A Cucurbituril-Based Gyroscane: A New Supramolecular Form**

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Cucurbit[*n*]uril, here abbreviated as Q*n* (Figure 1), are macrocyclic acid-catalyzed condensation products of glycoluril and formaldehyde.[1–6] These macrocycles have an intrinsic capacity to act as molecular hosts. Research on the most common cucurbituril, Q6, has demonstrated the binding of guests such as xenon,[7] water,[8] tetrahydrofuran,[9] toluene,[10] and pyridinium[11] and *p*-xylylenediammonium[12] ions within the cyclic host. Many alkyl diamines thread through the Q6 cavity.[4, 12] These guests can be functionalized to provide the basis for a family of rotaxane structures.[13] Metal complexes of tetraazamacrocycles contained within Q8,[14] and *cis*-[$SnCl_4(OH_2)_2$] within Q7,[15] have been described. *o*-Carborane also binds in Q7 as a globular guest.[16]

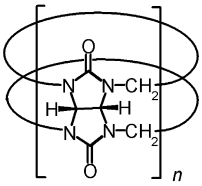

Figure 1. Schematic representation of cucurbit[*n*]uril.

Here we report the formation and characterization of a supramolecular form in which a smaller macrocycle, Q5, is located inside a larger macrocycle, Q10, with facile rotation of one relative to the other in solution. The image of a ring rotating independently inside another ring, which resembles a gyroscope, suggests the name gyroscane for this new class of supramolecular system.

We recognized the formation of this gyroscane while investigating the controlled synthesis of cucurbit[*n*]urils.[5] The ^{13}C NMR spectrum of each Q*n* contains three peaks: there is progressive change in the chemical shift of peaks associated with the methylene and methine carbon atoms that is dependent on *n*. Monitoring of the fractional crystallization of our crude Q*n* reaction mixture by ^{13}C NMR spectroscopy showed there to be two sets of unidentified Q*n* peaks: one set of peaks corresponded to the previously unknown Q10, whereas the other set of peaks did not correspond to either the known Q5 resonances or those predicted for Q4.[5b] The relative intensities of these two sets remained unchanged despite repeated recrystallizations. Only these two sets of resonances finally remained in the ^{13}C NMR spectrum of the crystalline material.

Electrospray mass spectrometry of this sample gave an ion that was equivalent to a Q15 species (as the $[Q15+2\,Cs]^{2+}$ ion, *m*/*z* 1378), which suggested that the unidentified ^{13}C resonances arose from Q5. The X-ray crystal structure[17] of single crystals grown in concentrated HCl unambiguously identifies this new supramolecular structure as Q5 encapsulated within Q10, namely Q5@Q10. We have isolated 65 grams of Q5@Q10 from a 1 kg scale synthesis.[5b]

The key feature of the crystalline structure of this gyroscane is the concentric location of Q5 inside Q10, with the molecular axis of Q5 inclined strongly (64°) to the axis of Q10. There is a Cl^- ion at the center of Q5,[18a] and a hydrogen atom from an OH_2 molecule or OH_3^+ ion bound over each of the two carbonyl portals of Q5 (Figure 2) such that the inner component of the gyroscane is $Cl@Q5\cdot(OH_2)_2$ (**1**), with a Cl^- ion and two water molecules coaxial with Q5.[18b] Figure 3 shows the location and orientation of **1** inside Q10. Each of the water molecules capping the Q5 portals is also well inside Q10 and near two of its carbonyl oxygen atoms, and hence has

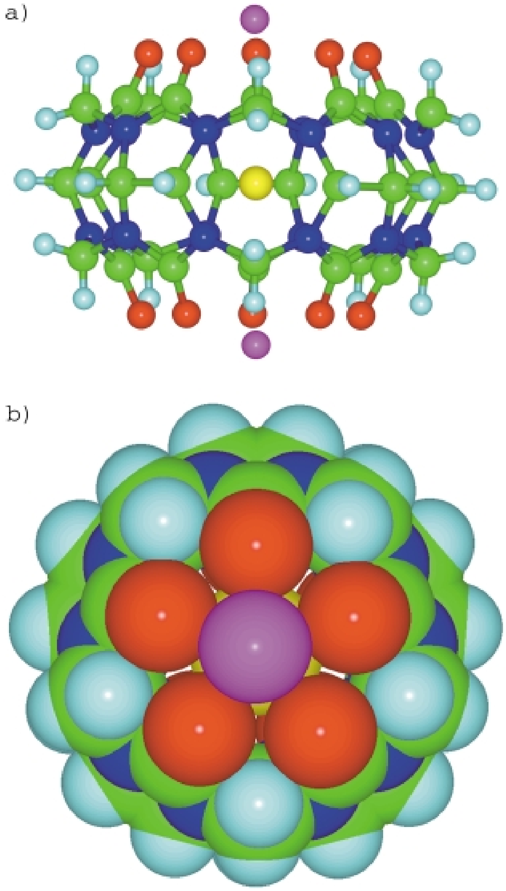

Figure 2. The inner component $Cl@Q5\cdot(OH_2)_2$ (**1**) of the gyroscane: a) side elevation (ball-and-stick representation; b) axial view of Q5 (space-filling representation). C: green, N: blue, O: red, H: cyan, Cl: yellow, O(water): magenta.

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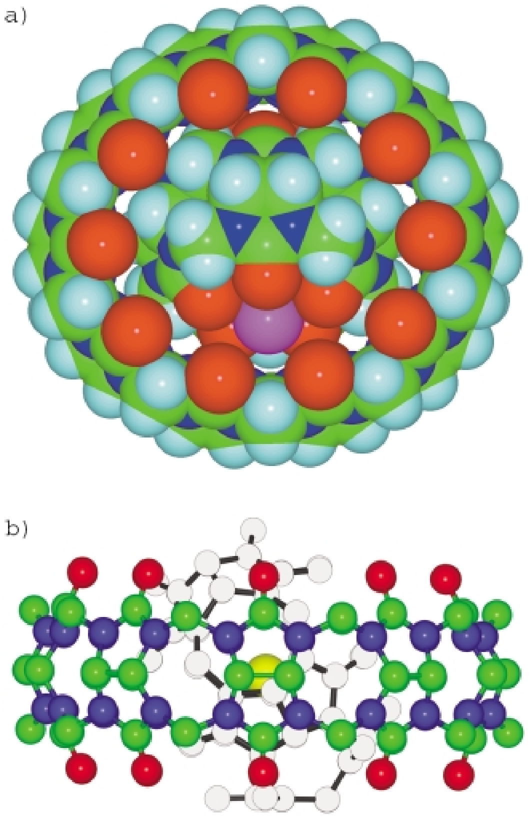

Figure 3. Inclusion of Q5 component (**1**) inside Q10: a) axial view of Q10 (space-filling representation); b) side elevation (ball-and-stick representation). The angle between the axis of the inner component and the axis of Q10 is 64°. C: green, N: blue, O: red, H: cyan, O(water): magenta.

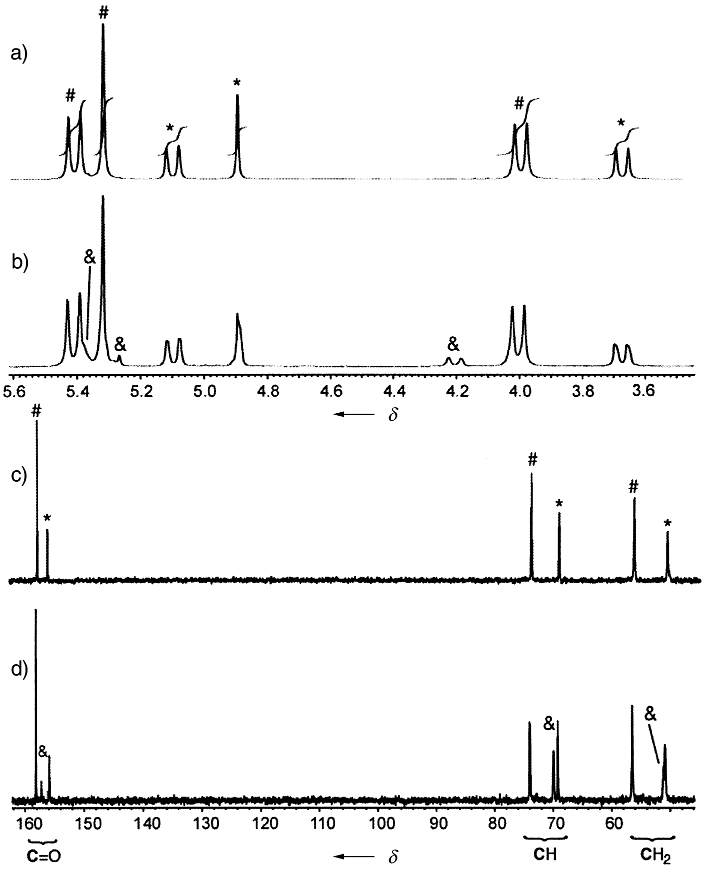

Figure 4. a) ^{1}H NMR spectrum of Q5@Q10 in 18% w/v DCl/D$_2$O; b) ^{1}H NMR spectrum of Q5@Q10 with additional Q5; c) ^{13}C NMR spectrum of Q5@Q10 in 18% w/v DCl/D$_2$O; d) ^{13}C NMR spectrum of Q5@Q10 with additional Q5. Note: In the ^{1}H NMR spectra, the methylene hydrogens are nonequivalent, and give rise to the pair of doublets observed for each cucurbit[*n*]uril. The methine hydrogen atom is observed as a singlet in each case. #, *, and & represent Q10, Q5 encapsulated in Q10, and unbound Q5, respectively.

a number of hydrogen-bonding possibilities. There is some protrusion of the inner component through the portals of the Q10 macrocyle (Figure 3b). The fivefold symmetry of Q5 means that when the axes of Q5 and Q10 are inclined, different surfaces of Q5 are exposed at the two portals of Q10: on one side a flat imidazolidinone ring is parallel to the face of the portal (revealed in Figure 3b), while at the other portal of Q10 the bismethylene linkage is exposed. The angled orientation of **1** within Q10 in the crystal is influenced by offset-face-to-face intermolecular interactions between exposed imidazolidinone faces of adjacent molecules of (Cl@Q5 · (OH$_2$)$_2$)@Q10. The interannular relationship between concentric cucurbituril molecules is geometrically analogous to a section of fullerene "onions".[19]

The integrity of Q5@Q10 in solution is demonstrated by the ^{1}H and ^{13}C NMR spectra of this gyroscane in 18% w/v DCl/D$_2$O. The spectra (Figure 4a) show no evidence of dissociated Q5 at concentrations down to 2×10^{-4} M, which indicates that the association constant for Q5@Q10 is $>10^6$. When Q5 is added to a solution of Q5@Q10, it appears in the ^{1}H and ^{13}C NMR spectra as resonances for unbound Q5 (Figure 4b, d). These spectra show that there is slow exchange between endo-annular Q5 and exo-annular Q5 on the NMR time scale. However, this exchange of Q5 does occur at room temperature within one hour, as revealed by the equilibrated ^{13}C spectrum when ^{13}C-labeled Q5 was added to Q5@Q10 in 18% w/v DCl/D$_2$O. The rate of exchange could not be determined, as the exchange is faster than the time required to accumulate sufficient data to achieve an acceptable spectrum (see the Supporting Information).

It is our view that the significant yield of Q10,[5b] albeit associated with Q5, occurs as a consequence of the association of Q5 with Q10. One explanation is that Q5 acts as a template in the synthesis of Q10. However, this appears unlikely, since the addition of Q5 to the reaction mixture does not affect the final yield of Q10. The synthesis of cucurbit[*n*]urils produces only trace amounts of Q9 (<1%),[5b] and even lower amounts of higher homologues, apart from Q10, which suggests that the higher homologues are unstable. By contrast, Q10 appears to be stabilized by Q5. At no time has Q10 been isolated, or detected, free of Q5.

Rapid re-orientation of Q5 in Q5@Q10 is revealed by the single set of ^{1}H and ^{13}C resonances for both components, and there is no evidence of signal broadening at 2 °C. There must be, therefore, rapid gyroscopic-like motion around the principal axes of both Q5 and Q10 for dynamic averaging of *both* the host Q10 and the guest Q5 to be achieved. Q5 undergoes both axial rotation and precessive rotation in the Q10 framework.

The O$\cdots$O diameters of the carbonyl portals of Q10 range from 12.07 to 14.73 Å (mean value: 13.13 Å). The maximum diameter, H$\cdots$H, of Q5 is 10.6 Å (including the van der Waals radii). Q5 can pass through the Q10 portal in the inclined conformation (Figure 3b). Other conformations of Q5@Q10, such as coaxial (Figure 5), would require distortion of the Q10 cage for egress to occur. The snug fit of Q5 in Q10 is consistent with its slow egress through the portal of Q10.

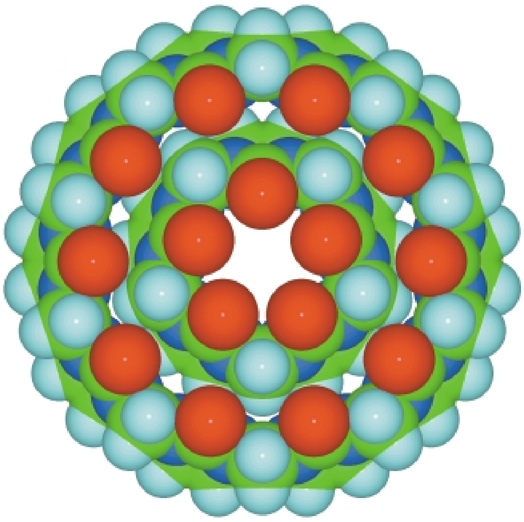

Figure 5. A probable coaxial conformation of Q5@Q10.

In summary, we have isolated and characterized the first example of a small cucurbituril contained within a large cucurbituril as a crystalline material that can be readily prepared in large amounts. The two macrocyclic rings are concentric but not coaxial in the crystal. It is evident that both rings are freely rotating relative to each other in solution. Facile axial and precessive motion of the inner ring relative to the outer ring represents the molecular analogy of the gyroscope: the gyroscane is a new potential molecular machine,[20] with analogy to carbon-nanotube linear bearings.[21]

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[17] Crystal data: colorless parallelepipeds $0.25 \times 0.15 \times 0.15$ mm, $(C_{60}H_{60}N_{40}O_{20})(C_{30}H_{34}N_{20}O_{12}Cl) \cdot 23.75\, H_2O \cdot 10\, HCl$, $M_r = 3321.14$, triclinic, space group $P\bar{1}$, $a = 20.047(4)$, $b = 20.064(4)$, $c = 23.978(5)$ Å, $\alpha = 67.44(3)$, $\beta = 84.93(3)$, $\gamma = 66.36(3)^\circ$, $V = 8134(3)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.662\ g\,cm^{-3}$, $T = 293$ K, Bruker-AXS SMART CCD diffractometer, $Mo_{K\alpha}$ ($\lambda = 0.71073$ Å), $\mu = 0.755\ cm^{-1}$, 59909 reflections measured for $\theta \leq 23^\circ$, R_1 ($I > 2\sigma(I)$) = 0.1255. Higher symmetry was excluded with the program PLATON, but it is possible that some twinning is present in the crystal investigated. A number (15.75) of the water molecules in the lattice are ill-defined, but the gyroscane complex is well-defined. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-169807. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[18] a) The Cl^- ion is 0.03 Å from the equatorial plane of Q5, and 0.04 Å from the equatorial plane of Q10; b) the relevant hydrogen atoms have not been located. It is not known whether the central species is Cl^-, HCl, or $HClH^+$. Around each Q5 portal water site there are seven O atoms (five from Q5 at about 2.7 Å and two from Q10 at about 3.4 Å) that are geometrically consistent with it possessing disordered hydrogen bonding of OH_2 or OH_3^+. The internal assembly could be $[H_3O \cdot H \cdot Cl \cdot H \cdot OH_3]^{3+}$.

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