

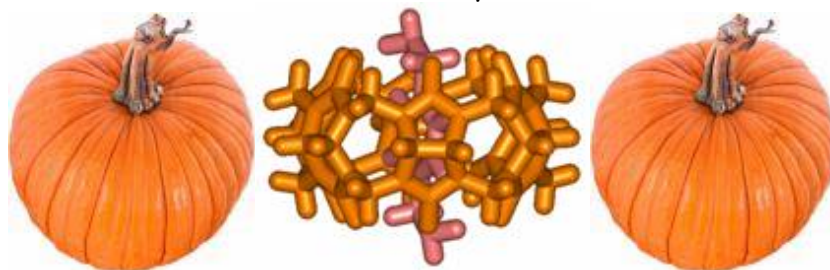
Cucurbituril

by

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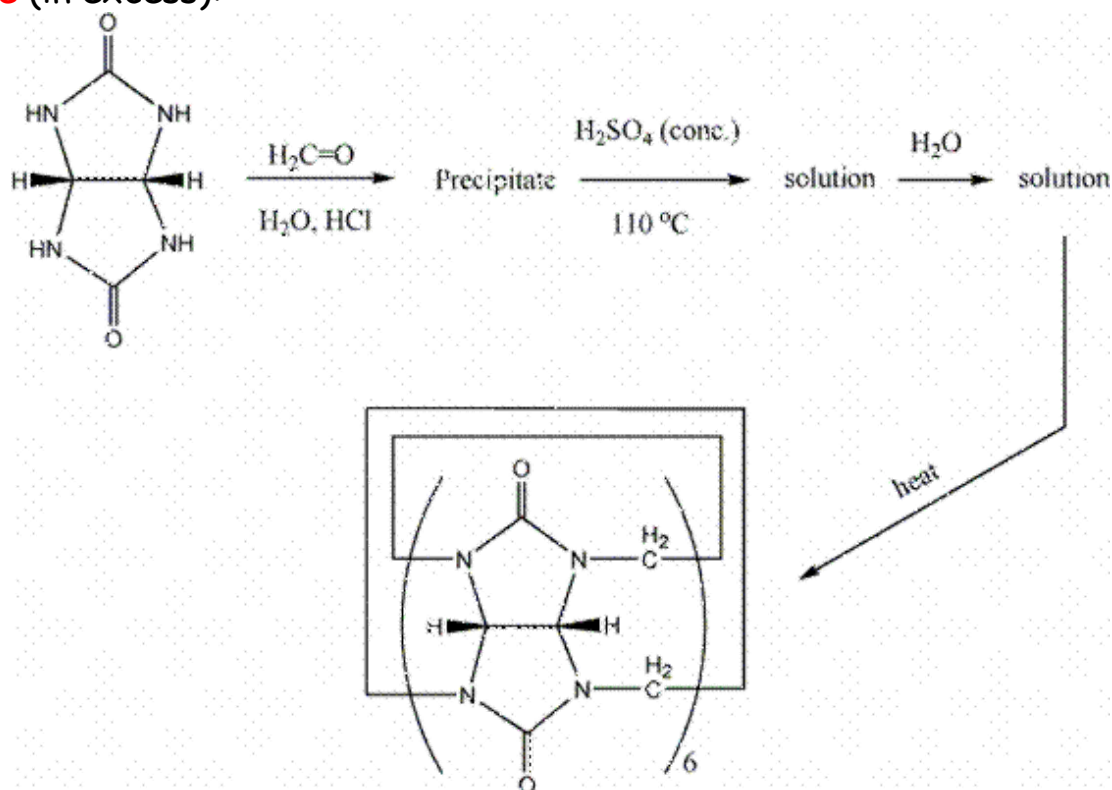
Sendai, Japan



Molecule of the Month - March 2006

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Cucurbituril (from *cucurbita* = pumpkin) is the fancy name given to the pumpkin-shaped macrocycle hexamer obtained from the condensation reaction between **glycoluril** and **formaldehyde** (in excess):



The story of cucurbituril, hereafter referred to as CB or CB[6], starts in 1905 (Einstein's magic year!!!) when three German chemists, Behrend, Meyer, and Rusche, published a paper on the illustrious *Liebigs Annalen der Chemie* 339 (1905) 1. Their paper described the reaction between glycoluril and an excess of formaldehyde (see the above Scheme) which yielded a cross-linked polymer (Behrend's polymer) that upon treatment with concentrated sulfuric acid produced a crystalline precipitate. Behrend characterized the crystalline precipitate as $C_{10}H_{11}N_7O_4 \times 2H_2O$. At that time, however, chemists could not make use of analytical techniques such as x-ray crystallography that are nowadays routinely employed to identify the atomic structure of molecules (note that in 1912, seven

years later the publication of Behrend's paper, Max von Laue observed the first diffraction pattern from crystals).

The molecular structure of CB remained unknown for about 76 years up until 1981 when a team of three American chemists working at the University of Illinois, Chicago, decided to repeat the 1905 synthesis of Behrend et al. Treatment of the precipitate (Behrend's polymer) with H_2SO_4 (conc.) and subsequent dissolution in hot water afforded a crystalline solid which, after being subjected to a single-crystal x-ray structure analysis, revealed the beautiful pumpkin-shaped molecule shown in Figure 1. In reference (4) of their landmark paper the authors state: *"The trivial name cucurbituril is proposed because of a general resemblance of CB to a gourd or pumpkin (family Cucurbitaceae), and by devolution from the similarly named (and shaped) component of the early chemists' alembic"*. And another nice chapter of the history of Chemistry was written!

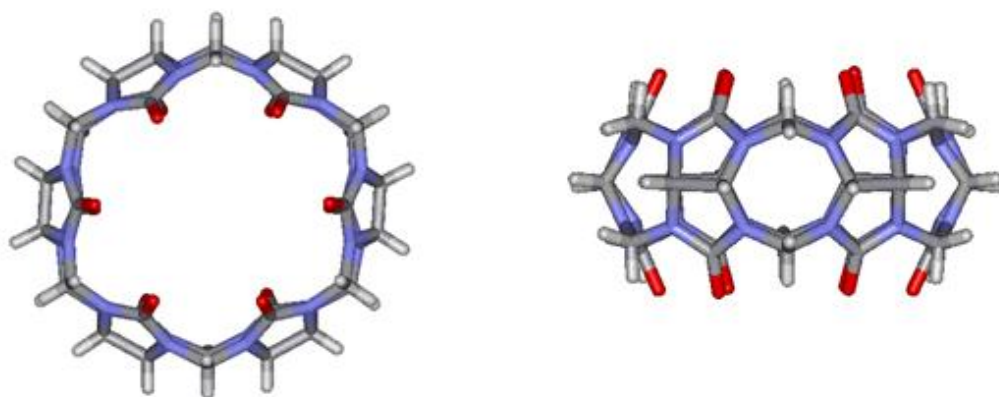


Figure 1. Molecular structure of cucurbituril: top (left) and lateral (right) views. (Click image for 3D structure).

The molecular dimensions of CB are as follows: the internal and external diameters are at 3.9 \AA and 5.8 \AA , respectively, the height at 9.1 \AA and the volume corresponds to 164 \AA^3 . In 1984, only three years after the publication of the JACS paper, Freeman publishes the crystal structure of the first host-guest complex of CB[6] which incorporates the *p*-Xylylenediammonium cation into the macrocycle's cavity. This structure, along with those of 11 other adducts also reported in this study, firmly established the *cavitand-like* character of CB. Note from Figure 2 that each N-H moiety forms a pair of H-bond interactions with two carbonyl (C=O) oxygen atoms on opposite portals.

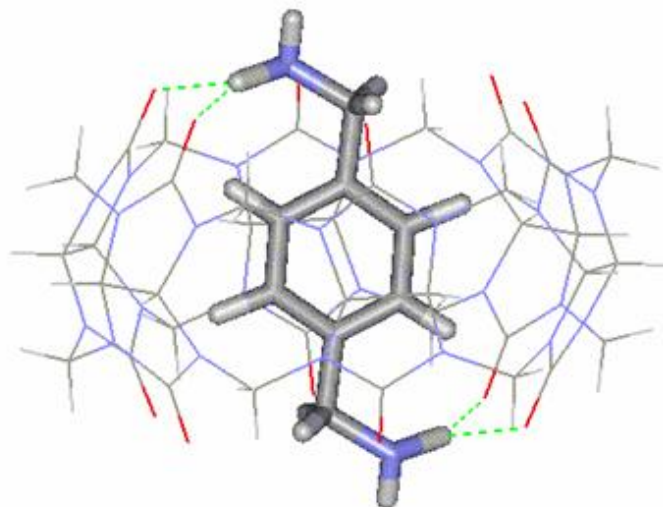


Figure 2. Molecular structure of the CB[6];*p*-Xylenediammonium complex

After the exciting discoveries of the early 80s, not much happened in the field of cucurbituril chemistry for a certain number of years. In the year 2000, however, another important breakthrough: Kimoon Kim and his group at Pohang University of Science and Technology (South Korea) present the syntheses and crystal structures of three **CB homologues**, namely CB[5], CB[7], and CB[8]. The crystal structure of CB[10] has been subsequently characterized by Day's group in 2002 (as its CB[5]@CB[10] complex - vide infra) and in 2005 by Isaacs's group (cucurbituril-free CB[10]) whereas those of CB[9] and CB[11] are yet to be determined. Note, however, that evidence about their existence is supported by the results of electrospray ionization mass spectrometry (EIMS) experiments.

Given the unique shape of the CB[*n*] molecules, it is perhaps not surprising that a large variety of interesting supramolecular architectures have been so far discussed in the scientific literature. Figure 3 shows an example of **molecular necklace** that results from the threading of three CB[6] macrocycles onto a molecular ring containing three Pt metal centres.

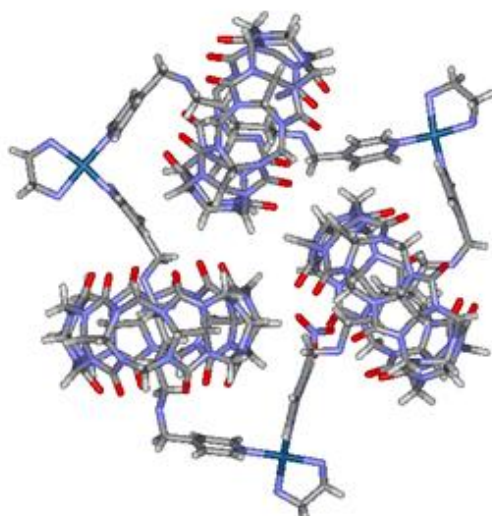


Figure 3. Molecular necklace made of three CB[6] units as beads

The space provided by the CB's cavity can be exploited to host selected molecular pairs, as shown in Figure 4. The aromatic molecules brought in close proximity can thus be activated either electrochemically or photochemically to yield products that are likely to differ from those obtained without the presence of the macrocycle. Hence, cucurbituril macrocycles can be employed as **molecular nanochambers** or **nanoreactors**.

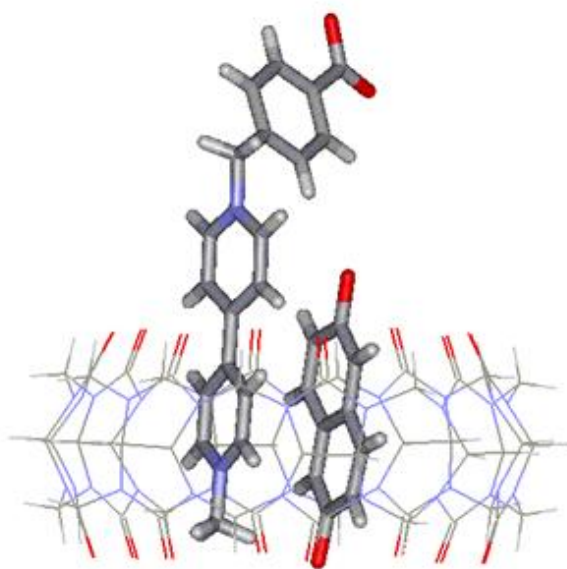


Figure 4. A molecular pair inside the cavity of CB[8]: an example of nanoreactor

Another interesting application of CBs is in the construction of **molecular machines**. According to Balzani and coworkers, *"a molecular-level machine can be identified as an assembly of a distinct number of molecular components that are designed to perform machine-like movements (output) as a result of an appropriate external stimulation (input)."* In this regard, Day and coworkers have succeeded in characterizing the structure and solution properties of the CB[5]@CB[10] complex shown in Figure 5. Because in solution CB[5] freely rotates inside the cavity of CB[10], the authors classified this complex as a **molecular gyroscope** (or gyroscope) in analogy with macroscopic devices that are employed to measure and maintain orientation during flight.

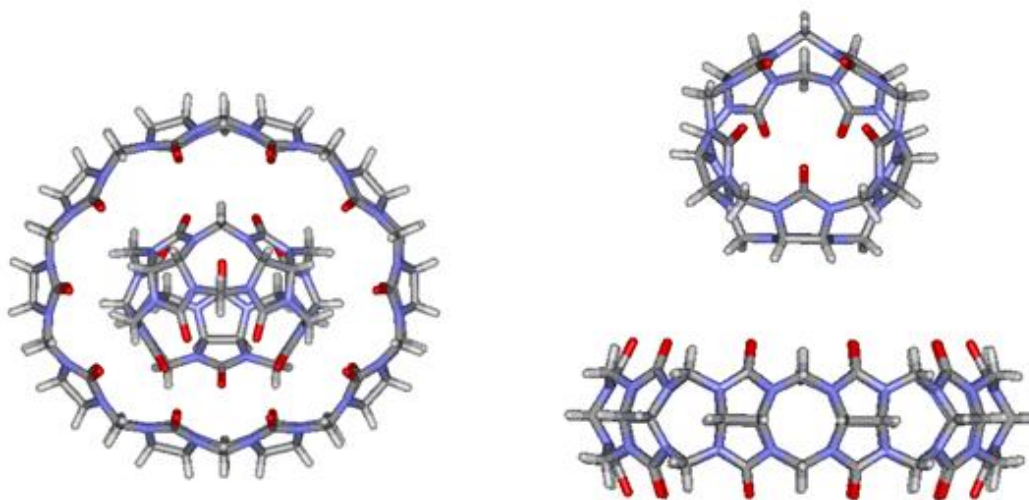


Figure 5. Molecular gyroscope made of the CB[5]@CB[10] complex

One of the main problems encountered with CB is its poor solubility in water. In this regard, Kim and coworkers have introduced a pair of hydroxyl groups (-OH) on each glycoluril unit as shown in the modified CB[6] macrocycle on the left side of Figure 6. This perhydroxylated CB[6] derivative shows good solubility in DMSO and can be further modified with groups that can increase its solubility in water. The same group was also able to introduce a carbon chain made of four methylene moieties attached to each glycoluril unit, as shown on the right side of Figure 6.

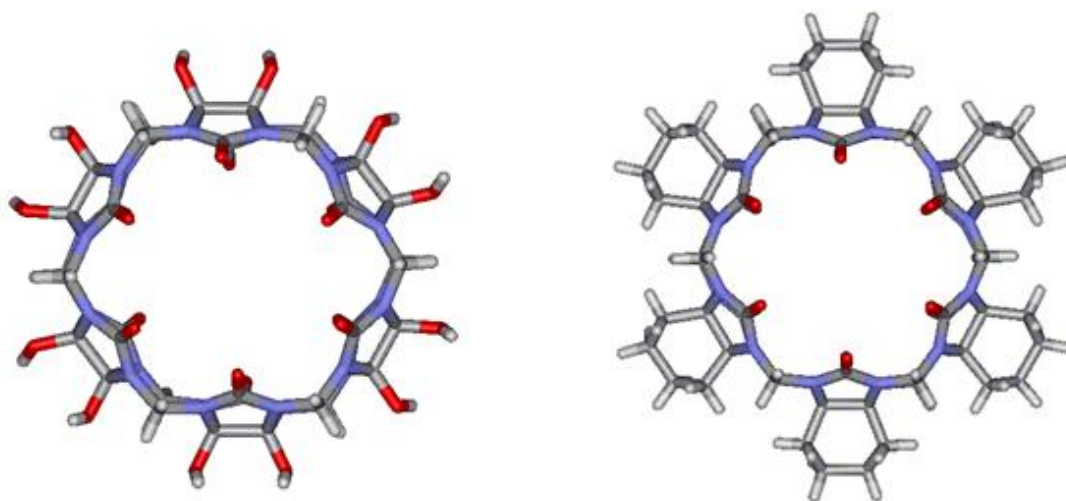


Figure 6. Modified CB[6] macrocycles

An interesting modification of CB is the replacement of its carbonyl oxygen atoms (C=O) with sulfur atoms (C=S) which yields the *thia-CB[6] analogue*. Computer-aided design studies have shown that *thia-CB* macrocycles can be soldered with transition metal ions such as Pd(II), Pt(II), or Hg(II) to produce molecular nanotubes of any desired length and selected diameters as the one shown in Figure 7. These new nanostructures, dubbed *cucurtubes*, might be useful in the development of future molecular-scale wires for nanoelectronics.

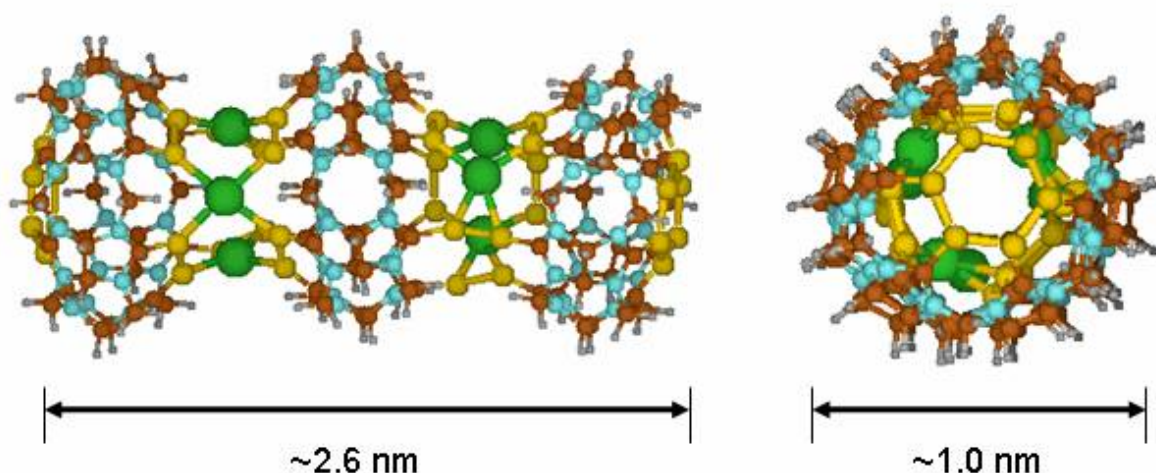


Figure 7. Structure of a cucurtube trimer (green spheres represent Hg^{2+} ions)

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The crystal structures depicted on this page were retrieved from the Cambridge Structural Database (CSD) maintained by the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge, CB2 1EZ, UK



I dedicate this MOTM page to my lovely family.



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