

A Bis-exTTF Macrocyclic Receptor That Associates C₆₀ with Micromolar AffinityHelena Isla,[†] María Gallego,[†] Emilio M. Pérez,^{†,‡} Rafael Viruela,[§] Enrique Ortí,^{*,§} and Nazario Martín^{*,†,‡}*Departamento de Química Orgánica, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain, IMDEA-Nanociencia, 28049 Madrid, Spain, and Instituto de Ciencia Molecular, Universidad de Valencia, 46980 Paterna, Spain*

Received November 30, 2009; E-mail: enrique.orti@uv.es; nazmar@quim.ucm.es

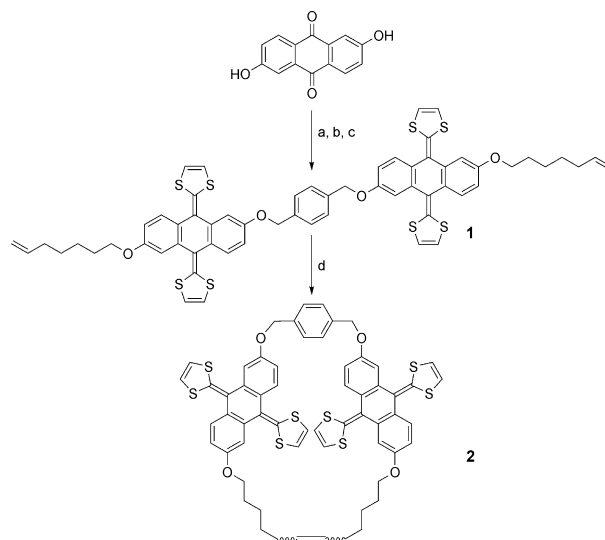
The search for molecular receptors for fullerenes is a very active area of research.^{1–3} Various receptors based on concave recognition motifs such as cyclotrimeratrylenes,^{4,5} corannulenes,^{6,7} cyclic paraphenyleneacetylenes,^{3,8–10} and π -extended tetrathiafulvalene derivatives^{11–14} have been reported, but to date, hosts that exploit porphyrins as recognizing motifs have dominated the literature both in quantity and binding strength.² The highest binding constants among porphyrin-based receptors correspond to Aida's bisporphyrin macrocyclic receptors. For example, a Zn(II) metalloporphyrin derivative shows a binding constant toward C₆₀ of $\log K_a = 5.8$, while the free base shows $\log K_a = 5.9$, both in benzene at room temperature.¹⁵ The world record for complex stability toward C₆₀, achieved by an Ir(III) metalloporphyrin, shows $\log K_a = 8.1$ in 1,2-dichlorobenzene (oDCB) at room temperature.¹⁶ It is noteworthy that in the latter case, Ir was found to bind a 6,6 junction of the fullerene in an η^2 fashion.

Making use of the perfect match between the concave aromatic surface of 2-[9-(1,3-dithiol-2-ylidene)anthracen-10(9H)-ylidene]-1,3-dithiole (exTTF) and the convex surface of the fullerenes, we reported the first exTTF-based receptor for fullerene, which was based on a very simple tweezers-like design.^{11,12,14} This receptor was shown to form complexes with C₆₀ of considerable stability considering its lack of preorganization ($\log K_a = 3.5$ in PhCl at room temperature).¹⁴ We now report the design, synthesis, and fullerene binding abilities of macrocycle **2**.

The design of the macrocyclic receptor conserves the basic features of the tweezers receptor but includes an alkyl linker with terminal alkenes to achieve macrocyclization through ring-closing metathesis. Molecular mechanics showed that the most suitable spacer would be heptene, which afforded flexible macrocyclic cavities of 11–13 Å. Macrocycle **2** was synthesized in just four steps (Scheme 1) and obtained as a chromatographically inseparable mixture of *E* and *Z* isomers that was used as such. The identity and purity of **2** and all of the synthetic intermediates were unambiguously established by standard spectroscopic and analytical techniques (see the Supporting Information).

The binding constants of macrocycle **2** toward C₆₀ and C₇₀ were estimated through three independent UV–vis titrations at room temperature. In a typical experiment, to a solution of **2** (1.0×10^{-5} M in PhCl) were added aliquots of a solution of C₆₀ or C₇₀ ($3\text{--}4 \times 10^{-5}$ M in PhCl) up to a total of 2–3 molar equiv, working at constant host concentration (see the Supporting Information).

The results of a titration experiment involving **2** and C₆₀ are shown in Figure 1a. The spectral features are similar to what we had previously observed for exTTF tweezers.^{11,14} With an increase in the concentration of C₆₀, a significant decrease in the absorption

Scheme 1. Synthesis of Macrocycle **2**^a

^a Conditions: (a) 7-bromo-1-heptene, K₂CO₃, NaI (cat), DMF, reflux, 2 h; (b) α,α' -*p*-dibromoxylene, K₂CO₃, NaI (cat), DMF, 60 °C, 4 h; (c) dimethyl 1,3-dithiol-2-ylphosphonate, BuLi, THF, –78 °C to rt, 2 h; (d) Grubb's first-generation catalyst, CH₂Cl₂, rt, 2 h.

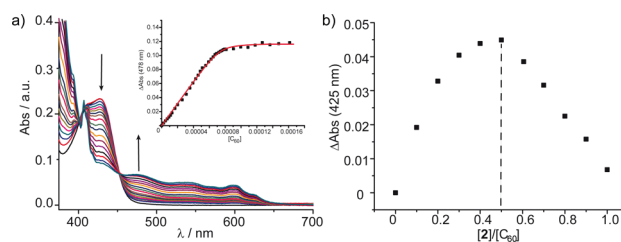


Figure 1. (a) Spectral changes in a UV–vis titration experiment for **2** vs C₆₀ in PhCl at room temperature; the inset shows the binding isotherm ($K_a = 1\,087\,200\text{ M}^{-1}$, $R^2 = 0.996$). (b) Job's plot demonstrating the 1:1 stoichiometry.

at $\lambda = 425\text{ nm}$ was observed, together with the appearance of a charge-transfer band centered at 478 nm with an isosbestic point at 450 nm. The expected 1:1 stoichiometry, suggested by the presence of the isosbestic point, was confirmed through continuous variation plots (Figure 1b). In the case of C₇₀, the spectral changes were less obvious because of spectral overlap (see the Supporting Information). The binding constant of **2** toward C₆₀ in PhCl at room temperature was found to be $\log K_a = 6.5 \pm 0.5$ (Specfit) or 6.1 ± 0.2 (Origin). This represents an increase of 3 orders of magnitude with respect to our previously reported receptors^{11,14} and is one of the highest binding constants toward C₆₀ reported in the literature,^{1–3} illustrating the dramatic effect of preorganization.¹⁷ In regard to

[†] Universidad Complutense.[‡] IMDEA-Nanociencia.[§] Universidad de Valencia.

C₇₀, the binding constant was too large to be calculated precisely through UV–vis titrations.¹⁸ With the aim of lowering the binding constant to a more reliable quantity, we changed to oDCB as the solvent. However, despite the fact that both **2** and the fullerenes are soluble in oDCB, when we approached 1:1 stoichiometry during the addition process, the solution immediately turned turbid, precluding UV–vis measurements. The mixture of *E* and *Z* isomers and the flexibility of **2** prevented the formation of single crystals suitable for X-ray diffraction, so we investigated the geometry of the complexes through density functional theory (DFT) calculations using the Becke “half-and-half” (BH&H) functional (see the Supporting Information for full computational details). Figure 2 shows the structure of the complex of (*Z*)-**2** with C₆₀ calculated at the BH&H/6-31G** level.¹⁹

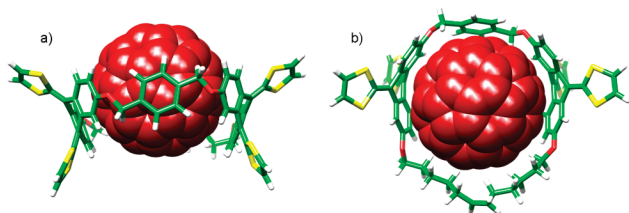


Figure 2. (a) Side view and (b) top view of the energy-minimized structure (BH&H/6-31G** level) of the (*Z*)-**2**–C₆₀ complex.

The DFT calculations confirmed that **2** is a close to perfect fit for C₆₀, with both exTTFs, the aromatic xylylene linker, and the alkyl spacer closely wrapping around the fullerene unit. BH&H/6-31+G** calculations including corrections for the basis-set superposition error predicted a binding energy of $-24.1 \text{ kcal mol}^{-1}$, which is significantly higher than that calculated for the exTTF tweezers under the same computational conditions,^{11,12} in agreement with the experimental results.

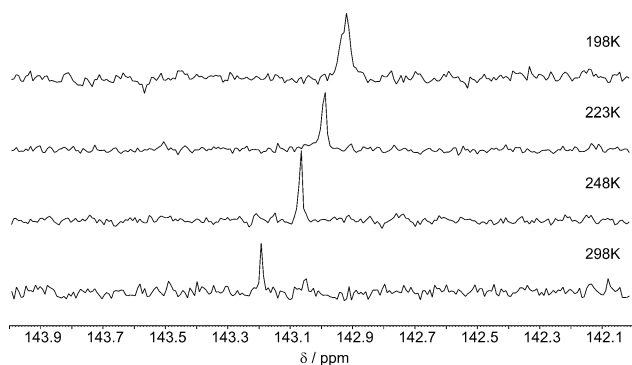


Figure 3. ¹³C NMR spectra (75 MHz) of a mixture of C₆₀ and **2** (1.5:1) in toluene-*d*₈ at several temperatures.

The binding event was also investigated by ¹³C NMR spectroscopy, which confirmed the association of **2** with C₆₀. Figure 3 shows variable-temperature ¹³C NMR spectra (75 MHz) for a mixture of C₆₀ and **2** (1.5:1) in toluene-*d*₈. The spectra were run with a sufficient number of scans to detect the signal of C₆₀ only. The signal shifted upfield and broadened upon cooling, as would be expected for the formation of the complex.²⁰ The association equilibrium remained rapid even at 198 K, although the significant broadening indicates that we were close to the temperature of coalescence.

In conclusion, we have described an exTTF-based macrocyclic receptor that associates C₆₀ with a binding constant that is 3 orders

of magnitude higher than the previous examples of exTTF-based receptors,^{11,12,14} nearly 2 orders of magnitude higher than those reported for metalloporphyrin tweezers,^{21,22} and even superior to most of Aida's porphyrin macrocycles, with the exception of the Rh(III)¹⁵ and Ir(III)¹⁶ congeners. These results definitely consolidate exTTF as one of the most suitable fragments for the molecular recognition of fullerenes. The simplicity of the synthetic route to obtain **2** augurs well for its utilization in the construction of electroactive nanostructures.^{23–25} This, together with the full structural optimization of the aromatic linker and the alkyl spacer, is the main objective of our future investigations.

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Supporting Information Available: Supporting figures and experimental and computational details. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (17) For comparison, the linear precursor **1** showed $\log K_a = 3.01$ in PhCl at room temperature.
- (18) Utilizing Specfit, we were able to approximate it as $\log K_a = 8.4 \pm 2.5$.
- (19) The BH&H functional has been shown to provide good performance for supramolecular systems dominated by dispersion interactions (see: Zhao, Y.; Truhlar, D. G. *J. Chem. Theory Comput.* **2007**, *3*, 289). The *Z* and *E* isomers define cavities of similar size.
- (20) As might be expected, the magnitude of the shielding effect is significantly smaller than that observed for porphyrin-based receptors (see ref 2) since in our case (as opposed to the strong ring currents of porphyrins) the shielding capacity of **2** is comparable to that of the aromatic solvent.
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