Shape-persistent macrocyclic amphiphiles: molecular reversible coats

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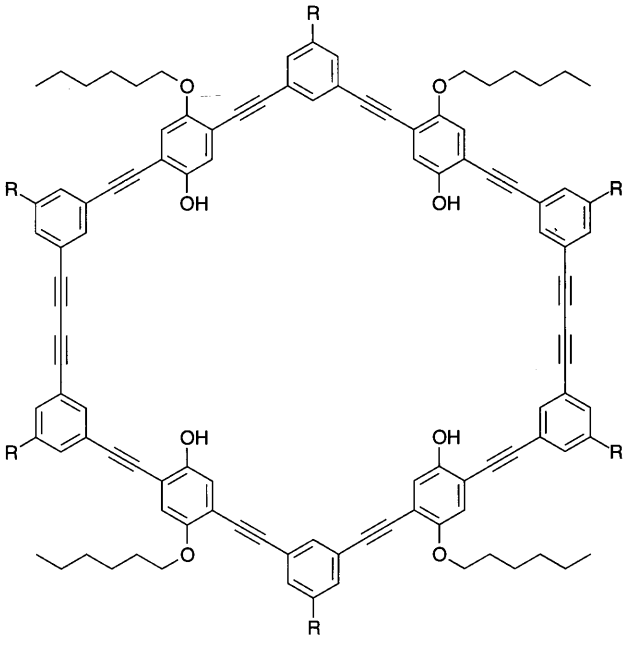
Shape-persistent macrocyclic host molecules 1 and 2 form complexes with guest molecules 3 and 4 due to the complementary arrangement of hydrogen bond donor phenol groups on the host molecules and hydrogen bond accepting amine groups on the guests.

Although the synthesis of artificial shape-persistent macrocycles with nanometre scale cavities have attracted intense interest during the last few years, the use of these molecules in host–guest chemistry has largely been unexplored.[1] However, nanometre size macrocycles can be designed to allow the complexation of organic molecules by specific interactions of complementary binding sites between the two molecules.[2] The ability to design either highly rigid structures capable of binding guest molecules (lock and key systems) or flexible structures with movable binding groups (induced fit systems) are amenable to shape-persistent macrocycles.[3]

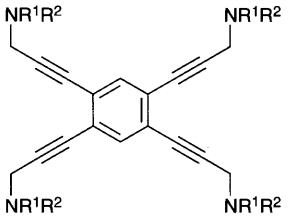
In our previous communication we described the synthesis and X-ray structure of a macrocyclic amphiphile with hydrophobic propyloxy residues and hydrophilic phenolic hydroxy side groups. The idea behind this design was the construction of a molecular framework, in which the arrangement of the amphiphilic functions of the macrocycle depend on the nature of the surrounding solvent or included guest molecules.[4]

In crystals grown from pyridine, the solvent is included as a solvate. The polar phenolic hydroxy groups point outside toward the polar solvate molecules and the macrocycle has a non-polar interior [Fig. 1(a)]. In accordance with our ideas, appropriate polar guest molecules should cause a conformational change of the amphiphilic portions of the macrocycle if polar interactions with the solvent are diminished [Fig. 1(b)].

Based on computer simulations, we identified and prepared guest molecules **3** and **4**, which fit well into the cavity of host molecules **1** and **2** when these adopt a conformation such that the polar phenolic hydroxy groups point toward the interior of the ring.‡ The driving force for this host–guest interaction is the



1 R = Me
2 R = Bu^t



3 R^1, R^2 = Me
4 R^1 = Me, R^2 = Bn

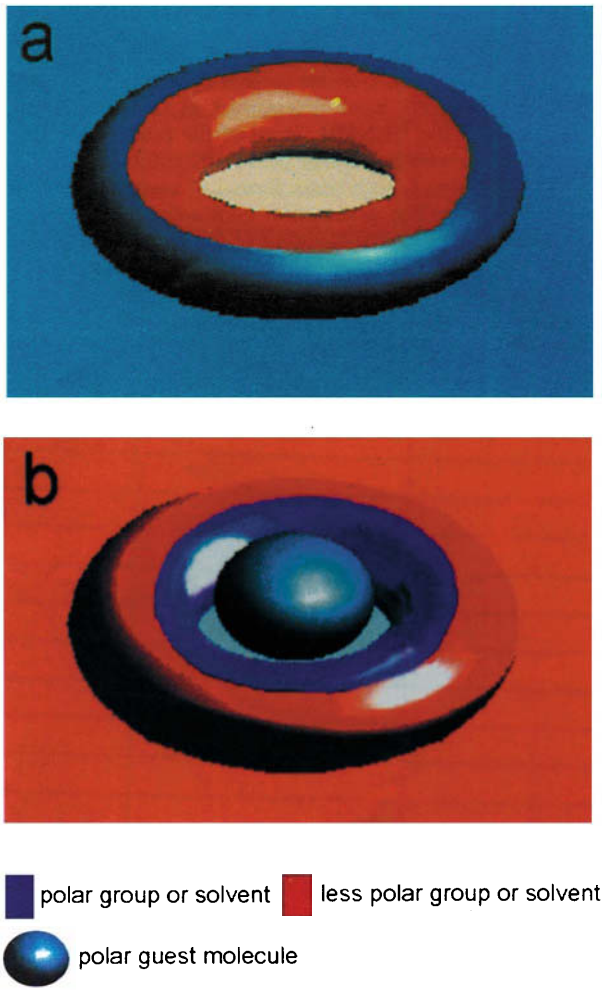


Fig. 1 Anticipated conformation of the macrocyclic amphiphile in (*a*) a more polar solvent, and (*b*) a less polar solvent, in the presence of a guest molecule

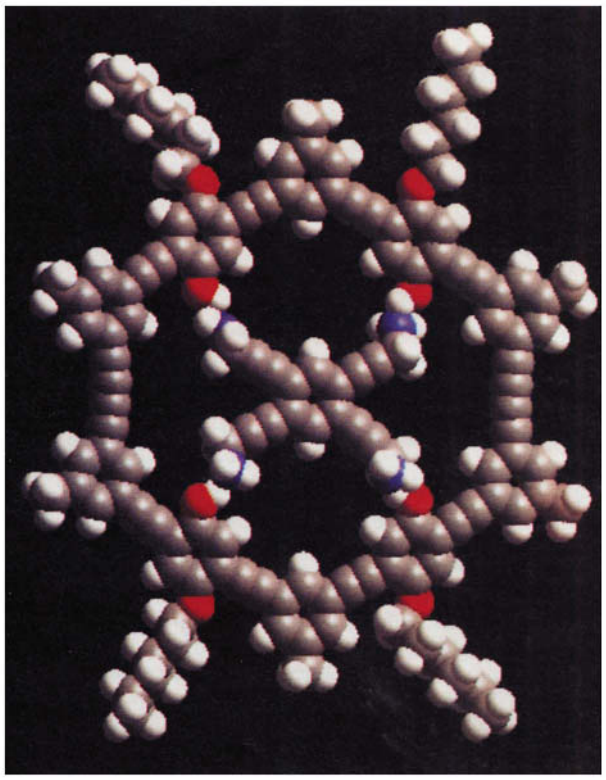


Fig. 2 Space-filling representation of the host–guest complexes. The substituents at the nitrogen atom are omitted for clarity.

attainment of a close contact between the acidic phenolic hydrogens and the basic amine groups of the guest.

Binding constants were determined in $C_2D_2Cl_4$ from the upfield shift of the ^1H NMR signal of the proton *ortho* to the phenolic group with increasing guest concentration at constant host concentration.[5] Both hosts form 1 : 1 complexes with the guest molecules. The association constants of the dimethylamino guest **3** with host molecule **1** (1.6×10^2 dm^3 mol^{-1}) and host molecule **2** (1.7×10^2 dm^3 mol^{-1}) at room temperature are of similar magnitude. Thus, the size of the *exo*-annular substituents on the ring, as expected, only has a negligible influence on the binding behaviour of the macrocycle. In contrast, the association constant decreases by more than one order of magnitude going from the complex **2·3** (1.7×10^2 dm^3 mol^{-1}) to the complex **2·4** (1×10^1 dm^3 mol^{-1}). Therefore, the steric demand of the substituents on the nitrogen atom of the guest molecule has a strong influence on the strength of binding.

The binding data support the structure of the host–guest complex shown in Fig. 2. The macrocycle adopts a conformation in which the phenolic hydroxy groups are pointing towards the interior of the ring, which is the reverse of the structure obtained from X-ray analysis of crystals with pyridine as solvate. Thus, the amphiphiles studied here behave like molecular reversible coats. The complementary arrangement of the binding sites of the substrate causes a conformational change of the receptor and therefore induce the fit. Further studies of this behaviour for these macrocycles are in progress.

Footnotes

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‡ The guest molecules were prepared by Hagihara coupling of the corresponding propargylamines with 1,2,4,5-tetraiodobenzene.

References

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5 The experimental data were analysed by non-linear least-squares fitting programs: (*a*) ASSOCIATE, ver. 1.6, Blake Peterson, Ph.D. Dissertation, University of California at Los Angeles 1994, provided by Professor F. Diederich, ETH Zürich; (*b*) SIMPLEX, written and provided by Professor H. Whitlock, University of Wisconsin, Madison, USA.

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