Chirality from achiral components: *N*,*N*′-bis(4-dimethylaminobenzyl)dodecane-1,12-diammonium in cucurbit[8]uril†

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The long alkyl chain of *N*,*N*′-bis(4-dimethylaminobenzyl)-dodecane-1,12-diamine (C_{12}DA) adopts different chiral helical conformations, one left-handed and the other right-handed, when bound within the cavities of two distorted cucurbit[8]uril (Q[8]) units, as unequivocally established by X-ray crystallography.

Alkanes usually adopt fully extended conformations in solution, the gas phase and the solid state, that minimizes steric interactions and maximizes surface area.[1] However, alkanes can adopt contorted conformations, such as helices or U-shapes, when bound within some natural and synthetic hydrophobic receptors. This phenomenon is attracting growing interest in host–guest chemistry[2–5] because folded or bent conformations of alkanes in cavitands provide unique opportunities to study new types of stereoisomerism and molecular recognition. More importantly, the cavitand microenvironments provide ideal vessels for unusual reactions and unusual conformations.

Cucurbit[*n*]urils (*n* = 5–8; hereafter abbreviated as Q[*n*]; Fig. 1), a family of macrocyclic cryptands self-assembled from acid-catalyzed condensation reactions of glycoluril and formaldehyde, have a hydrophobic cavity and two identical carbonyl-laced portals.[6] In the past decade, much attention has been focused on the host–guest chemistry of the Q[*n*] family and excellent progress has been made by the research groups of Mock, Kim, Isaacs, Fedin, *etc*.[7] In particular, Kim and co-workers reported the formation of an intramolecular charge-transfer complex induced by inclusion in the cavity of Q[8], which led to unusual back-folding of the guest molecule.[5] More recently, they established unequivocally that alkyl chains adopt a U-shaped conformation in the cavity of Q[8] by using NMR spectroscopy, ITC and X-ray crystallography.[5] Q[8] offers a special microenvironment in which the conformations of alkyl chains may be regulated due to the large hydrophobic cavity. With this background, we set out to see if chirality can be created from achiral alkyl chains bound to Q[*n*]. Herein, we report for the first time that the dodecanyl chain of an *N*,*N*′-bis(4-dimethylaminobenzyl)dodecane-1,12-diamine guest (hereafter abbreviated as C_{12}DA) is coiled in different directions to produce chiral helical conformations within the cavity of the host molecule Q[8].

Fig. 2 shows ^{1}H NMR spectra of C_{12}DA, (a) in the absence of Q[8] and (b) in the presence of 1.0 equiv. of the Q[8] host, in neutral D_2O solution. Compared to the spectrum of the unbound guest (Fig. 2a), only one set of signals due to the bound C_{12}DA guest is observed in the corresponding ^{1}H NMR spectrum (Fig. 2b). The resonances of the protons of the whole dodecanyl chain (e′–j′) are shifted upfield, while those of the protons of the two terminal 4-dimethylaminobenzyl moieties (a′–d′) of C_{12}DA exhibit slight downfield shifts, indicating that the long alkyl chain is entirely encapsulated within the cavity of the host Q[8] and that the two terminal 4-dimethylaminobenzyl moieties are located at the portals of Q[8]. Thus, a symmetric pseudorotaxane shape of C_{12}DA@Q[8] is formed. Close inspection reveals that the 8.8 × 9.1 Å (equatorial width × depth) cavity of Q[8] definitely cannot entirely contain the 17.5 Å length of the dodecanyl chain in extended conformation, but could contain a folded conformation, such as a helix or U-shape, although it is impossible to presume the exact dimensional conformation by ^{1}H NMR spectroscopy.

X-Ray crystal structure analysis provided unequivocal proof of the helical conformation of the alkyl chains. Slow vapor diffusion of hydrogen chloride into an aqueous solution containing the guest and Q[8] host resulted in the formation of crystals of complex **1**, which crystallized in space group $P2_1/n$. The X-ray crystal structure of complex **1** (Fig. 2) clearly reveal that there are two host–guest inclusion complexes in the unit cell, and that in each inclusion complex the entire alkyl chain of the C_{12}DA guest is encapsulated within the Q[8] host by adopting a folded conformation, while the two terminal

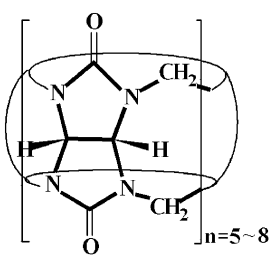

Fig. 1 Molecular structure of cucurbit[*n*]urils (*n* = 5–8).

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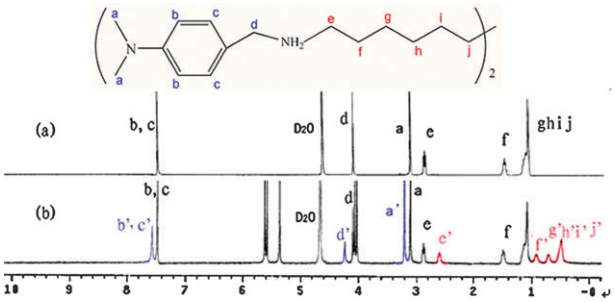

Fig. 2 ^{1}H NMR spectra of C_{12}DA in the (a) absence of Q[8] and in the (b) presence of 1.0 equivalent of Q[8] in D_2O at 20 °C.

4-dimethylaminobenzyl moieties of the C_{12}DA guest reside at the respective portals of the Q[8] host. In the crystal structure of complex **1**, each host–guest inclusion complex is surrounded by six neighbours, stacking into a one-layer hexagonal packing. The space between the layers is filled with water molecules, chloride anions and $[ZnCl_4]^{2-}$ anions, and they interact to form a complicated hydrogen-bonding network.

Most interestingly, both host–guest inclusion complexes of complex **1** in the unit cell have 1 : 1 stoichiometry between the host and the guest and the respective aliphatic chains of the guest adopt the same folded conformation in the Q[8] cavity. However, the two alkyl chains in the respective host–guest inclusion complexes have opposite chirality. As shown in Fig. 3, one helical chain in complex **1** exhibits right-handedness (a) while the other exhibits left-handedness (b).

Deformation of the Q[8] host during encapsulation was also observed. The host Q[8] molecule has a certain degree of steric rigidity and a D_{8h} symmetrical conformation. To accommodate the helical alkyl chains, both Q[8] hosts in the unit cell undergo severe ellipsoidal deformation. In complex **1**, the O···O diameters of the carbonyl portals of the Q[8] host range from 9.347 to 10.322 Å.

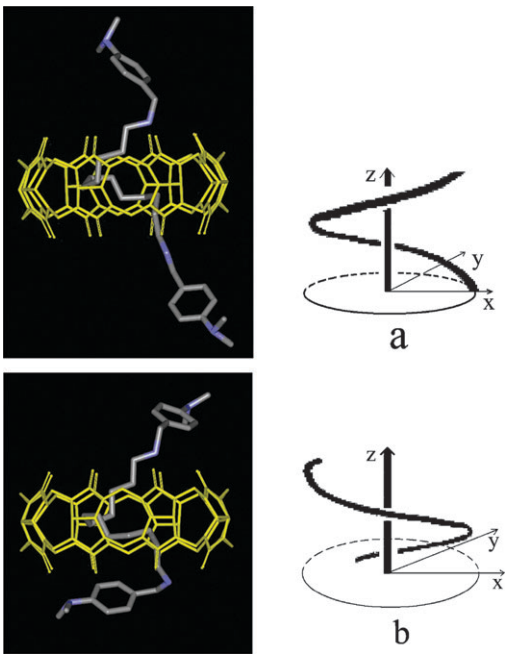

Fig. 3 X-Ray crystal structure of the two host–guest inclusion complexes in complex **1**; (a) right-handed helix (b) left-handed helix. Solvate water molecules and anions are omitted for clarity.

Obviously, in order to accommodate the helical alkyl guest and to provide a complementary shape, the Q[8] host has to modulate its conformation spontaneously during the encapsulation process. As a result, the empty space of Q[8] is filled with the helical alkyl chain and a more reciprocal conformational inclusion complex is formed.

There might be several reasons for the formation of the unusual helical conformation of the host–guest complex. First, ion–dipole interactions between the quaternized nitrogens on the guest and the carbonyl oxygens at the portals of the Q[8] host stabilize the host–guest complex. There are clearly still strong electrostatic interactions between the host–guest partners. Second, the hydrophobic effect of the Q[8] cavity drives the formation of the host–guest inclusion complex. The surfaces of the extended alkyl chain and the interior of the cavity are covered with solvent molecules, such as water and hydrochloric acid, and the release of solvent from these surfaces is favorable to the entropic and enthalpic changes as the inclusion complex forms.[8] Third, size and shape complementarity of the receptor and the helical alkyl chain must be taken into account. As has been mentioned, longer alkane chains are seen to twist into helical conformations to avoid empty spaces. At the same time, the Q[8] molecule is ellipsoidally deformed to accommodate the helical alkyl chain. These reciprocal conformational changes maximize the host–guest interactions.

To quantify the interaction between Q[8] and C_{12}DA, a ratio-dependent study was carried out by recording electronic absorption and fluorescence spectra. The free host Q[8] shows no absorbance at $\lambda > 210$ nm. Fig. 4(a) shows the variation in the UV spectra obtained for aqueous solutions containing a fixed concentration of C_{12}DA (20 mM) and variable concentrations of Q[8]. The absorption band of the guest C_{12}DA exhibits a progressively lower absorbance with a red shift to 267 nm as the Q[8]/C_{12}DA ratio is increased. The data for absorbance (A) *vs.* the ratio of the number of moles (N) of the host Q[8] and guest C_{12}DA (Q[8]/C_{12}DA) can be fitted by a 1 : 1 binding model for the Q[8]–C_{12}DA system at λ_{max} 250 nm. This behavior is consistent with the results of the ^{1}H NMR study.

Similar experiments were performed using fluorescence spectroscopy. Fig. 5(b) shows emission spectra of the guest C_{12}DA obtained from aqueous solutions containing a fixed concentration of C_{12}DA (20 mM) and variable concentrations of Q[8]. The emission spectra of the guest C_{12}DA exhibit a progressive change in fluorescence intensity with a blue-shift as the $N_{Q[8]}/N_{C12DA}$ ratio is increased. The curve of fluorescence intensity (I_f) at λ_{max} 369 nm *vs.* Q[8]/C_{12}DA can also be fitted by a 1 : 1 binding model for the Q[8]–C_{12}DA system.

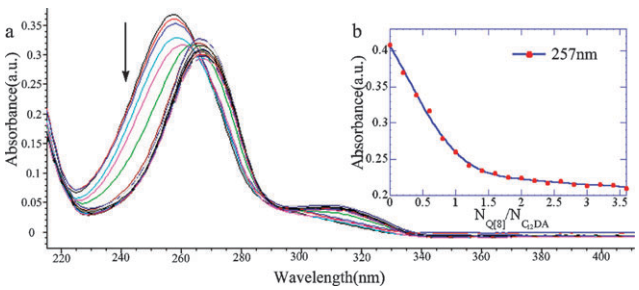

Fig. 4 UV spectra of C_{12}DA with increasing concentrations of Q[8] and A *vs.* $N_{Q[8]}/N_{C_{12}DA}$ curve.

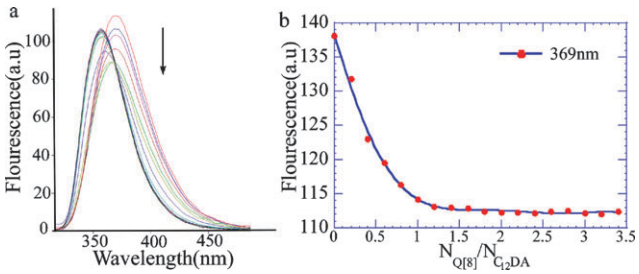

Fig. 5 Fluorescence spectra of $C_{12}DA$ with increasing concentrations of Q[8] and I_f *vs.* $N_{Q[8]}/N_{C_{12}DA}$ curve.

The absorption spectrophotometric data yielded a calculated binding constant (K) of 1.7×10^5 L mol^{-1}, while the fluorescence spectroscopy analysis yielded a value of 2.0×10^5 L mol^{-1}.

In summary, we have shown that the two identical long alkyl chains adopt distinct coiled conformations with different chirality when bound to two distorted Q[8] molecules. Such different chiral conformations within the same host are rare and may represent a key advance in understanding the origin of chirality in life. Control of the ratio of left-handed to right-handed helical conformations and the preparation of homochiral complexes remain challenging issues. Work along these lines is currently ongoing in our laboratory.

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