Structure, Electronic Properties and NMR-Shielding of Cucurbit[n]urils

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Abstract

Geometries, electronic properties and NMR-shielding of cucurbit[5]uril, decamethylcucurbit[5]uril, cucurbit[6]uril, cucurbit[7]uril, and cucurbit[8]uril are investigated with DFT calculations. All molecules are highly symmetrical with a distinct geometric flexibility. In addition with a characteristic partial charge distribution these findings account for their chemical complex building ability.

Introduction

The scientific interest in cucurbit[n]urils as macrocyclic ligands increases from year to year. The first synthesis has been reported by R. Behrend and coworkers in 1905 [1]. From the reaction of glycoluril with an excess of formaldehyde in strong acidic solution he obtained a white crystalline product, which is nowadays named cucurbit[6]uril. Without the knowledge of its structure R. Behrend described the formation of crystalline compounds in the presence of some salts e.g. KBr, NH_4Cl and $AgNO_3$. At this time no scientist could know that the formation of complexes between neutral molecules and cations or anions takes place. However R. Behrend already observed the solubilization of cucurbit[6]uril in the presence of acids. After dilution with water the ligand precipitates again. He reports that only in the presence of salts no precipitate is formed. With the knowledge of the complex formation between cucurbit[6]uril and cations this observation is understandable.

It lasted until 1984 before this ligand was rediscovered from the literature by W.L. Mock [2] and the crystal structure reported by W.A. Freeman [3]. The macrocyclic ligand cucurbit[6]uril possesses a relatively rigid structure and the hydrophobic cavity of this ligand is accessible by two polar portals formed by carbonyl groups. Thus, this ligand is able to complex cations [4] as well as neutral molecules [5]. Even the inclusion of gases has been reported [6]. During the last years the synthesis of smaller and larger sized cucurbit[n]urils has been described in the literature [7–12]. The thermodynamics and kinetics of host-guest chemistry of cucurbit[6]uril was the subject of a detailed study [13]. Due to the interesting complexation behaviour of cucurbit[6]uril more information about the electron distribution within these molecules is essential for a more detailed understanding. Unfortunately in case of the cucurbit[n]urils only one theoretical study has been published up to now [14]. In contrast for cyclodextrins extensive calculations have been reported in the literature [15, 16]. They demonstrate very clear the hydrophobic and hydrophilic surface regions of the cyclodextrins. In the following paper we like to present the results of detailed calculations concerning cucurbit[n]urils.

Methods

The quantum chemical calculations were performed with Gaussian [17]. Molecular graphics were generated with GaussView [18]. Geometries were optimized from chemical intuitive start geometries with the semiempirical PM3 method and then refined with Density Functional Theory (DFT) using the B3LYP hybrid functional with the 6–31G(d) basis set. Calculation of nuclear magnetic shielding tensors for the optimized molecular geometries was performed with the Gauge-Independent Atomic Orbital (GIAO) method and the B3LYP/6–31G(d) model chemistry. Reported shifts are relative to those of optimized tetramethylsilane calculated with the same model chemistry [19–22].

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Results and discussion

Optimized geometries

Repeated potential energy surface (PES) minimization procedures of the cucurbit[n]uril molecules from different start geometries converge to minimum energy structures with practically the same minimum energy values but distinct geometric differences. A PES difference of less than 0.1 kcal/mol can transform Cuc[6] from a perfect D_{6h} symmetry into a perfect C_{2v} symmetry with differences in e.g. opposing oxygen distances within a portal of up to 0.5 Å. Cuc[8] exhibits a vertical curvature which distorts its native D_{8h} symmetry into a C_2 symmetry. These findings indicate very flat energy minima with regard to symmetrical distortions. On the other hand this ability for symmetrical low energy distortions reveals a distinct flexibility in portal geometry of the cucurbit[n]uril molecules which supports complex building also with a priori geometrically unfavourable ligand molecules.

The optimized geometries of Cuc[5], DMCuc[5], Cuc[6] and Cuc[7] are consistent with intuitive chemical expectations as well as earlier experimental and modelling results (see Table 1, Figure 1a) [14]. The intramolecular distance of the oxygen portals is nearly identical from Cuc[5] to Cuc[8] (6.23–6.26 Å). The value of DMCuc[5] with 6.17 Å is slightly smaller which corresponds to the slightly smaller approximated oxygen portal area of 18.7 Å^2 in comparison with the value of 19.3 Å^2 for Cuc[5]. The portal area can be regarded as a geometric measure of the accessibility of the cavity for ligand molecules. The geometric differences between Cuc[5] and DMCuc[5] may contribute to the experimentally observed difference in chemical complex building reactivity where Cuc[5] is the more and DMCuc[5] the less reactive complex builder.

It should be noted that geometry refinements with the B3LYP/6-31G(d) model chemistry are necessary in order to get plausible geometries: The semiempirical PM3 calculations lead to strong asymmetrical distortions in the eight-membered $(CNCN)_2$-rings for all cucurbit[n]uril molecules.

Electronic properties

The electron densities with mapped electrostatic potentials of all cucurbit[n]uril molecules show the negatively charged oxygen portals connected by a hydrophobic uncharged cavity and the slightly positive charged hydrogens of the outer perimeter (see Figure 1b). These distinct partial charge distribution accounts for the well-known chemical complex building ability of the cucurbit[n]urils.

The highly symmetrical highest occupied molecular orbital (HOMO) is mainly located at the carbamide groups of the oxygen portals and is of identical shape in Cuc[5], DMCuc[5], Cuc[6], Cuc[7] and Cuc[8] (see Figure 1c). The same picture results for the lowest unoccupied molecular orbital (LUMO) with the exception of DMCuc[5] which shows a distinct LUMO occupation of the outward methyl groups (see Figure 1d, e). As far as HOMO and LUMO energies are concerned there is a linear decrease from Cuc[5] to Cuc[8] (see Table 2). DMCuc[5] differs significantly from this line. This is also found for the HOMO-LUMO gap that is nearly identical for Cuc[5] to Cuc[8] (7.16–7.21 eV) but differs from that of DMCuc[5] (6.80 eV). The electronic differences between Cuc[5] and DMCuc[5] may again contribute to the different complex building reactivity mentioned above.

NMR shifts

Like all highly symmetrical molecules the cucurbit[n]urils show simple NMR spectra. The ^{1}H-NMR-spectrum of Cuc[5] to Cuc[8] consists of three proton signals, labelled H_A, H_B and H_C (see Figure 1a). The calculated chemical shifts of these signal groups are nearly identical for Cuc[5] to Cuc[8] (see Table 3). For the corresponding signal groups DMCuc[5] shows comparable chemical shifts and has two additional signal groups at 1.0 ppm and 2.0 ppm which belong to the outer methylene protons (and will combine into one signal in a experimental spectrum due to methylene group rotation). Compared to experimental ^{1}H-NMR-spetra of the chemical entities under investigation the calculated chemical shifts of the signal groups show distinct different values but the same signal sequence for spectra-structure correlation. So the calculated results may be regarded as consistent within the calculation framework (similar structures show similar shifts on the same level of theory) but reveal distinct offsets up to 1 ppm in comparison with the experimental values. These deviations are well known in chemical shift calculations due to the sensitivity of NMR calculations

Table 1. Optimized geometries

	Cuc[5]	DMCuc[5]	Cuc[6]	Cuc[7]	Cuc[8]
Symmetry	D_{5h}	D_{5h}	D_{6h}	D_{7h}	D_{8h}
Intramolecular distance between oxygene portals[a] [Å]	6.25	6.17	6.23	6.25	6.26
Diameter of oxygene portal[b] [Å]	5.40	5.34	7.21	8.54	10.30
Area of oxygene portal[c] [Å^2]	19.3	18.7	33.7	52.4	75.0

[a] see Figure 1a; reported is the O-O distance as indicated in Figure 1.
[b] see Figure 1a; reported is the mean value of all distances of opposing oxygen atoms of both portals.
[c] see Figure 1a; the value of the polygonal area is calculated with the individual O–O distances.
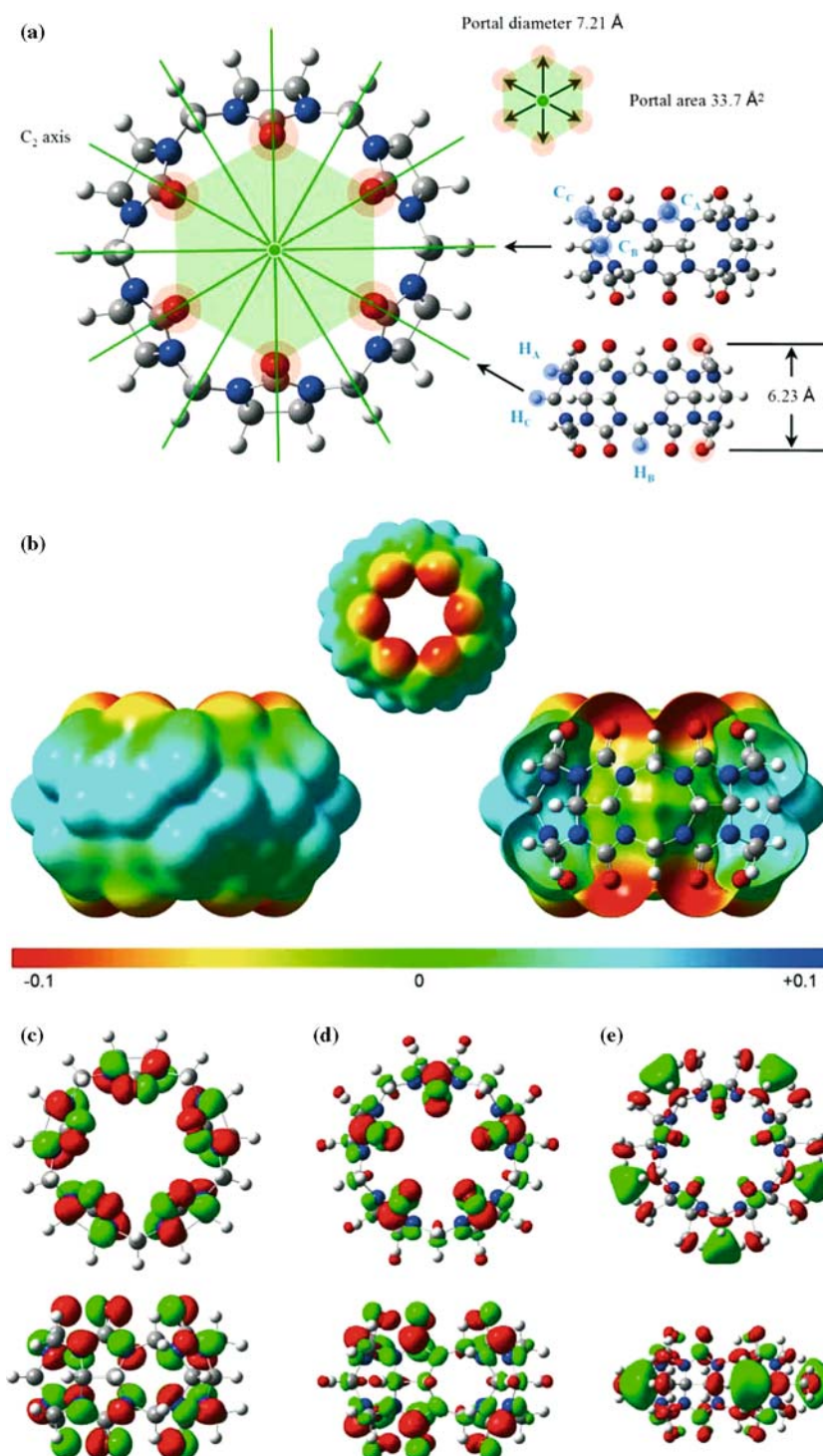
Figure 1. (a) Cuc[6]: Geometry measures and NMR atom types. (b) Cuc[6]: Electrostatic potential mapped on the molecular "size surface" with electronic density isovalue of 0.002 a.u. (c) Cuc[5]: HOMO. (d) Cuc[5]: LUMO. (e) DMCuc[5]: LUMO.

Table 2. Frontier orbitals

	Cuc[5]	DMCuc[5]	Cuc[6]	Cuc[7]	Cuc[8]
HOMO [eV]	−6.34	−5.99	−6.42	−6.50	−6.59
LUMO [eV]	0.82	0.82	0.79	0.71	0.63
HOMO-LUMO gap [eV]	7.16	6.80	7.21	7.21	7.21

to small differences in the optimized geometries and the calculated electron densities.

The ^{13}C-NMR-spectra of Cuc[5] to Cuc[8] consists of three carbon signals, labelled C_A, C_B and C_C (see Figure 1a). The calculated chemical shifts of these signal groups are again comparable (see Table 3). The C_B shift of DMCuc[5] with 75.5 ppm differs significantly due to connection to the outer methylene carbon and there is

Table 3. Calculated NMR shifts

	Cuc[5]	DMCuc[5]	Cuc[6]	Cuc[7]	Cuc[8]
[1]H-shift of atom type H_A [ppm]	3.3	3.5	3.2	3.2	3.2
[1]H-shift of atom type H_B [ppm]	5.9	6.0	6.0	6.1	6.1
[1]H-shift of atom type H_C [ppm]	4.6	-	4.6	4.5	4.4
[13]C-shift of atom type C_A [ppm]	141.3	141.6	141.7	142.1	142.6
[13]C-shift of atom type C_B [ppm]	67.6	75.5	68.9	69.9	70.6
[13]C-shift of atom type C_C [ppm]	50.0	44.4	51.5	52.8	53.7

an additional signal group at 19.4 ppm of this outer methylene carbon.

The NMR calculations indicate that it will be difficult to differentiate between Cuc[5], Cuc[6], Cuc[7] and Cuc[8] on the basis of experimental ^{1}H-NMR spectra alone but it should be possible with high quality experimental ^{13}C-NMR-spectra. DMCuc[5] can be easily detected due to its extra signals.

Conclusions and prospects

The investigated cucurbit[n]urils are highly symmetrical with a distinct geometrical flexibility. Their characteristic partial charge distribution accounts for their chemical complex building ability. Their frontier orbitals are similar in energy and shape and so are their characteristic NMR shift sequences. Obvious differences in geometry and electronic properties between Cuc[5] and DMCuc[5] are likely to be responsible for their different complex building reactivity.

The calculation of chemical shift distortions in cucurbit[n]uril host-ligand complexes in comparison with the isolated molecules and corresponding spectra-structure correlation will be especially valuable in the difficult structure elucidation of cucurbit[n]uril host-ligand complexes which will be shown in a subsequent publication.

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