ORGANIC LETTERS

2004
Vol. 6, No. 7
1091−1094

p-(1*H*-Phenanthro[9,10-*d*]imidazol-2-yl)-Substituted Calix[4]arene, a Deep Cavity for Guest Inclusion

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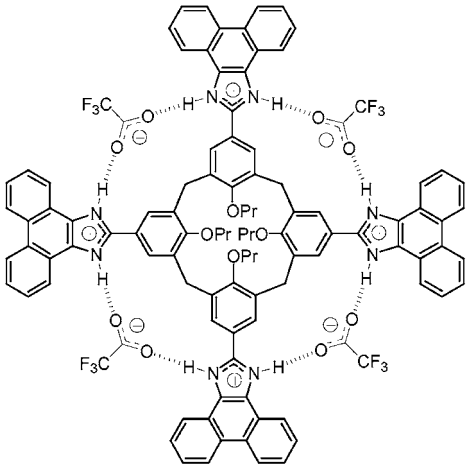
Received November 24, 2003

ABSTRACT



The reaction of tetra-*p*-formyltetra-*O*-propylcalix[4]arene with phenanthrenequinone in the presence of NH_4OAc affords compound 2, a new class of calixarene with an expanded aromatic cavity, that could be stabilized by hydrogen-bonded bridges and/or ion pairing, thus preventing collapse into fully stacked pinched cone conformations as depicted. Two partially protonated calixarenes interdigitate in the solid state to give rise to a self-assembled face-to-face dimer, stabilized by π–π stacking interactions.

Calixarenes are useful building blocks for the selective recognition of cations, anions, and neutral molecules.[1] In calix[4]arenes, the relatively small cavity of the macrocycle restrains its role to be a platform where the binding groups are attached and oriented for recognition, which usually takes place outside the cavity. Although sizable holes may arise from the larger, less accessible, and more flexible calix[*n*]-arenes ($n = 5, 6, 8$), the increased flexibility results in poor preorganization and frequent collapse.[2]

The calix[4]arene platform, easily fixed into a cone conformation by *O*-alkylation of the phenolic groups with groups larger than ethyl, could be expanded and deepened by attachment of further aromatic planar surfaces at the para

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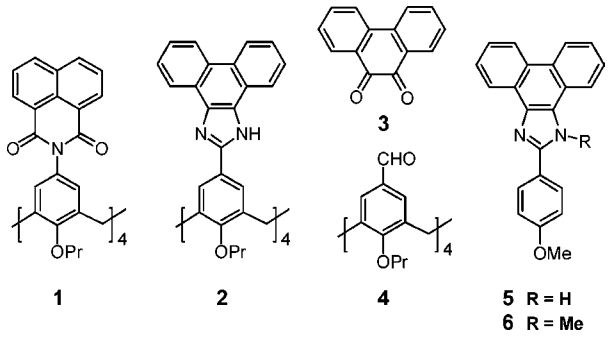
10.1021/ol036287x CCC: $27.50
Published on Web 03/02/2004

positions of the phenol rings. However, extended surfaces such as styrene, 1-naphthyl, or carbazol-9-yl attached at two opposite rings give rise to "pinched" cone structures stabilized by $\pi-\pi$ interactions, so no permanent cavities are available for guest encapsulation.[3] Introduction of four substituents instead of two does not contribute either to prevent collapse. For instance, attachment of four 1,8-naphthalene imides to the wider rim of a calix[4]arene yields the deep structure **1**, which is again collapsed into a pinched cone conformation.[4] Moreover, X-ray analysis reveals that the outer aromatic imides are almost perpendicular to the respective phenol rings, whereas the inner ones are twisted 60° to reach an optimal stacking and to minimize the repulsions between the adjacent carbonyl groups. Consequently, no encapsulation was reported.



1 **2** **3** **4** **5** R = H **6** R = Me

We describe herein calix[4]arene **2**, a deep cone-shaped macrocycle bearing four coplanarly oriented 1*H*-phenanthro[9,10-*d*]imidazol-2-yl groups. The location of imidazole N and NH heteroatoms within the ensemble opens the possibility to preventing full collapse or stabilize the shape into a more preorganized conical conformation by linking the large planar aromatic surfaces through hydrogen-bonded ion pairs.[5,6] In addition, the phenanthroimidazole moiety is a stable chromophore endowed with high extinction coefficients and fluorophoric properties.[7]

Calixarene **2** was readily obtained in 65% yield by reaction of tetrakis-*p*-formylcalix[4]arene[8] (**4**) with 8 equiv of 9,10-phenanthrenequinone (**3**) in refluxing acetic acid in the presence of an excess ammonium acetate.[9] Model compound **5**[10] was prepared similarly and, together with its *N*-methyl derivative **6**, used as a control.

The structure of **2** was mainly established by MALDI-TOF (m/z = 1458.6 $[M + H]^+$) and ESI (m/z = 1458.7 $[M + H]^+$, 729.6 $[M + 2H]^{2+}$) mass spectrometries, as well as by ^{1}H and ^{13}C NMR and elemental analysis.

The compound was almost insoluble in most organic, nonprotic solvents, but addition of ca. 25% methanol or protic acids, such as trifluoroacetic acid (TFA) or HCl, to a suspension in chloroform resulted in clean solutions. Broad signals were observed in the ^{1}H NMR spectrum ($CDCl_3$/MeOD or CD_2Cl_2/MeOD) (Figure 1a), even at low temperature (188 K), probably due to a slow equilibrium between several conformers.[11]

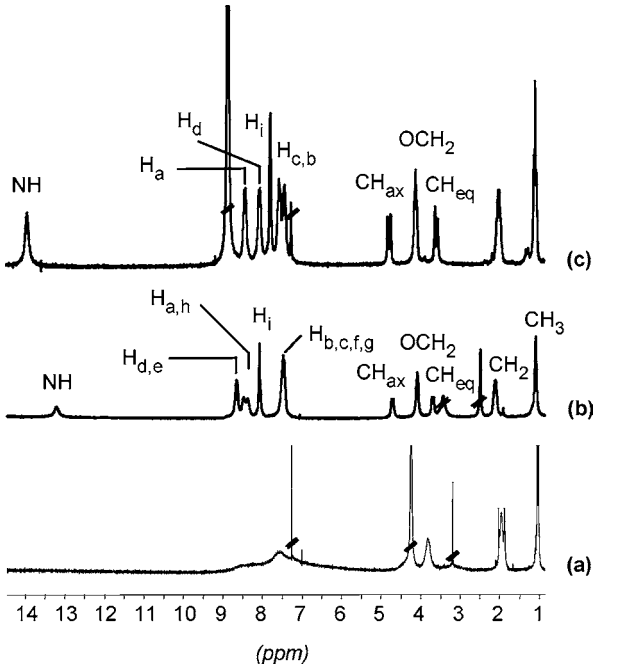


Figure 1. ^{1}H NMR spectra of **2**: (a) in $CDCl_3$/MeOD, (b) in DMSO-d_6, (c) in $CDCl_3/CF_3CO_2H$. The highest peaks marked with a double line are solvent peaks.

On the contrary, the spectrum in DMSO-d_6 was well resolved and could be fully assigned through a ROESY experiment (Figures 1b and 2). The $ArCH_2Ar$ protons appear as an AX system (δ = 4.71 and 3.69 ppm), typical for a C_{4v} conical structure or for pinched conformers in rapid equilibrium.

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(11) A similar behavior has been described for calix[4]arene **1** endowed with four naphthalene imides, although a well-resolved spectrum, accounting for a stable pinched cone, was observed at −58°C (see ref 4).

Remarkably, a slow annular tautomerism of the imidazole rings was observed, as evidenced by the split signals for H_a and H_h or for H_d and H_e (see the Supporting Information). The structure becomes symmetric at 413 K, and coalescence was found at 318 K (Figure 3). In contrast, control compound **5** displays a rapid tautomeric equilibrium at room temperature, as expected. Both the slow in the tautomeric equilibrium and the well-resolved structure in solution could be explained by the presence of bridges between the heterocyclic subunits, established through a complement of hydrogen bond donors and acceptors, such as water or DMSO molecules, as depicted in Figure 2.

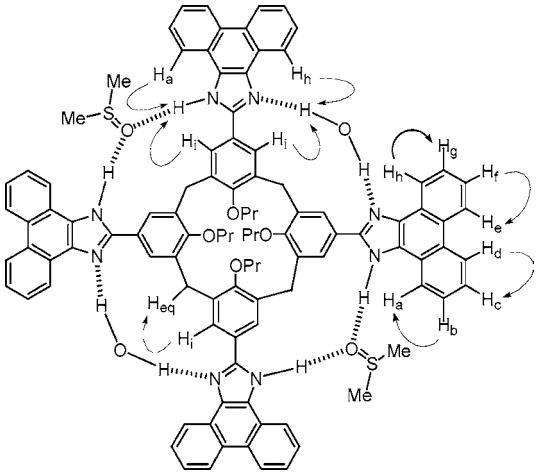

Figure 2. Proposed structure for **2** in DMSO-d_6. Arrows indicate the main NOE cross-peaks found in the ROESY spectrum.

Oxoanions could also act as hydrogen acceptor bridges between the subunits. Indeed, a well-resolved spectrum in $CDCl_3$/TFA compatible with a C_4-symmetric cone conformation was obtained at room temperature (Figure 1c). Interestingly, the singlet at 13.93 ppm (imidazolium NH) does not average with the TFA signal. However, splitting of signals is observed at 233 K, in agreement with the presence of two equivalent distorted or pinched cones in equilibrium (see the Supporting Information).

In $CDCl_3$/HCl, the spectrum of **2** was too broad to be analyzed by NMR. Thus, protonation of the imidazole rings is not the only requirement to obtain well-resolved spectra. Likely, TFA establishes four hydrogen-bonded, ion-paired bridges that prevent rotation of the phenanthroimidazole moieties on top of the calixarene platform (see in the Abstract graphic).

Attempts to obtain crystals from a dichloromethane/TFA mixture failed, but suitable crystals for X-ray analysis were grown by slow evaporation of a 1:4 ratio of **2** and TFA in a solution of CH_2Cl_2/MeOH (3:1).[12] The structure **7** contains molecule **2** with three of its phenanthroimidazole groups protonated by three TFA molecules, respectively (Figure 4).

Two out of the three TFA molecules bridge the neighboring imidazole groups through strong hydrogen bonds (lengths

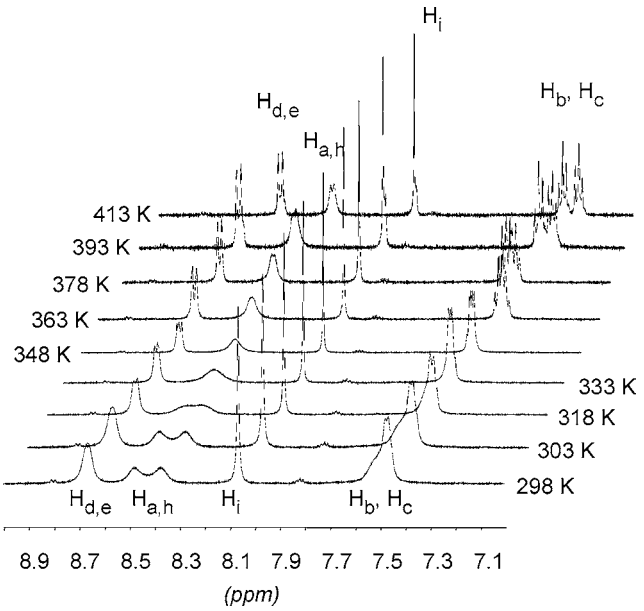

Figure 3. ^{1}H NMR spectrum of **2** (aromatic region) in DMSO-d_6.

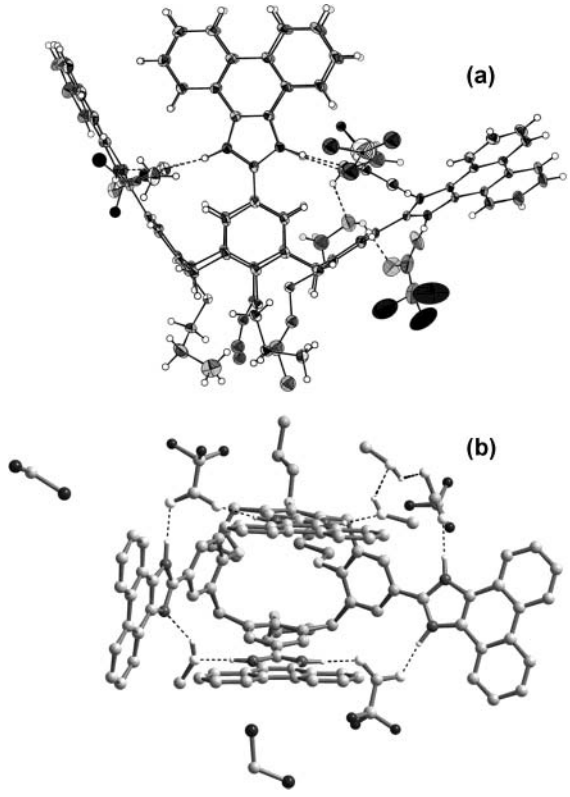

Figure 4. X-ray structure **7** with one calix[4]arene **2**, three TFA, and three MeOH bridging molecules: (a) side view, (b) top view. Hydrogens are omitted for clarity.

from 1.679 to 1.821 Å). The third TFA is hydrogen bonded to one imidazole hydrogen and also involved in a pattern of hydrogen bonds including two methanol molecules and a

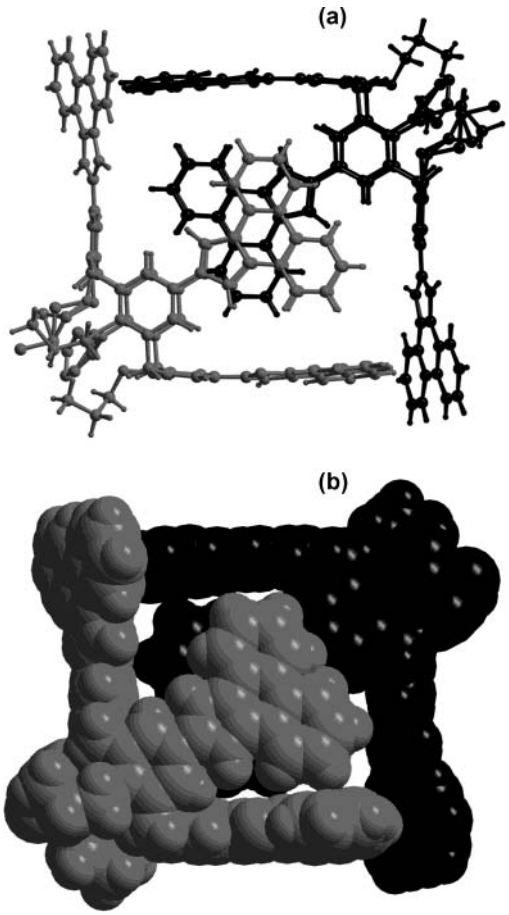

Figure 5. Packing of two interleaved calixarenes in the crystal showing the offset face-to-face $\pi-\pi$ interactions: (a) ball-and-stick representation; (b) CPK model.

protonated imidazole. The TFA creates a bridge between the imidazole groups together with the two methanol molecules. The fourth bridge involves a methanol molecule. The hydrogen bonding was clearly observable despite the rotational disorder of the trifluoromethyl groups of the TFA molecules.

The bridging results in a distorted, pinched cone conformation which is further stabilized by dimerization with the paired phenanthroimidazole arms gripping one another by offset face-to-face $\pi-\pi$ interactions (Figure 5). The winged phenanthroimidazole arms participate in the dimerization by accepting CH$-\pi$ hydrogen bonds. The CH$-\pi$ (centroid) distance is 2.913(2) Å and the $\pi-\pi$ interaction lengths range from 3.496(1) to 3.797(1) Å.

In good agreement with those results in the solid state, compound **2**, in the presence of TFA, interacts also *in solution* with suitable guests. Thus, addition of *N*-methyl model **6** to a solution of **2** in $CDCl_3$/TFA resulted in a 0.2−0.4 ppm upfield shift of the ^{1}H NMR signals for the aromatic CH protons, which are likely inside the cavity, while the OCH_3 signal, at the outside, remained essentially unchanged. The *N*-methyl signal of **6** was hardly seen at room temperature, due to extensive broadening, but showed a remarkable upfield shift (ca. 1.2 ppm) at 233 K, accounting for its inclusion deeply into the cavity. Upon cooling, the calixarene conformation equilibria frozen and signals for both the complex and free host and guest components are neatly resolved at 233 K in a 35:65 ratio. Moreover, the signals corresponding to the NH protons of the host were split into four signals in the complex, accounting for the loss of symmetry induced by the guest upon encapsulation (see the Supporting Information).

In summary, we have described a new deep calixarene whose cavity can be stabilized by hydrogen-bonded bridges and/or ion pairing, suitable for encapsulation of sizable guests. The presence of imidazole subunits opens the possibility of establishing a more robust array of covalent bridges by alkylation and quaternization with suitable difunctionalized spacers. In resorcinarenes (the calix[4]arene resorcinol analogues), the flexible structure can be rigidified into the so-called cavitands by short spacers.[13] A similar strategy with phenanthroimidazole calix[*n*]arenes such as **2**, would lead to polycationic permanent well preorganized cavities useful for molecular recognition, catalysis or molecular materials. Our results in these directions will be reported on due time.

Acknowledgment. We are grateful to "Ministerio de Ciencia y Tecnología" of Spain for financial support (Grant No. BQU2002-03536).

Supporting Information Available: Experimental procedures for the synthesis of **2**−**6**, NMR spectra for compounds **2**, **5**, **6**, and complex **2•6**, as well as crystal structure data for **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Crystallographic measurement at 123.0(1) K using an Enraf Nonius Kappa-CCD diffractometer, Mo Kα radiation. Structure solution by direct methods, full matrix least-squares refinement on F_2, no absorption correction: $C_{111}H_{83}O_{13}N_8Cl_4F_9$, M 2049.65, crystal size 0.40 × 0.30 × 0.15 mm, triclinic, space group *P*-1 (No. 2), a = 14.7972(2) Å, b = 16.9446(3) Å, c = 22.5701(3) Å, α = 97.406(1)°, β = 106.599(1)°, γ = 109.447(1)°, V = 4964.2(1) Å^3, Z = 2, D_c = 1.374 g/cm^3, i = 0.205 mm^{-1}, 32705 reflections, 16844 independent, R_{int} = 0.0409, R_1 = 0.1021, wR_2 = 0.2687 for $I > 4\sigma(I)$, 1298 parameters, S = 1.064.

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