Boron–nitrogen macrocycles: a new generation of calix[3]arenes

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The simple condensation reaction of 3,5-di-tert-butyl salicylaldehyde and 3-aminophenylboronic acid leads to a trimeric macrocyclic compound. The ability of this molecule to include small organic molecules was in a first approximation analyzed by ^{1}H NMR spectroscopy and X-ray crystallography.

The increasing interest in the development of calixarenes and related macrocycles is certainly due to their versatile applications in host–guest chemistry as well as their use as supramolecular building blocks.[1] As a result of the hydrophobic cavities present in calixarenes, weak forces between alkyl groups and π-systems often play a decisive role for host–guest interactions.[2] The volume and the electronic properties of calixarenes have been changed by modification of both the upper and lower rims of the calix, as well as by replacement of the connecting methylene groups by heteroatoms.[1,3] In contrast to the calix[4]arenes, calix[3]arene derivatives have received less attention.[3a,4] Recently, a silacalix[3]-phosphaarene has been reported to possess strong π-acceptor properties and its ability to coordinate tungsten was demonstrated.[5] Oxacalix[3]arene derivatives have shown high selectivity for the separation of alkaline and lanthanide metal ions.[6]

Herein, we describe the one-step preparation of an air-stable boron–nitrogen bridged macrocycle having a calix[3]arene-like conformation and its host–guest chemistry with small organic molecules. The title compound 1 was prepared by reaction of 3-aminophenylboronic acid with 3,5-di-tert-butylsalicylaldehyde under reflux of methanol in 92% yield (Scheme 1).† FAB-MS analysis revealed a peak at $m/z = 1047$, proving that a trimeric structure was obtained. Compound 1 is stable against moisture and can be stored in the presence of air for weeks without decomposition.

In the ^{1}H and ^{13}C NMR spectra recorded at room temperature in CDCl₃, a single set of signals was observed, indicating a structure with C_3 symmetry. A fast dynamic equilibrium between the two conformations normally observed for calix[3]arenes[7] was excluded, since the ^{1}H NMR spectrum remained unchanged between 213 and 333 K. A possible reason might be the rigidity of the six-membered heterocyclic connecting groups between the aromatic rings that

suppress rotation and favor the higher symmetrical cone conformer. AM1 semi-empirical calculations also predict that the cone-like conformation is more stable than the partial cone conformation by 4.7 kcal mol⁻¹. In the ^{11}B NMR spectrum only one broad signal was observed at $\delta = 4.7$ ppm, showing that the boron atoms are in a tetrahedral environment.[8]

In contrast to other boron complexes with central macrocyclic structures,[9] compound 1 is soluble in all common organic solvents, which may be attributed to the presence of six tert-butyl groups in the molecule. The solubility of the boron–nitrogen calix[3]arene enables this compound to act as a host for small organic molecules. In the solid state, two types of inclusion complexes have been detected during this study.‡ When the reaction mixtures of the starting materials required for the formation of 1 in either THF–MeOH or MeOH–CH₃COOH (9 : 1) are slowly cooled down, the crystallographic analysis showed that solvent molecules are trapped in the interstitial cavity of the host to form the 1·THF and 1·AcOMe inclusion complexes, respectively. In contrast, on recrystallization of 1 from concentrated solutions in either benzene or THF, clathrate complexes having a host–guest ratio of 1 : 5 are formed rather than simple inclusion complexes: of the five solvent molecules present in the cubic crystal lattice, only one is completely included in the cavity of the calix[3]arene-like host. Attempts to obtain solvent free diffraction grade crystals of 1 were unsuccessful, but at the same time showed the great versatility of 1 to trap solvent molecules.

A detailed analysis of the four X-ray structures, confirmed that the boron–nitrogen macrocycle 1 adopts a cone-like conformation (Fig. 1) and the presence of strong coordinative B–N bonds was observed, having an average distance of 1.620 Å. All three methoxy groups are pointing outward from the cavity, and the tert-butyl groups function as stoppers for the guest (this has been observed also for conventional calixarenes[2c]). The cavity can be considered as hydrophobic, since only aromatic rings and part of the tert-butyl groups point to its interior.

In principle, two sites can be considered for guest inclusion: (i) the cavity formed by the aromatic groups of the boronic acid base
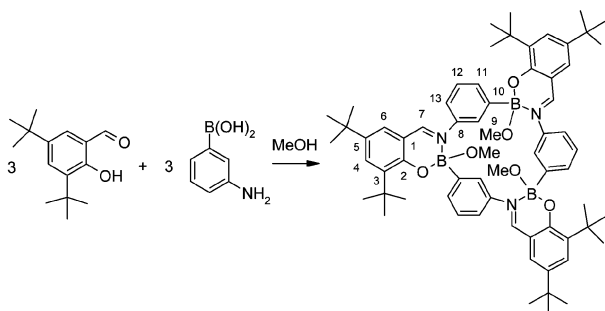
Scheme 1 One-pot synthesis of compound 1.
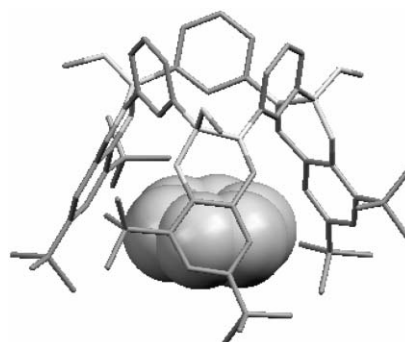
Fig. 1 Side view of the 1·C₆H₆ inclusion complex using a stick model for the host and a space filling model for the guest.
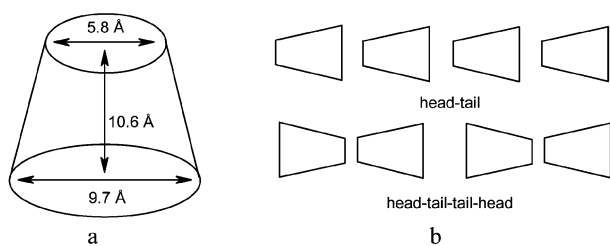
Scheme 2 Schematic representation of (a) the synthetic receptor **1** showing the size and shape of its cavity and (b) the two different supramolecular arrangements observed for the inclusion complexes of **1**.

(upper rings) and (ii) the cavity formed by the salicylaldehyde base moieties (lower rings). So far, we have achieved inclusion only into the second type of cavity. The dimensions of the overall cavity in **1** can be estimated from the cone obtained considering the diameters in the lower and upper rings (Scheme 2a).[10] The volume calculated is similar for all four cases, although different guests are present, and has an average value of approximately 160 Å^3 considering the van der Waals radii.

Interestingly, the guest molecules can have two different orientations within the host. While THF has a vertical orientation, AcOMe and benzene molecules are oriented horizontally with respect to the C_3 molecular axis. As far as we know, this isomerism has not been observed so far in calix-type macrocycles. For the two types of crystal systems found for the host–guest complexes of **1**, two different supramolecular arrangements of the host molecules were observed. In the triclinic systems of **1**·THF and **1**·AcOMe, these are organized in a *head–tail* orientation (Scheme 2b) with a separation of 3.6 Å between each other,[11] forming infinite channels along the *a* axis. In the cubic systems of **1**·5 C$_6$H$_6$ and **1**·5 THF, a *head–tail–tail–head* arrangement is observed in the [111] direction, with distances of 7.7 and 19.7 Å for the "*head–head*" and "*tail–tail*" orientations, respectively (Scheme 2b).[11]

For all four cases, the host–guest ratio observed in the solid-state was in accordance with the ^{1}H NMR data measured in CDCl$_3$, but no significant changes were observed comparing the chemical shifts for the different host–guest complexes. Furthermore, the chemical shifts of the guest molecules were also not significantly different from the ones measured in the absence of the hosts. This behavior may be explained by considering that CDCl$_3$ molecules could also act as guest molecules and thus compete for the receptor cavities. To examine the complexation abilities of **1** in solution further, we made preliminary inclusion studies using primary ammonium cations as guest molecules. Methylamine (MA), propylamine (PA), and heptylamine (HA) hydrochlorides were selected for this study for two reasons: first, RNH$_3^+$ moieties posses C_3 symmetry, which is consistent with the symmetry of the host, and second, it is known that ammonium cations interact with aromatic systems through N–H···π interactions.[2b] Measuring the ^{1}H NMR spectrum of **1** in the presence of one equivalent of the ammonium salt in CDCl$_3$, it was observed that the signal of the CH$_3$ protons is shifted upfield by $\Delta\delta = 0.22$ ppm when MA is used as guest. For PA, the signals of the NCH$_2$, NCH$_2$*CH$_2$* and CH$_3$ groups are shifted also upfield ($\Delta\delta = 0.20$, $\Delta\delta = 0.12$ and $\Delta\delta = 0.02$ ppm, respectively). In the case of HA, no significant changes were observed for the signals of the methylene groups. In all three cases, the signals corresponding to the host are barely affected by the complexation ($\Delta\delta = 0.01$–0.02 ppm). A molecular model shows that the ammonium salts' inclusion is located in the middle of the lower aromatic rings supported by N–H···π interactions, in accordance with the literature.[2b] The recognition ability of **1** for ammonium ions is affected by the chain length of the organic substituent attached to the polar head, smaller length leads to better inclusion. In summary, the above results have shown that compound **1** possesses a calix[3]arene-like conformation with a cavity large enough to trap small organic molecules.

Notes and references

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10 The diameter is defined by the circles that circumscribe the three carbon atoms located on the top of the upper rings, and the three carbon atoms located on the bottom of the *tert*-butyl groups of the lower rings. The diameters found are similar for all four cases and average values are given.

11 At the supramolecular level, the distances between the host molecules were measured from the center of the circles described in ref. 10.