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Aryl–Aryl Linked Bi-5,5′-*p*-*tert*-butylcalix[4]arene Tweezer for Fullerene Complexation

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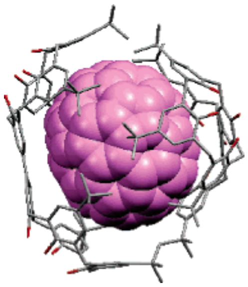
ABSTRACT



We report the synthesis and complexing properties of the new cavity-extended receptor 1, a C,C-linked bi-calix[4]arene that selectively binds [70]fullerene in a 2:1 tennis-ball fashion.

Recognition of quasi spherically shaped fullerenes by several molecular receptors based in hollow structures has been reported.[1−4] Particularly interesting is the separation of fullerene mixtures on the basis of *p*-*tert*-butylcalix[8]arene for the selective precipitation of fullerene C_{60}.[5] On the other hand, receptors containing two or more calixarene subunits have attracted special attention as a result of their enhanced complexation properties.[6] In most cases, a flexible spacer acts as a linker between the two calixarene cavities, resulting in a poorly preorganized overall structure.[7] The search for new fullerene receptors prompted us to examine the formation of wide-rim "head-to-head" double *p*-*tert*-butylcalix[4]arenes directly linked through their wider rims. We expected that the *tert*-butyl groups at the rings not directly involved in the connection would result in deeper and more rigid cavities, with an improved complementarity to the fullerene surface and likely enhanced selectivity. To date, the only examples of "head-to-head" bicalix[n]arenes (n = 4,5,6,8) directly connected through their wide rims, have been reported by Neri et al.[8] and Gutsche et al.[9] and arise from the oxidative coupling of the corresponding *p*-unsubstituted moieties. In the solid state, both cavities of bicalix[4]arene

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(1) Calixarenes: (a) Wang, J.; Gutsche, C. D. *J. Org. Chem*. **2002**, *67*, 4423−4429. (b) Mizyed, S.; Georghiou, P. E.; Ashram, M. *J. Chem. Soc., Perkin Trans. 2* **2000**, 277−280. (c) Haino, T.; Yanase, M. C.; Fukunaga, L.; Fukazawa, Y. *Tetrahedron* **2006**, *62*, 2025−2035 and references therein.

(2) Thiacalixarenes: Kunsagi-Mate, S.; Szabo, K.; Bitter, I.; Nagy, G.; Kollar, L. *Tetrahedron Lett*. **2004**, *45*, 1387−1390.

(3) Cyclotriveratrylenes: (a) Steed, J. W.; Junk, P. C.; Atwood, J. L.; Barnes, M. J.; Raston, C. L.; Burkhalter, R. S. *J. Am. Chem. Soc*. **1994**, *116*, 10346−10347. (b) Zhang, S.; Palkar, A.; Fragoso, A.; Prados, P.; de Mendoza, J.; Echegoyen, L. *Chem. Mater*. **2005**, *17*, 2063−2068.

(4) Cyclodextrins: (a) Andersom, T.; Wastman, G.; Stenhagen, G.; Sundahl, M.; Wennerström, O. *Tetrahedron Lett*. **1995**, *36*, 597−600. (b) Kim, H.-S.; Jeon, J.-S. *Chem. Commun*. **1996**, 817−818.

(5) (a) Atwood, J. L.; Koutsantonis, G. A.; Raston, C. L. *Nature* **1994**, *368*, 229−231. (b) Suzuki, T.; Nakashima, K.; Shinkai, S. *Chem. Lett*. **1994**, 699−702.

(6) (a) Böhmer, V. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 713−745. (b) Gutsche, C. D. *Calixarenes Revisited*; The Royal Society of Chemistry: Cambridge, U.K., 1998.

(7) Ikeda, A.; Shinkai, S. *Chem. Rev*. **1997**, *97*, 1713−1734.

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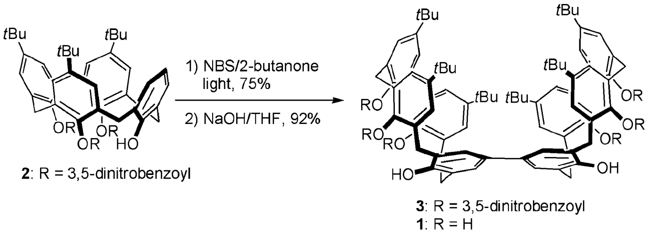
display an anti orientation.[8a] Among these receptors, only the de-*tert*-butylated bicalix[5]arene described by Gutsche et al.[9] has been found to complex fullerenes with association constants of 43 M^{-1} for C_{60} and 233 M^{-1} for C_{70} in CS_2, as determined by UV−vis titrations. As expected for the dimeric nature of this receptor, these values were about 1 order of magnitude higher than those observed for the parent calix[5]arene. However, the selectivity toward C_{70}, of the bicalix[5]arene, measured as the ratio K_{C70}/K_{C60} was 30 times lower.[9] To the best of our knowledge, there is no example of a fullerene receptor based on "head-to-head" linked calix[4]arenes, despite the inherently simpler synthetic chemistry of calix[4]arene as compared with that of its higher homologues. We report herein the synthesis, molecular structure, and fullerene encapsulation properties of 5,5′-bi-(11,11′,17,17′,23,23′-hexa-*p*-*tert*-butyl)calix[4]arene **1**.

The synthesis of **1** was achieved in two steps from tris-*O*-3,5-dinitrobenzoyl calix[4]arene **2** (see Supporting Information). Initially, we tried to perform the oxidative coupling with $FeCl_3$ in acetonitrile, as previously reported,[8,9] but this reaction resulted in the formation of the corresponding quinone as the major product, along with traces of **1**. Therefore, we choose the classical biphenyl formation via halogen derivatives. Because attempts to directly brominate the *p*-position of **2** with $Br_2/CHCl_3$ prior to aryl−aryl coupling failed, we tried *N*-bromosuccinimide. Surprisingly, bicalixarene **3** was formed directly (Scheme 1).[10] Removal of the aroyl protecting groups under basic conditions afforded **1** in a 69% yield overall from **2**.

Scheme 1. Synthesis of Receptor **1**



2: R = 3,5-dinitrobenzoyl

3: R = 3,5-dinitrobenzoyl
1: R = H

In solution, both linked calixarenes display a flattened cone conformation, as indicated by the presence of two broad high-field AX systems in the ^1H NMR spectrum ($CDCl_3$) and two signals at ∼32 ppm for the methylene bridges in the ^{13}C NMR spectrum.[11] This structure was confirmed in the solid state. Crystals suitable for X-ray analysis were obtained by the slow evaporation of a dichloromethane solution of **1**.

Unlike its *p*-unsubstituted analogue,[8a] both calixarene subunits are syn oriented in **1** (Figure 1a), with the biphenyl linkage tilted by 43°. As a result, the *tert*-butyl groups are lined up around a wall that deepens the cavity and increases its volume. Moreover, several CH−π and CH−O interactions stabilize the structure. Most interestingly, the crystal packing shows that two molecules of **1** are "head-to-head" oriented, forming a pseudocage in which up to four solvent molecules are included (Figure 1b).

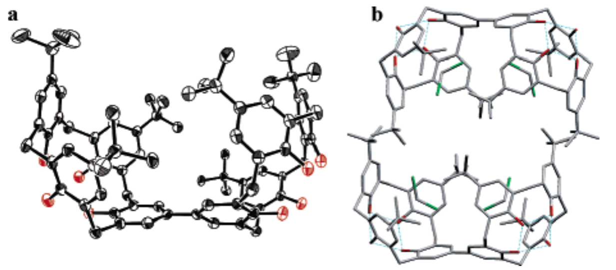


Figure 1. (a) X-ray structure of **1**. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level. (b) Wireframe representation of the pseudocage formed by two molecules of compound **1** in the solid state.

Complexation of C_{60} and C_{70} was investigated by UV−vis titrations in toluene. Both fullerenes gave stable complexes whose guest/host stoichiometries ranged from 1:1 to 1:2, depending on the concentration (Job plot analysis, Figure 2). At submillimolar concentrations, both stoichiometries coexist, especially in the case of C_{70}. At higher concentrations, however, the formation of a 1:2 complex is more evident, as indicated by the maximum close to $\chi = 0.67$. The titration data was analyzed using global multivariate factor analysis[12] for a guest/host stoichiometry of 1:2 and considering the parent fullerene and its complex as a colored species (see Supporting Information). Thus, the stability constants for the formation of a 1:2 complex were evaluated

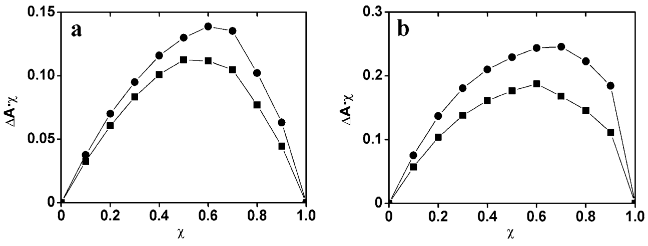


Figure 2. Job plots for the complexation of **1** with C_{60} (a) and C_{70} (b) at 0.14 mM (■) and 1.4 mM (●).

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[8] "Head-to-head" bicalix[4]arenes: (a) Neri, P.; Bottino, A.; Cunsolo, F.; Piattelli, M.; Gavuzzo, E. *Angew. Chem., Int. Ed.* **1998**, *37*, 166−169. (b) Bottino, A.; Cunsolo, M. F.; Piattelli, M.; Gavuzzo, E.; Neri, P. *Tetrahedron Lett.* **2000**, *41*, 10065−10069. Bicalix[6] and [8]arenes: (c) Bottino, A.; Cunsolo, F.; Piattelli, M.; Garozzo, D.; Neri, P. *J. Org. Chem.* **1999**, *64*, 8018−8020.

[9] "Head-to-head" bicalix[5]arenes: Wang, J.; Borige, S. G.; Watson, W. H.; Gutsche, C. D. *J. Org. Chem.* **2000**, *65*, 8260−8263.

[10] A radical pathway for the aryl−aryl coupling is likely, as the reaction does not occur in the dark. TLC and MS analysis revealed that the *p*-bromo derivative is formed in the first stages of the reaction but is rapidly transformed into **3**. Interestingly, when the reaction was attempted on 11,17,23,29-tetra-*p*-*tert*-butyl-32,33,34,35-tetra-(3,5-dinitrobenzoyloxy)calix[5]arene, no coupling was observed.

[11] Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sánchez, C. *J. Org. Chem.* **1991**, *56*, 3372−3376.

as $\log K_{12} = 4.2 \pm 0.2$ and 5.1 ± 0.4 for C_{60} and C_{70}, respectively (Figure 3).[13]

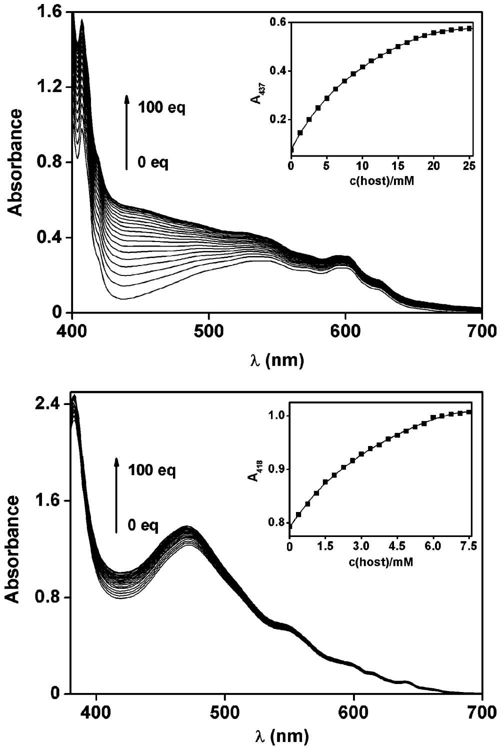

Figure 3. Variations on the UV−vis spectra of 0.5 mM C_{60} (top) and 0.15 mM C_{70} (bottom) upon addition of **1** in toluene at 295 K. The titration curves at selected wavelengths are shown in the inset.

Thus, **1** binds C_{70} about eight times more strongly than C_{60}. This behavior differs markedly from that reported by Gutsche et al. for a bicalix[5]arene, which only forms a relatively weak 1:1 complex with both fullerenes.[9] Selectivity toward C_{70} could arise from a better fitting of this fullerene into a dimeric cage made from two bicalix[4]arenes orthogonally oriented in a "tennis-ball" fashion, with intertwining *tert*-butyl groups. Indeed, an examination of optimized molecular models suggests that the "egg-shaped" form of C_{70} fits better than the "soccer-ball" shaped C_{60} into the dimeric cavity (Figure 4).

The only previous examples of fullerene complexation by related receptors correspond to calix[4]naphthalenes[1b] or thiacalix[4]arenes.[2] Therefore, to the best of our knowledge, this is the first example of the complexation of fullerenes by *p*-*tert*-butyl calix[4]arenes.

The complexation of C_{60} by **1** was also studied by electrochemical techniques. The cyclic voltammogram (CV) of a 1 mM solution of C_{60} in a 5:1 toluene/acetonitrile mixture showed the three characteristic cathodic waves corresponding to its first, second, and third reductions, respectively (Figure 5a).[14] The peak-to-peak separation is relatively large (200−220 mV) most likely a result of uncompensated resistance effects provoked by the low

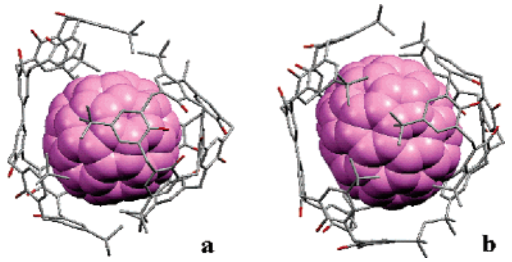

Figure 4. Side views of optimized structures of the 1:2 complexes of **1** with (a) C_{60} and (b) C_{70} (Insight II/Discovery in vacuo, cvff force field calculation).

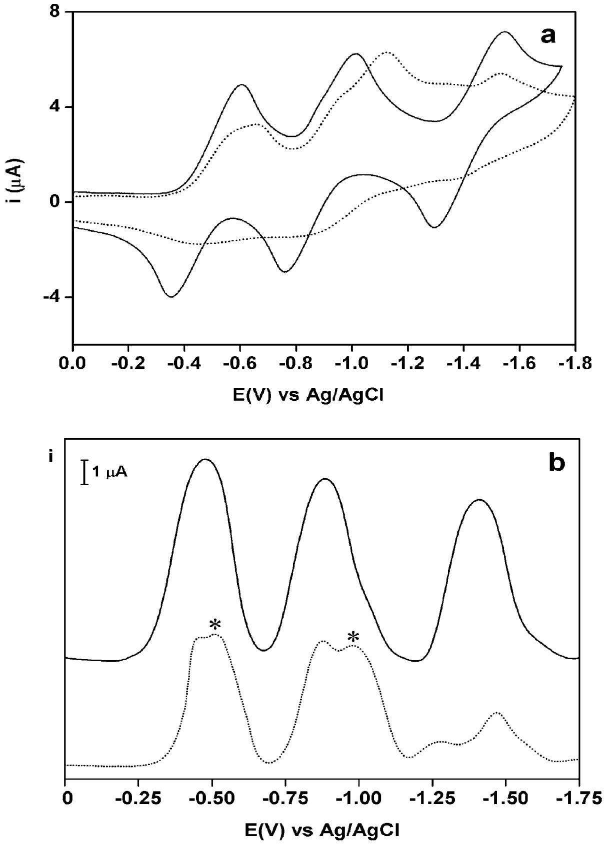

Figure 5. CV (a) and DPV (b) responses of 1 mM C_{60} (—) and in the presence of 1 equivalent of **1** (···) in toluene/acetonitrile, 5:1. Supporting electrolyte: 0.1 M NBu_4PF_6. Working electrode: 0.03 cm^2 Pt disk. Scan rate: 100 mV/s.

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(12) (a) *SPECFIT*, version 3.0; Spectra Software Associates. (b) Gampp, H.; Maeder, M.; Meyer, C. J.; Zuberbühler, A. D. *Talanta* **1985**, *32*, 95−101. (c) Gampp, H.; Maeder, M.; Meyer, C. J.; Zuberbühler, A. D. *Talanta* **1986**, *33*, 943−951.

(13) For a 1:1 binding model, the association constants would translate into $\log K_{11} = 1.9 \pm 0.2$ and 2.3 ± 0.3 for C_{60} and C_{70}, respectively.

(14) Echegoyen, L.; Echegoyen, L. E. *Acc. Chem. Res.* **1998**, *31*, 593−601.

polarity of the solvent. Upon addition of 1 equiv of **1**, the signal intensity decreases by about 40%, indicating the formation of a C_{60}−**1** complex that reduces the diffusion rate of C_{60} to the electrode. Interestingly, the reduction waves are split into two signals, as is more evident by examining the differential pulse voltammograms (DPV; Figure 5b). As can be seen, the first two reduction signals show two peaks, one at the same potential of free C_{60} and a second one that is shifted to more negative potentials (indicated with an asterisk), which might correspond to the C_{60}−**1** complex. This means that electron incorporation to the complex is less favored in the presence of **1**, as expected as a result of its electron-rich character. The $i_{p\,\mathrm{free}}/i_{p\,\mathrm{complex}}$ ratio for the first and second reduction steps were 0.95 and 1.16, respectively. These values correlate reasonably well with the concentrations of free and complexed C_{60} because, according to the distribution diagram for this system, at 1 mM C_{60} and 1 mM **1**, the concentrations of C_{60} and C_{60}−**1** were 0.56 mM and 0.44 mM, respectively, with $[C_{60}]/[C_{60}-\mathbf{1}] = 1.27$. It should also be noted that the second reduction is more difficult than the first one, as evidenced by the increased cathodic shift of this peak (−100 mV) when compared with the gain of the first electron (−30 mV). A similar signal spitting has been previously observed and was also explained in terms of host−guest complexation.[15,16] In these cases, however, the CV changes were observed only after several days of interaction, in contrast to the present results where splitting was immediately observed. This accounts for a relatively fast complexation of C_{60} by **1**. The almost complete absence of anodic currents in the CV indicates that the electrochemical process is now chemically and electrochemically irreversible. After 1 h, the voltametric response of free C_{60} is partially recovered due to decomposition of the complex.

In summary, we have reported the synthesis of the new cavity-extended receptor **1**, which represents the first example of fullerene complexation by a *p-tert*-butylcalix[4]arene. The complexing ability of this receptor toward other guests as well as the preparation of higher homologues is currently under study.

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Supporting Information Available: Synthetic procedure and crystallographic data for **1** and complexation studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Chen, Z.; Fox, J. M.; Gale, P. A.; Pilgrim, A. J.; Beer, P. D.; Rosseinsky, M. J. *J. Electroanal. Chem.* **1995**, *392*, 101−105.

(16) Olsen, S. A.; Bond, A. M.; Lazarev, G.; Mahon, P. J.; Raston, C. L.; Tedesco, V.; Compton, R. G.; Marken, F.; Webster, R. D. *J. Phys. Chem. A* **1998**, *102*, 2641−2649.