

A New Macrocavitand from the Head to Tail Four-point Capping of *p*-*tert*-Butylcalix[8]arene with a Calix[4]arene

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The synthesis of a partially rigid calix[8]arene with a deep cavity, obtained by capping *p*-*tert*-butylcalix[8]arene **1** with tetramethoxy-*p*-tetrachloromethylcalix[4]arene **2** in the presence of CsF is reported.

Calix[4]- and calix[6]-arenes have been widely studied as molecular receptors for the inclusion of neutral molecules or as molecular platforms for anchoring binding groups which are able to complex selectively metal ions or polar organic molecules.¹ The conformational mobility of the macrocycles has also been reduced by suitable functionalization, including capping, at the lower rim.² On the contrary, calix[8]arenes and their simple derivatives, which are very attractive for the synthesis of molecular receptors for large organic molecules, experience a very high conformational mobility^{1,3} which reduces their molecular recognition abilities. Only very recently examples of 1,5-*intra*-bridged calix[8]arene derivatives, having reduced conformational mobility, have been reported.⁴

In this paper we report the first example of a calix[8]arene C_4 -symmetrically capped at the lower rim with a calix[4]arene derivative, which has a large cavity and shows reduced mobility.

Examination of CPK molecular models suggested that tetramethoxy-*p*-tetrachloromethylcalix[4]arene **2** could be a suitable capping unit with a possible coupling in 1,3,5,7-positions of *p*-*tert*-butylcalix[8]arene. The reaction of *p*-*tert*-butylcalix[8]arene **1** with tetramethoxy-*p*-chloromethylcalix[4]arene **2**⁵ in the presence of CsF and NaI in refluxing acetone, under high dilution conditions, gives the capped calix[8]arene **3** in 30% yield (Scheme 1).[†]

The CI mass spectrum ($m/z = 1825$) shows the calix[8]-calix[4] coupled product, and the ¹H NMR spectra[‡] (Fig. 1) reflect the symmetry expected for **3**.

Fig. 1 shows the ¹H NMR spectrum of **3** in (CD₃)₂SO at 370 K§ in which the two AX quartets of the methylene bridges of the calix[4]- and the calix[8]-arene units indicate C_4 -symmetry. Interestingly, the ¹H NMR spectrum of **3** in C₂D₂Cl₄ at 330 K¶ is more complex and so complete assignment of all signals was obtained by 2D-COSY and NOESY experiments. The most important feature of this spectrum is the presence of two signals for each group of protons belonging to the calix[4]arene unit, which is in agreement with a C_{2v} symmetry for the molecule. In particular the two aromatic signals at δ 7.60 and 6.74 indicate a flattened cone conformation for this unit, in which the protons of one pair of aromatic nuclei are shielded by the anisotropic effect of the other pair.⁶ As a consequence of this particular conformational preference of the capping unit, the calix[8]arene macrocycle assumes a more elongated, elliptical conformation. On this basis the symmetry observed in (CD₃)₂SO at high temperature can be explained as a fast exchange between two elliptical structures (Fig. 2).

In conclusion compound **3** is the first example of a lower rim capped calix[8]arene in which the flipping motion of the four-

point bridged aromatic groups is inhibited by the cap and a deep cavity is created. The unsubstituted phenolic groups are conformationally mobile whereas the residual mobility of the calix[4]arene unit between two flattened cone conformations confers an elliptical shape to the calix[8]arene macrocycle. This reduces the complexation ability of macrocycle **3** as evidenced by preliminary experiments with several aromatic guest molecules. These results are in line with our recent findings, using

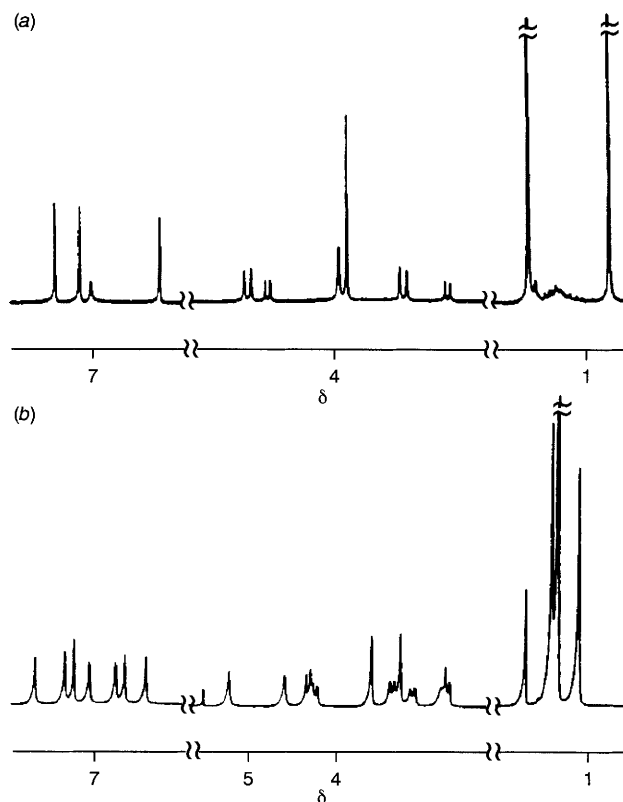
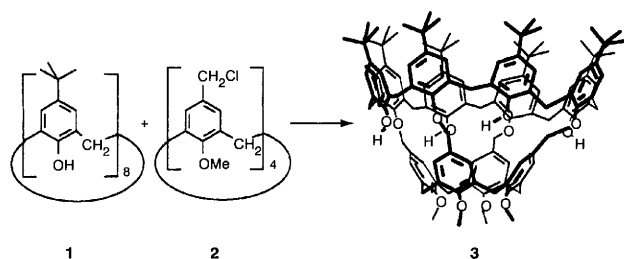


Fig. 1 ¹H NMR spectra of **3** (a) in (CD₃)₂SO at 370 K and (b) in C₂D₂Cl₄ at 330 K (400 MHz)



Scheme 1 Reagents and conditions: CsF, NaI, acetone, reflux

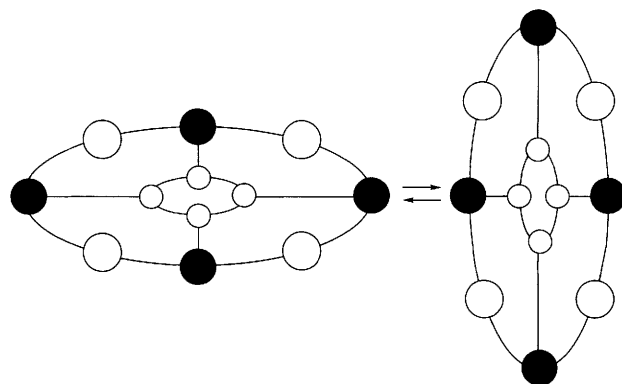


Fig. 2 Conformational interconversion of calix[8]arene macrocoring (○ = calix[8]arene unbridged aromatic rings, ● = calix[8]arene bridged aromatic rings, ○ = calix[4]arene aromatic rings)

calix[4]arene hosts, that rigidity is an essential prerequisite to ensure complexation of neutral molecules both in the gas phase and in apolar solvents.⁷ Therefore the alkylation of the free OH groups in compound **3** and the capping of *p*-*tert*-butylcalix[8]arene **1** with more rigid units is currently under investigation.

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Footnotes

† Compound **3** was prepared as follows: to a mixture of *p*-*tert*-butylcalix[8]arene **1** (0.280 g, 0.22 mmol) and dry CsF (0.260 g, 1.71 mmol) in refluxing acetone (280 ml), tetramethoxy-*p*-chloromethylcalix[4]arene **2** (0.150 g, 0.22 mmol) and NaI (0.140 g, 0.95 mmol) were added. After 3 d, the resulting mixture was evaporated, taken up into HCl solution (10%) and extracted with ethyl acetate (2 × 100 ml). The organic phase was washed with a solution of Na₂S₂O₅ (10%) and then with water. Purification by column chromatography (ethyl acetate–hexane 15:85) afforded **3** in 30% yield. Mp > 350 °C; MS(Cl, CH₄): *m/z* 1826 (MH⁺ + 1, 80), 1825 (MH⁺, 100); IR (KBr) ν/cm^{-1} 3440, 2940, 1580. As verified with other calixarenes⁸ the elemental analytical value for this compound is rather poor.

‡ Similar results were obtained in C₆D₆, CDCl₃, CD₂Cl₂. The mobility of the molecule is affected by the nature of the solvent used.

§ The solubility of compound **3** in DMSO at room temp. is very low.

¶ The signal at δ 3.69 and 3.45 are very broad at room temp.

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