Stability and DFT Calculated Structure of Protonated Tetraethyl *p-tert*-Butyltetrathiacalix[4]arenetetraacetate in the *cone* Conformation

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Summary. From extraction experiments in the two-phase water-nitrobenzene system and γ-activity measurements, the stability constant of protonated tetraethyl *p-tert*-butyltetrathiacalix[4]arenetetraacetate (*cone*) in nitrobenzene saturated with water was determined. Three different structures of the resulting complex species were indicated by means of the DFT calculations.

Keywords. Calixarenes; Macrocycles; Protonation; Stability; DFT.

Introduction

Calix[*n*]arenes are a well-known family of macrocyclic molecules with many potential applications in various branches of chemistry. Because of their simple one-pot preparation, easy derivatization, and unique complexation abilities, calix[*n*]arenes are widely used as the building blocks for the constructions of more sophisticated molecular systems. Their unique three-dimensional pre-organization make them very attractive as the receptors for the complexation of cations, anions, and even neutral molecules [1].

The well-established chemistry of the "classical" calix[*n*]arene family was "rejuvenated" by the discovery of so called thiacalix[4]arenes. The presence of four sulfur atoms instead of methylene groups makes thiacalix[4]arenes very promising molecules with many novel features [2] if compared with the chemistry of "classical" calixarenes.

Recently, experimental evidence for the *p-tert*-butylcalix[4]arenetetrakis(*N,N*-diethylacetamide)·H_3O^+ complex species has been advanced [3] and its complex structure has been derived [4]. Further, NMR evidence for protonated tetramethyl *p-tert*-butylcalix[4]arenetetraketone in nitrobenzene−d_5 has been given [5]. In the present work, the stability constant of protonated tetraethyl *p-tert*-butyltetrathiacalix[4]arenetetraacetate in the *cone* conformation ($\mathbf{1} \cdot H_3O^+$) is evaluated in water saturated nitrobenzene and its DFT calculated structure is solved.

Results and Discussion

Extraction Experiments

In terms of previous papers [6–8], the two-phase water-HCl/nitrobenzene-Na*DCC*-**1** (**1** = tetraethyl *p-tert*-butyltetrathiacalix[4]arenetetraacetate (*cone*)) extraction system, chosen for determination of stability constant of the complex $\mathbf{1} \cdot H_3O^+$ in nitrobenzene saturated with water, can be characterized by the main chemical equilibrium (1) to which the equilibrium extraction constant (Eq. (2)) corresponds; aq

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and nb denote the presence of the species in the aqueous and nitrobenzene phases.

$$H_3O^+\,(aq) + 1 \cdot Na^+\,(nb) \leftrightarrows 1 \cdot H_3O^+\,(nb) + Na^+\,(aq);$$
$$K_{ex}(H_3O^+, 1 \cdot Na^+) \quad (1)$$
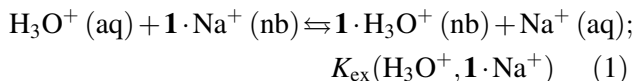
$$K_{ex}(H_3O^+, 1 \cdot Na^+) = \frac{[1 \cdot H_3O^+]_{nb}[Na^+]_{aq}}{[H_3O^+]_{aq}[1 \cdot Na^+]_{nb}} \quad (2)$$

It is necessary to emphasize that **1** is a considerably hydrophobic ligand, practically present in the nitrobenzene phase only, where this ligand forms – with H_3O^+ and Na^+ – the relatively stable complexes $1 \cdot H_3O^+$ and $1 \cdot Na^+$.

Taking into account the conditions of electroneutrality in the organic and aqueous phases of the system under study, the mass balances of H_3O^+ and Na^+ ions at equal volumes of the nitrobenzene and aqueous phases, as well as the measured equilibrium distribution ratio of sodium, $D_{Na} = [1 \cdot Na^+]_{nb}/[Na^+]_{aq}$, combined with Eq. (2), we get the final expression for the mentioned extraction constant (Eq. (3)); $C_{HCl}^{in,nb}$ is the initial concentration of HCl in the aqueous phase and $C_{NaDCC}^{in,nb}$ denotes the initial concentration of Na*DCC* in the organic phase of the system under consideration.

$$K_{ex}(H_3O^+, 1 \cdot Na^+) = \frac{1}{D_{Na}} \frac{C_{NaDCC}^{in,nb}}{(1 + D_{Na})C_{HCl}^{in,aq} - C_{NaDCC}^{in,nb}} \quad (3)$$

From the extraction experiments and γ-activity measurements by using Eq. (3), the following value of the constant K_{ex} (H_3O^+, $1 \cdot Na^+$) was evaluated as $\log K_{ex}(H_3O^+, 1 \cdot Na^+) = -0.8 \pm 0.1$. Moreover, with respect to Refs. [8–10], for the exchange extraction constant K_{ex} (H_3O^+, Na^+) corresponding to the equilibrium H_3O^+ (aq) + Na^+ (nb) $\leftrightarrows$ H_3O^+ (nb) + Na^+ (aq) and for the extraction constant $K_{ex}(H_3O^+, 1 \cdot Na^+)$ defined above, as well as for the stability constants of the complexes $1 \cdot Na^+$ and $1 \cdot H_3O^+$ in nitrobenzene saturated with water, denoted by $\beta_{nb}(1 \cdot Na^+)$ and $\beta_{nb}(1 \cdot H_3O^+)$, one gets Eq. (4).

$$\log \beta_{nb}(1 \cdot H_3O^+) = \log \beta_{nb}(1 \cdot Na^+)$$
$$+ \log K_{ex}(H_3O^+, 1 \cdot Na^+)$$
$$- \log K_{ex}(H_3O^+, Na^+) \quad (4)$$

Using the value $\log K_{ex}(H_3O^+, Na^+) = 0.3$ inferred from Ref. [7], the constant $\log K_{ex}(H_3O^+, 1 \cdot Na^+)$

given above and $\log \beta_{nb}(1 \cdot Na^+) = 6.2 \pm 0.1$, determined from the distribution of sodium picrate in the water-nitrobenzene extraction system containing also **1** [11], and applying Eq. (4), we obtain the stability constant of the $1 \cdot H_3O^+$ complex in water saturated nitrobenzene at 25°C as $\log \beta_{nb}(1 \cdot H_3O^+) = 5.1 \pm 0.2$. This means that in the mentioned medium the stability constant of the considered complex $1 \cdot H_3O^+$ is somewhat lower than that of the $1 \cdot Na^+$ complex.

Quantum Mechanical Calculations

The quantum mechanical calculations were carried out at the density functional level of theory (DFT, *B3LYP* functional) using the Gaussian 03 suite of programs [12]. The 6-31G(d) basis set was used and the optimization was unconstrained. The optimizations were done *in vacuo* as no reliable correction for the influence of the solvent is at hand at this precision level. Although a possible influence of a polar solvent on the detailed structures of **1** and $1 \cdot H_3O^+$ could be imagined, our quantum calculations in similar cases, performed in an analogous way, showed very good agreement of experiment with theory [13, 14].

In the model calculations, we optimized the molecular geometry of the parent thiacalixarene ligand **1** and its complex with H_3O^+. The optimized structure of **1** is shown in Fig. 1. From this figure it follows that the most stable conformation of the thiacalixarene ligand **1** forms a *pinched cone* structure [1] with C_2 symmetry.
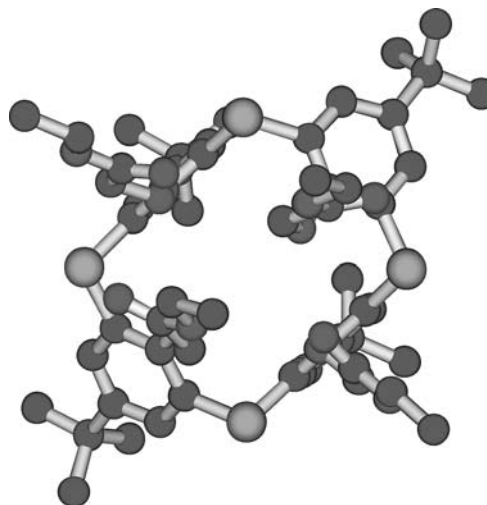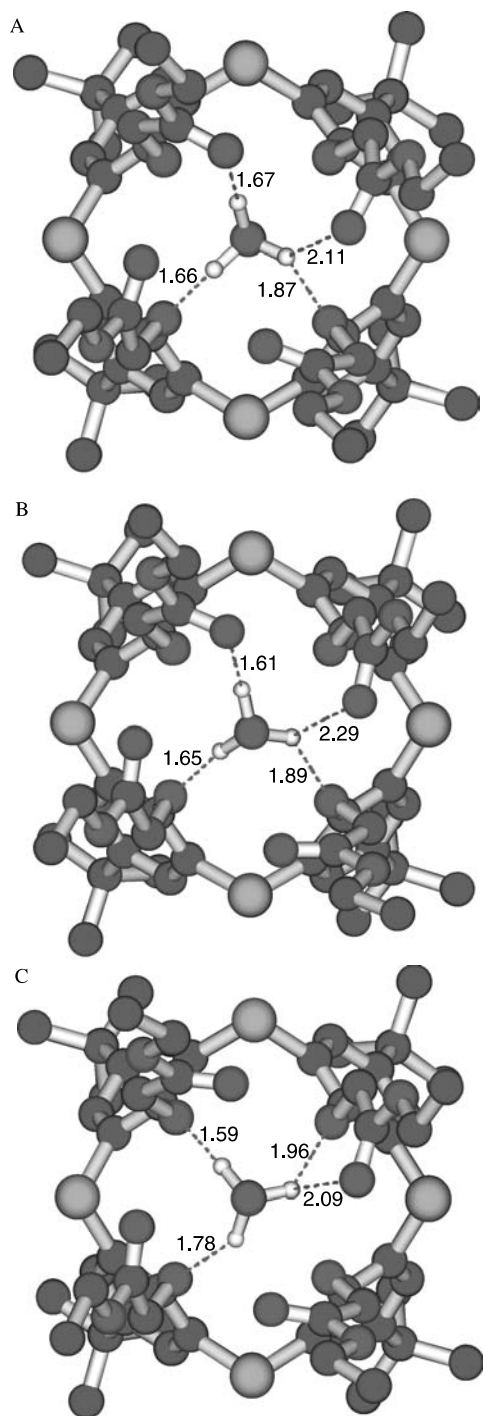

Fig. 1. DFT optimized structure of free **1** (*B3LYP*/6-31G(d))

A

B

C

Fig. 2. DFT optimized structures (A, B, C) of the $1 \cdot H_3O^+$ complex ($B3LYP$/6-31G(d)) with the lengths of the corresponding hydrogen bonds. Structure A: H-bond lengths of H_3O^+ to phenoxy oxygens of **1**: 1.87 and 1.66 Å; H-bond lengths of H_3O^+ to carbonyl oxygens of **1**: 1.67 and 2.11 Å. Structure B: H-bond lengths of H_3O^+ to phenoxy oxygens of **1**: 1.89 and 1.66 Å; H-bond lengths of H_3O^+ to carbonyl oxygens of **1**: 1.61 and 2.29 Å. Structure C: H-bond lengths of H_3O^+ to phenoxy oxygens of **1**: 1.69, 1.96, and 1.78 Å; H-bond length of H_3O^+ to carbonyl oxygen of **1**: 2.09 Å

In Fig. 2, the structures A, B, and C of the $1 \cdot H_3O^+$ complex obtained by DFT optimization are illustrated together with the lengths of the corresponding hydrogen bonds (in Å). Compared to free ligand **1** (Fig. 1), the thiacalixarene part of the complex $1 \cdot H_3O^+$ is more open and very close to the C_4 symmetry. The hydroxonium ion H_3O^+, placed in the coordination cavity formed by the thiacalixarene lower-rim groups, is bound by strong hydrogen bonds to the phenoxy oxygen atoms of **1** (structures A, B, and C) and also to one carbonyl oxygen of **1** (structure C) or two carbonyl oxygens of **1** (structures A and B). Finally, the calculated stabilization energies corresponding to the structures A, B, and C of the $1 \cdot H_3O^+$ complex under study are gradually -429.7, -427.2, and $-420.1 \, kJ \, mol^{-1}$.

In conclusion, it should be noted that the structures A, B, and C of the $1 \cdot H_3O^+$ complex are apparently in the dynamic equilibrium characterized by the highest equilibrium portion of the structure A. Besides, from this point of view, the experimentally determined value of $\log \beta_{nb}(1 \cdot H_3O^+) = 5.1 \pm 0.2$ can be obviously considered as a certain "average" stability constant of the three DFT calculated structures.

Experimental

Cesium dicarbollylcobaltate (Cs*DCC*) was purchased from Katchem, Řež, Czech Republic. A nitrobenzene solution of H*DCC* [15] was prepared from Cs*DCC* by the procedure described in Ref. [16]. The equilibration of the nitrobenzene solution of H*DCC* with stoichiometric NaOH, which was dissolved in an aqueous solution of NaCl ($0.2\,M$), yielded the corresponding Na*DCC* solution in nitrobenzene. Compound **1** (5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis[(ethoxy-carbonyl)methoxy]-2,8,14,20-tetrathiacalix[4]arene (*cone*)), called also tetraethyl *p-tert*-butyltetrathiacalix[4]arenetetra-acetate (*cone*), was kindly supplied by Dr. *M. Kyrš*, Prague. The other chemicals used (Lachema, Brno, Czech Republic) were of reagent grade purity. The radionuclide $^{22}Na^+$ (DuPont, Belgium) was of standard radiochemical purity.

The extraction experiments were carried out in $10\,cm^3$ glass test-tubes covered with polyethylene stoppers: $2\,cm^3$ of an aqueous solution of HCl of a concentration in the range from 1×10^{-4} to $1 \times 10^{-3}\,M$ and microamounts of $^{22}Na^+$ were added to $2\,cm^3$ of a nitrobenzene solution of **1** and Na*DCC*, whose initial concentrations varied also from 1×10^{-4} to $1 \times 10^{-3}\,M$ (in all experiments, the initial concentration of **1** in nitrobenzene, $C_1^{in,nb}$, was equal to the initial concentration of Na*DCC* in this medium, $C_{NaDCC}^{in,nb}$). The test-tubes filled with the solutions were shaken for 24 h, using a laboratory shaker. Then the phases were separated by centrifugation. Afterwards, $1\,cm^3$ samples were taken from each phase and their γ-activities were measured using a well-type NaI(Tl) scintilla-

tion detector connected to a γ-analyzer NK 350 (Gamma, Budapest, Hungary). The equilibrium distribution ratio of sodium, D_{Na}, was determined as the ratio of the measured radioactivities of Na^+ in the nitrobenzene and aqueous samples.

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