van der Waals diameter ($ca.$ 10.5 Å) reasonably fits the size of the macrocycle cavity, which could also slightly adapt due to the presence of alkyl chains linking the two hept-HBC units.

The resonances of both ^{1}H and ^{13}C NMR spectra of mixtures of cyclophane **1** and C$_{60}$ or C$_{70}$ were shifted in comparison with those of the free host and guests, thus indicating the establishment of π interactions between them and the formation of host-guest complexes (Figures 3 and S44-S45, S47-S48 and S50-S51). In particular, the signals of He and Hf, located in the equatorial region of the receptor, are shifted to lower frequencies due to the shielding by the curved guest. ^{1}H NMR titration of receptor **1** with C$_{60}$ or C$_{70}$ in [D$_4$]-o-DCB allowed us to determine the binding constants as K_a = 420 ± 2 M^{-1} with C$_{60}$ and K_a = (6.49 ± 0.23) × 10^3 M^{-1} with C$_{70}$ (Figure 3 and the Supporting Information).
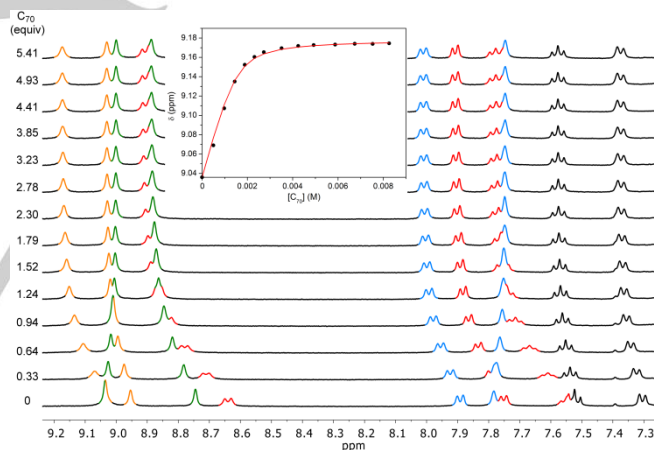

Figure 3. Partial ^{1}H NMR (400 MHz, [D$_4$]-o-DCB) spectra for the titration of **1** with increasing amounts of C$_{70}$. Inset: Fitting of δ for the signal initially at 9.04 ppm (labelled in orange in the NMR spectra) with [C$_{70}$].

Remarkably, the association between heptagon-containing macrocycle **1** and C$_{70}$ is one order of magnitude stronger than that with C$_{60}$. As a result, when the host was added to an excess of a 1:1 mixture of both fullerenes, the macrocycle selectively bound to C$_{70}$. This was confirmed by comparison of the ^{13}C NMR signals of the fullerenes before and after the host addition, which revealed a shift toward lower frequencies of the C$_{70}$ signals ($\Delta\delta$ = −0.17−0.24 ppm) while the ^{13}C signal of C$_{60}$ remains essentially unaltered ($\Delta\delta$ = −0.02 ppm) (Figure S52).

The host-guest complexes were also modelled by DFT calculations at the ωB97XD/def2SVP level in *o*-DCB (Figure 4). The optimized structures of the *syn*-**1** complexes show the inclusion of the fullerene guests inside its cavity. The calculation predicts C_{60} to be located in the center of the cavity, being the closest distance to both hept-HBC units quite similar (*ca*. 3.4 Å). On the contrary, C_{70} adopts, due to its prolate-like shape, a tilted orientation to maximize contact with the hept-HBC π surface. The computational methods also predict that the *anti*-**1** conformer can be a receptor for fullerene guests (see the Supporting Information).
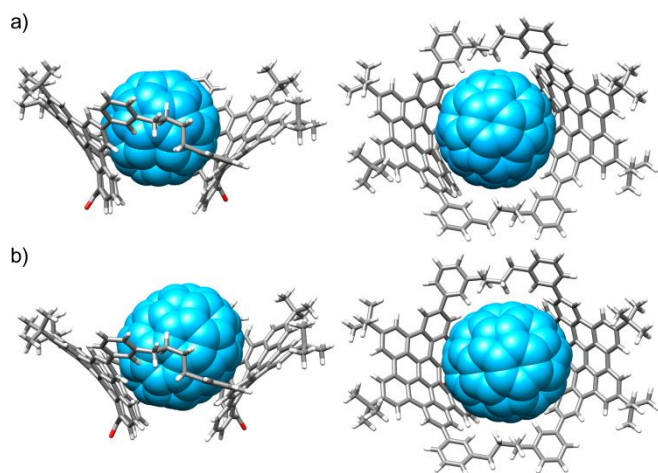
a)

b)

Figure 4. Side (left) and top (right) views of the calculated DFT (ωB97XD/def2SVP in *o*-DCB) structure of: a) *syn*-**1**⊂C_{60}; b) *syn*-**1**⊂C_{70}. Colour coding: C, gray or light blue; H, white; O, red.

In summary, we have synthesized the first example of a new type of macrocycle incorporating curved heptagon-containing extended PAH units. This cyclophane can act as supramolecular receptor of curved π systems. Thus, it forms host-guest complexes with C_{60} and C_{70} as demonstrated by NMR titration experiments. The curvature induced by the heptagon allows sufficient shape complementarity to fullerenes to enable the accommodation of the latter within the macrocycle cavity by means of π interactions. This proof-of-concept system shows that saddle shaped HAPs, such as the hept-HBC unit, can play an important role, yet to be explored, in the design of new macrocycles which could address receptor abilities, opening the door to a future development of variety of structures.

Acknowledgements

[1] a) H. Isobe, S. Hitosugi, T. Yamasaki, R. Iizuka, *Chem. Sci.* **2013**, *4*, 1293-1297; b) T. K. Ronson, A. B. League, L. Gagliardi, C. J. Cramer, J. R. Nitschke, *J. Am. Chem. Soc*. **2014**, *136*, 15615-15624; c) M. Yoshizawa, J. K. Klosterman, *Chem. Soc. Rev.* **2014**, *43*, 1885-1898; d) T. Matsuno, S. Sato, R. Iizuka, H. Isobe, *Chem. Sci.* **2015**, *6*, 909-916; e) T. K. Ronson, W. Meng, J. R. Nitschke, *J. Am. Chem. Soc.* **2017**, *139*, 9698-9707; f) K. Yazaki, L. Catti, M. Yoshizawa, *Chem. Commun.* **2018**, *54*, 3195-3206; g) D. Lu, Q. Huang, S. Wang, J. Wang, P. Huang, P. Du, *Front. Chem.* **2019**, *7*, 668; h) Y. Xu, M. von Delius, *Angew. Chem. Int. Ed.* **2020**, *59*, 559-573; *Angew. Chem.* **2020**, *132*, 567-582.

[2] a) G. Povie, Y. Segawa, T. Nishihara, Y. Miyauchi, K. Itami, *Science* **2017**, *356*, 172-175; b) K. Y. Cheung, S. Gui, C. Deng, H. Liang, Z. Xia, Z. Liu, L. Chi, Q. Miao, *Chem* **2019**, *5*, 838-847; c) X. Lu, T. Y. Gopalakrishna, Y. Han, Y. Ni, Y. Zou, J. Wu, *J. Am. Chem. Soc.* **2019**, *141*, 5934-5941.

[3] M. D. Watson, F. Jäckel, N. Severin, J. P. Rabe, K. Müllen, *J. Am. Chem. Soc.* **2004**, *126*, 1402-1407.

[4] S. Akine, T. Onuma, T. Nabeshima, *New J. Chem.* **2018**, *42*, 9369-9372.

[5] S. E. Lewis, *Chem. Soc. Rev.* **2015**, *44*, 2221-2304.

[6] a) M. Quernheim, F. E. Golling, W. Zhang, M. Wagner, H.-J. Räder, T. Nishiuchi, K. Müllen, *Angew. Chem. Int. Ed.* **2015**, *54*, 10341-10346; *Angew. Chem.* **2015**, *127*, 10482-10487; b) D. Lu, H. Wu, Y. Dai, H. Shi, X. Shao, S. Yang, J. Yang, P. Du, *Chem. Commun.* **2016**, *52*, 7164-7167; c) D. Lu, G. Zhuang, H. Wu, S. Wang, S. Yang, P. Du, *Angew. Chem. Int. Ed.* **2017**, *56*, 158-162; *Angew. Chem.* **2017**, *129*, 164-168; d) S. Cui, G. Zhuang, D. Lu, Q. Huang, H. Jia, Y. Wang, S. Yang, P. Du, *Angew. Chem. Int. Ed.* **2018**, *57*, 9330-9335; *Angew. Chem.* **2018**, *130*, 9474-9479; e) Q. Huang, G. Zhuang, H. Jia, M. Qian, S. Cui, S. Yang, P. Du, *Angew. Chem. Int. Ed.* **2019**, *58*, 6244-6249; *Angew. Chem.* **2019**, *131*, 6310-6315; f) Y. Nakagawa, R. Sekiguchi, J. Kawakami, S. Ito, *Org. Biomol. Chem.* **2019**, *17*, 6843-6853; g) H. Jia, G. Zhuang, Q. Huang, J. Wang, Y. Wu, S. Cui, S. Yang, P. Du, *Chem. Eur. J.* **2020**, DOI: 10.1002/chem.201905396.

[7] a) I. R. Márquez, S. Castro-Fernández, A. Millán, A. G. Campaña, *Chem. Commun.* **2018**, *54*, 6705-6718; b) S. H. Pun, Q. Miao, *Acc. Chem. Res.* **2018**, *51*, 1630-1642.

[8] a) K. Yamamoto, T. Harada, M. Nakazaki, T. Naka, Y. Kai, S. Harada, N. Kasai, *J. Am. Chem. Soc.* **1983**, *105*, 7171-7172; b) J. Luo, X. Xu, R. Mao, Q. Miao, *J. Am. Chem. Soc.* **2012**, *134*, 13796-13803; c) K. Kawasumi, Q. Zhang, Y. Segawa, L. T. Scott, K. Itami, *Nat. Chem.* **2013**, *5*, 739-744; d) K. Y. Cheung, X. Xu, Q. Miao, *J. Am. Chem. Soc.* **2015**, *137*, 3910-3914; e) N. Fukui, T. Kim, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2017**, *139*, 9075-9088; f) S. H. Pun, C. K. Chan, J. Luo, Z. Liu, Q. Miao, *Angew. Chem. Int. Ed.* **2018**, *57*, 1581-1586; *Angew. Chem.* **2018**, *130*, 1597-1602.

[9] a) T. Fujikawa, Y. Segawa, K. Itami, *J. Org. Chem.* 2017, *82*, 7745-7749; b) C. M. Cruz, S. Castro-Fernández, E. Maçôas, J. M. Cuerva, A. G. Campaña, *Angew. Chem. Int. Ed.* **2018**, *57*, 14782-14786; *Angew. Chem.* **2018**, *130*, 14998-15002; c) C. M. Cruz, I. R. Márquez, I. F. A. Mariz, V. Blanco, C. Sánchez-Sánchez, J. M. Sobrado, J. A. Martín-Gago, J. M. Cuerva, E. Maçôas, A. G. Campaña, *Chem. Sci.* **2018**, *9*, 3917-3924; d) C. M. Cruz, I. R. Márquez, S. Castro-Fernández, J. M. Cuerva, E. Maçôas, A. G. Campaña, *Angew. Chem. Int. Ed.* **2019**, *58*, 8068-8072; *Angew. Chem.* **2019**, *131*, 8152-8156.

[10]   a) T. Lenosky, X. Gonze, M. Teter, V. Elser, *Nature* **1992**, *355*, 333-335; b) N. Park, M. Yoon, S. Berber, J. Ihm, E. Osawa, D. Tománek, *Phys. Rev. Lett.* **2003**, *91*, 237204; c) D. Odkhuu, D. H. Jung, H. Lee, S. S. Han, S.-H. Choi, R. S. Ruoff, N. Park, *Carbon* **2014**, *66*, 39-47.

[12]   S. Castro-Fernández, C. M. Cruz, I. F. A. Mariz, I. R. Márquez, V. G. Jiménez, L. Palomino-Ruiz, J. M. Cuerva, E. Maçôas, A. G. Campaña,, *Angew. Chem. Int. Ed.* **2020***,* DOI:10.1002/anie.202000105; *Angew. Chem.* **2020***,* DOI:10.1002/ange.202000105

[12]   I. R. Márquez, N. Fuentes, C. M. Cruz, V. Puente-Muñoz, L. Sotorrios, M. L. Marcos, D. Choquesillo-Lazarte, B. Biel, L. Crovetto, E. Gómez-Bengoa, M. T. González, R. Martin, J. M. Cuerva, A. G. Campaña, *Chem. Sci.* **2017**, *8*, 1068-1074.

[13]   The presence of the *syn* and *anti* conformers is also supported by the two sets of signals in a slow exchange regime observed in the ^{1}H NMR spectrum of **4** recorded at 256 K (Figures S13-S14).

[14]   The effective size was calculated by substracting twice the van der Waals radius of C (1.7 Å) to the measured distances.

[15]   Miao and co-workers reported the cocristallization of an extended heptagon-containing PAH with C_{60}, suggesting the establishment of supramolecular interactions between both components. However, as pointed by the authors, the poor quality of the data precluded the full refining of the structure, which was not presented. X. Gu, H. Li, B. Shan, Z. Liu, Q. Miao, *Org. Lett.* **2017**, *19*, 2246-2249.

[16]   Y. Guan, M. L. Jones, A. E. Miller, S. E. Wheeler, *Phys. Chem. Chem. Phys.* **2017**, *19*, 18186-18193.

[17]   M. Chu, A. N. Scioneaux, C. S. Hartley, *J. Org. Chem.* **2014**, *79*, 9009-9017.

[18]   Non-linear least-squares curve fitting were carried out with the online software Bindfit. Website: http://supramolecular.org/

[19]   P. Thordarson, Chem. *Soc. Rev.* **2011**, *40*, 1305-1323.

[20]   a) D. Canevet, E. M. Pérez, N. Martín, *Angew. Chem. Int. Ed.* **2011**, *50*, 9248-9259; *Angew. Chem.* **2011**, *123*, 9416-9427; b) E. M. Pérez, N. Martín, *Chem. Soc. Rev.* **2015**, *44*, 6425-6433; c) C. García-Simón, M. Costas, X. Ribas, *Chem. Soc. Rev.* **2016**, *45*, 40-62; d) A. Sygula, *Synlett* **2016**, *27*, 2070-2080; e) S. Selmani, D. J. Schipper, *Chem. Eur. J.* **2019**, *25*, 6673-6692.

Entry for the Table of Contents (Please choose one layout)

Layout 1:

COMMUNICATION

Carbon nanobasket: a new cyclophane bearing two units of heptagon-containing hexa-*peri*-hexabenzocoronene is presented. The resulted macrocyclic offers an unusual aromatic calix-shape cavity able to interact with fullerenes. Selective binding of C_{70} over C_{60} is demonstrated.
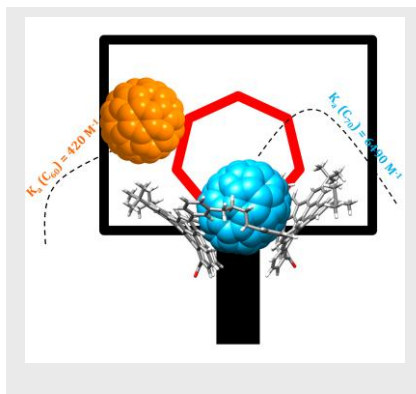
Vicente G. Jiménez, Arthur H. G. David, Juan M. Cuerva, Victor Blanco,* Araceli G. Campaña*

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