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ORIGINAL PAPER

Theoretical study on the protonation of cucurbit[6]uril

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Abstract The most probable structures of the cucurbit[6]uril·H_3O^+ and cucurbit[6]uril·$(H_3O^+)_2$ cationic complex species have been derived by quantum mechanical DFT calculations. In these two complexes, each of the H_3O^+ ions is bound by three strong linear hydrogen bonds to three carbonyl oxygen atoms of the parent macrocycle.

Keywords Cucurbiturils · Macrocycles · Protonation · Ab initio calculations · Complex structure

Introduction

Cucurbit[*n*]urils are macrocyclic compounds consisting of *n* glycoluril units connected by 2*n* methylene bridges. The shape of the macrocycle resembles a hollow barrel with a hydrophobic interior and partially negatively charged rims of carbonyl groups on both sides of the macrocycle. This structure makes the macrocycles suitable for binding organic guests bearing one or more positive charges in their structures [1–3].

Cucurbit[6]uril (**1**, Scheme 1) is the oldest and the most accessible representative of the CB family of macrocycles and its supramolecular interactions with various guests have been extensively investigated [1, 2]. The ability of **1** to behave as a synthetic receptor was described in detail by Mock and co-workers, together with the discovery of the macrocyclic structure of the molecule [4]. They reported the formation of complexes of **1** with aliphatic amines and diamines. Guest positioning and complex stability strongly depended on the length of the alkyl chain of the guest [5–8]. Since then, complexation between **1** and many organic guests has been studied, including polyamines [9, 10], viologen derivatives [11], organic dyes [12], polypeptides [13], and amino acids and dipeptides [14].

Recently, protonation of valinomycin, some calix[4]arenes, dibenzo-18-crown-6, and a hexaarylbenzene-based receptor has been investigated in detail [15–27]. Protonation of **1** has been proved experimentally in acidic aqueous solutions [28]. The structures of the protonated **1** species have not yet been solved, however. Therefore, in the work reported in this paper, the structures of the **1**·H_3O^+ and **1**·$(H_3O^+)_2$ cationic complex species were predicted by means of quantum mechanical DFT calculations.

Results and discussion

To increase numerical accuracy and reduce oscillations during the molecular geometry optimization, two-electron integrals and their derivatives were calculated by use of the pruned (99,590) integration grid with 99 radial shells and 590 angular points per shell; this was requested by means of the Gaussian 03 keyword “Int=UltraFine”.

Although a possible effect of a polar solvent on the detailed structures of **1**, **1**·H_3O^+, and **1**·$(H_3O^+)_2$ could be

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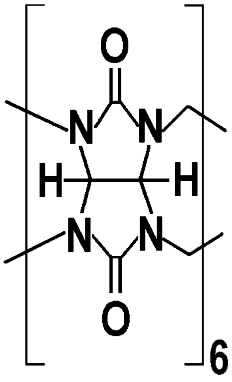
Scheme 1



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imagined, our results from quantum mechanical calculations in similar cases, performed analogously, were in very good agreement with experimental results [29–35].

In the model calculations, we optimized the molecular geometry of the parent macrocycle **1** and its complex species with H_3O^+. The optimized structure of the free macrocyclic receptor **1** with C_6 symmetry is illustrated in Fig. 1.

In Fig. 2, the structure obtained by full DFT-optimization of the $\mathbf{1}\cdot H_3O^+$ complex having C_3 symmetry is depicted, together with the lengths of the corresponding bonds (in Å; 1 Å = 0.1 nm). It follows from this figure that complexation with the H_3O^+ cation changes the overall shape of the parent macrocycle **1** only slightly. In the resulting $\mathbf{1}\cdot H_3O^+$ cationic complex species, which is most energetically favoured, the “central” cation H_3O^+ is bound by three strong linear hydrogen bonds to three carbonyl oxygen atoms (1.80, 1.80, and 1.80 Å) of the parent receptor **1**.

The lowest-energy-level structure obtained by full DFT-optimization of the $\mathbf{1}\cdot(H_3O^+)_2$ cationic complex species is shown in Fig. 3, together with the lengths of the corresponding hydrogen bonds (in Å). Compared with the free macrocycle **1** (Fig. 1), the cucurbit[6]uril part of the complex $\mathbf{1}\cdot(H_3O^+)_2$ is only slightly distorted, so its structure has C_3 symmetry. In this complex species, each of the two H_3O^+ cations is bound by three strong linear H-bonds to three carbonyl oxygen atoms (1.79, 1.79, and 1.79 Å) of the parent macrocycle. The distance between the two oxygen atoms of the two H_3O^+ cations is 5.00 Å.

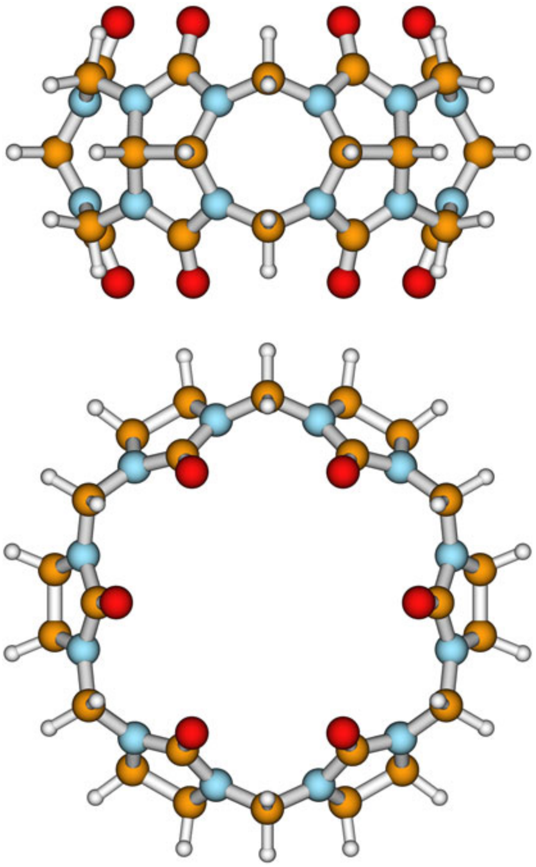

Fig. 1 Two projections of the DFT-optimized structure of free **1** [B3LYP/6-31G(d)]

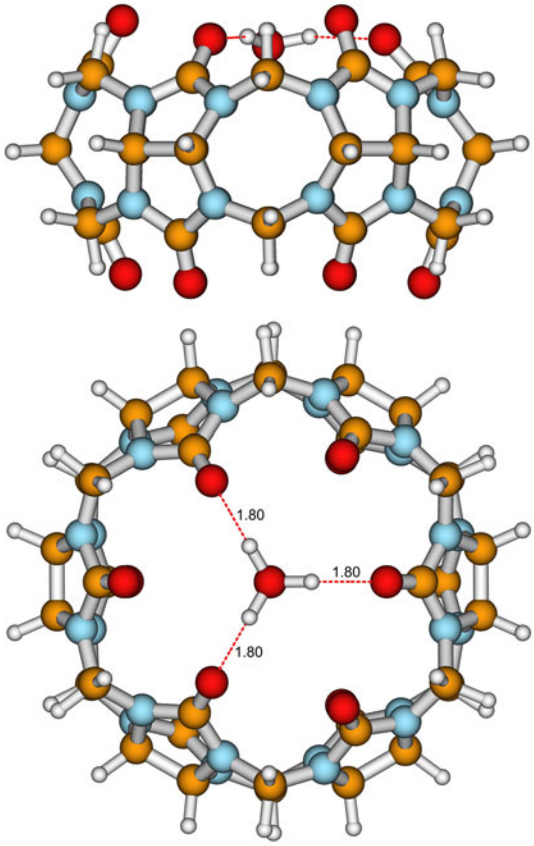

Fig. 2 Two projections of the DFT-optimized structure of the $\mathbf{1}\cdot H_3O^+$ complex [B3LYP/6-31G(d)]. Hydrogen bond lengths of H_3O^+ to the three corresponding carbonyl oxygen atoms of **1** are 1.80, 1.80, and 1.80 Å

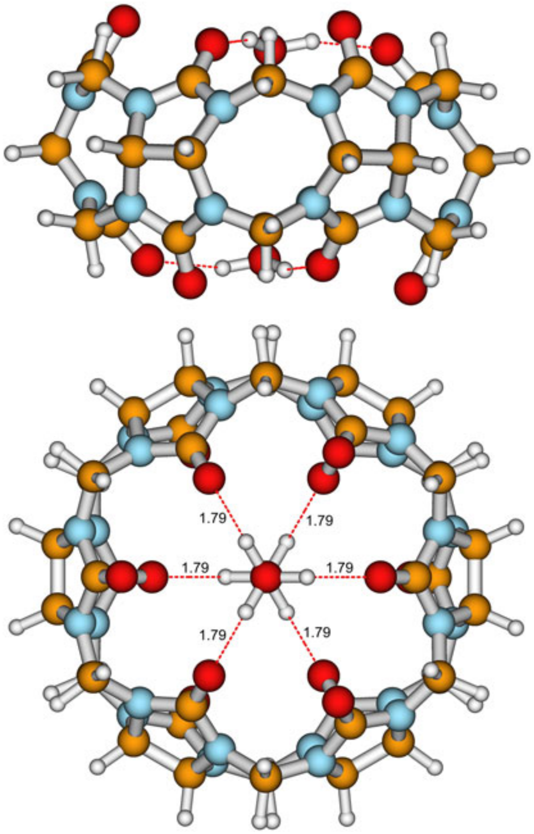

Fig. 3 Two projections of the DFT-optimized structure of the **1**·$(H_3O^+)_2$ complex [B3LYP/6-31G(d)]. Hydrogen bond lengths of the two H_3O^+ to the six carbonyl oxygen atoms of **1** are 1.79, 1.79, 1.79, 1.79, 1.79, and 1.79 Å

Finally, the calculated binding energies of the complexes **1**·H_3O^+ and **1**·$(H_3O^+)_2$ are −404.8 and −608.5 kJ/mol, confirming the relatively high stability of these cationic complex species.

In conclusion, it is possible to assume that other cucurbituril compounds (e.g., cucurbit[5]uril, cucurbit [7]uril, and cucurbit[8]uril) can form—naturally, under suitable conditions—complex CB structures involving the cations H_3O^+ or $H_5O_2^+$.

Methodology

The quantum mechanical calculations were carried out at the density functional level of theory (DFT, B3LYP functional) [36, 37] using the Gaussian 03 software suite [38]. The 6-31G(d) basis set was used and the optimizations were unconstrained.

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