

Hemicucurbit[6]uril a Macrocyclic Ligand with Unusual Complexing Properties[†]

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Abstract

The complex formation of the macrocyclic ligand hemicucurbit[6]uril with various salts has been studied in aqueous solution. Due to the low solubility of this ligand the formation of complexes results in an increase of the amount of ligand present in solution. From these measurements the stability constants of the complexes formed are calculated. Hemicucurbit[6]uril only forms cation complexes with cobalt(II), nickel(II) and the uranylion. All other cations examined e.g. silver(I), lead(II) and copper(II) do not form detectable complexes in aqueous solution. For a better understanding of the complexation behaviour some quantum mechanical chemical calculations are performed with Gaussian.

Introduction

In recent years the number of publications dealing with cucurbit[n]uril have increased consistently [1, 2]. The first cucurbituril was synthesized by Behrend in 1905 [3]. He described the formation of solid complexes with salts and dyes without the knowledge of the structure of this ligand. The characterization of this compound relating to its structure and properties was achieved many years later by Mock *et al.* [4, 5]. Cucurbiturils are formed from glycoluril monomers linked by pairs of methylene bridges. The resulting molecules have a very rigid structure with a well-defined internal cavity. The hydrophobic cavity is accessible by two portals formed by carbonyl groups. As a result cucurbit[n]urils are able to complex cations [6–8] at the portals and to include neutral molecules and even gases [9–12] within their cavities.

Recently the synthesis of a new member of the ‘cucurbituril family’ has been reported [13]. Effectively this new member is only half of a cucurbit[6]uril, equivalent to half of a ‘hollow pumpkin’ sliced through the molecular equator, see Figure 1. This macrocyclic ligand possesses six carbonyl groups. It was named hemicucurbit[6]uril (hmCuc6)1.

It was expected due to the similarity to crown ethers and related macrocyclic ligands, that this macrocyclic

ligand would also be suitable for the complexation of cations. Against all expectations only the formation of complexes with thiocyanate and propargyl alcohol have been observed in aqueous solution [13]. The crystal structures of the adduct with chloride and of the complex with propargyl alcohol have been reported [13]. Since the initial report of complex formation we have published the stability constants of the complexes with thiocyanate and iodide anions [14]. No cation complexes of hemicucurbit[6]uril were known before this study. In this study we examined a number of complexation reactions of transition metal cations.

Experimental

The ligand hemicucurbit[6]uril (hmCuc6) is synthesized by mixing equimolar amounts of ethyleneurea (19 g, 0.2 mol) and formaldehyde solution (36%, 15.3 ml) in 30 ml 4 N hydrochloric acid at room temperature as described by Miyahara [13]. The mixture is stirred and after 30 min the formation of white crystals is complete. After filtration they are washed several times with water and dried at 80 °C. Yield 18.8 g (83.9%), mp 324–325 °C (dec).

Anal. calcd. for C₂₄H₃₆O₆N₁₂·0.8H₂O: C, 47.80; H, 6.28; N, 27.87. Found: C, 47.93; H, 6.03; N, 27.64.

All the salts used Co(NO₃)₂, Co(ClO₄)₂, Ni(NO₃)₂, Ni(ClO₄)₂, Cu(NO₃)₂, AgNO₃, CdNO₃, TlNO₃, PbNO₃, CeCl₃, TmCl₃, LuCl₃, UO₂(NO₃)₂ and UO₂Cl₂ were

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[†]Dedicated to Prof. H. Möhwald on the occasion of his 60th birthday.

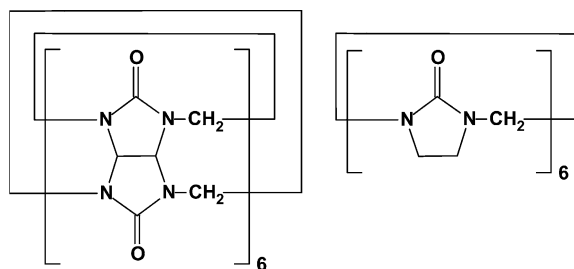


Figure 1. Chemical structures of cucurbit[6]uril (left) and hemicucurbit[6]uril (right).

commercial of the highest purity available. Doubly distilled water was used for all experiments.

To study the complex formation of hmCuc6 with cations or anions one can take advantage of the low solubility of this ligand in aqueous solution (5×10^{-5} mol/l) [13]. The addition of a sufficient amount of solid ligand to salt solutions (2×10^{-3} – 2×10^{-2} mol/l) results in the formation of saturated solutions with respect to the ligand [15–17]. To ensure the formation of a saturated solution the solutions were stirred for at least 24 h after this time still solid ligand remained. The solutions were passed through membrane filters (Polycarbonate, $0.2 \mu\text{m}$) and were analysed by measuring the total organic carbon content TOC (TOC-5050, Shimadzu). The solubility of the ligand was calculated from the TOC values of aqueous saturated solutions. All solutions were thermostated at 25°C .

For a better understanding of the complexation behaviour some quantum mechanical calculations were performed with Gaussian. Molecular graphics were generated with GaussView. The geometries were optimised from schemical intuitive starting 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 [18].

Mathematical treatment of the experimental TOC-values

Under the assumption that the salt used is completely dissociated and the ligand L only forms complexes with the cation M^{n+} the reaction is given by equation (1):



The stability constant of the cation complex is given by:

$$K = \frac{[LM^{n+}]}{[L][M^{n+}]} \quad (2)$$

All concentrations are in mol/l. The total concentration of the ligand c_{tot} increases in solution due to complex formation:

$$c_{\text{tot}} = [L] + [LM^{n+}] \quad (3)$$

The total concentration c_{tot} of the ligand can be measured by the TOC value of the solution. From the known elemental composition of the ligand the molar ligand concentration can be calculated using the following equation:

$$c_{\text{tot}} = \frac{(\text{TOC}) \cdot 10^3}{12.011 \cdot n_C} \quad (4)$$

with the number of carbon atoms of the ligand n_C

Since all the salt solutions contained an excess of undissolved ligand, the first term in the equation (3) is constant:

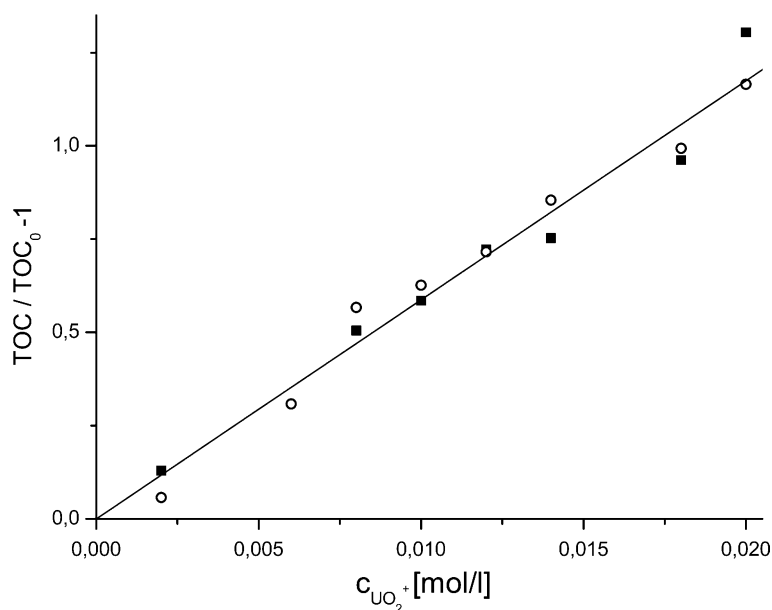


Figure 2. Variation of $\left(\frac{\text{TOC}}{\text{TOC}_0} - 1\right)$ of saturated solutions of the ligand hmCuc6 as a function of the concentration of uranium salts (■ UO_2Cl_2 , ○ $\text{UO}_2(\text{NO}_3)_2$) in aqueous solution at 298 K.

$$[L]_{\text{sat}} = \frac{(\text{TOC})_0 \cdot 10^3}{12.011 \cdot n_C} \quad (5)$$

From equations (2) and (5) and using the equations of the material balances:

$$c_L = [L] + [LM^{n+}]$$

and

$$c_{\text{salt}} = [M^{n+}] + [LM^{n+}]$$

equation (3) can be rearranged to equation (6):

$$c_{\text{tot}} = [L]_{\text{sat}} + \frac{K \cdot [L]_{\text{sat}}}{1 + K \cdot [L]_{\text{sat}}} \cdot c_s \quad (6)$$

Equation (6) can be transformed to equation (7) using equations (4) and (5):

$$\frac{(\text{TOC})}{(\text{TOC})_0} - 1 = \frac{K}{1 + K \cdot [L]_{\text{sat}}} c_{\text{salt}} \quad (7)$$

Plotting $\left(\frac{(\text{TOC})}{(\text{TOC})_0} - 1\right)$ as a function of the total salt concentration c_{salt} one expects a straight line with a slope b , this is shown e.g. for UO_2^{2+} in Figure 2. The slope b can be used to calculate the stability constant of the complex formed:

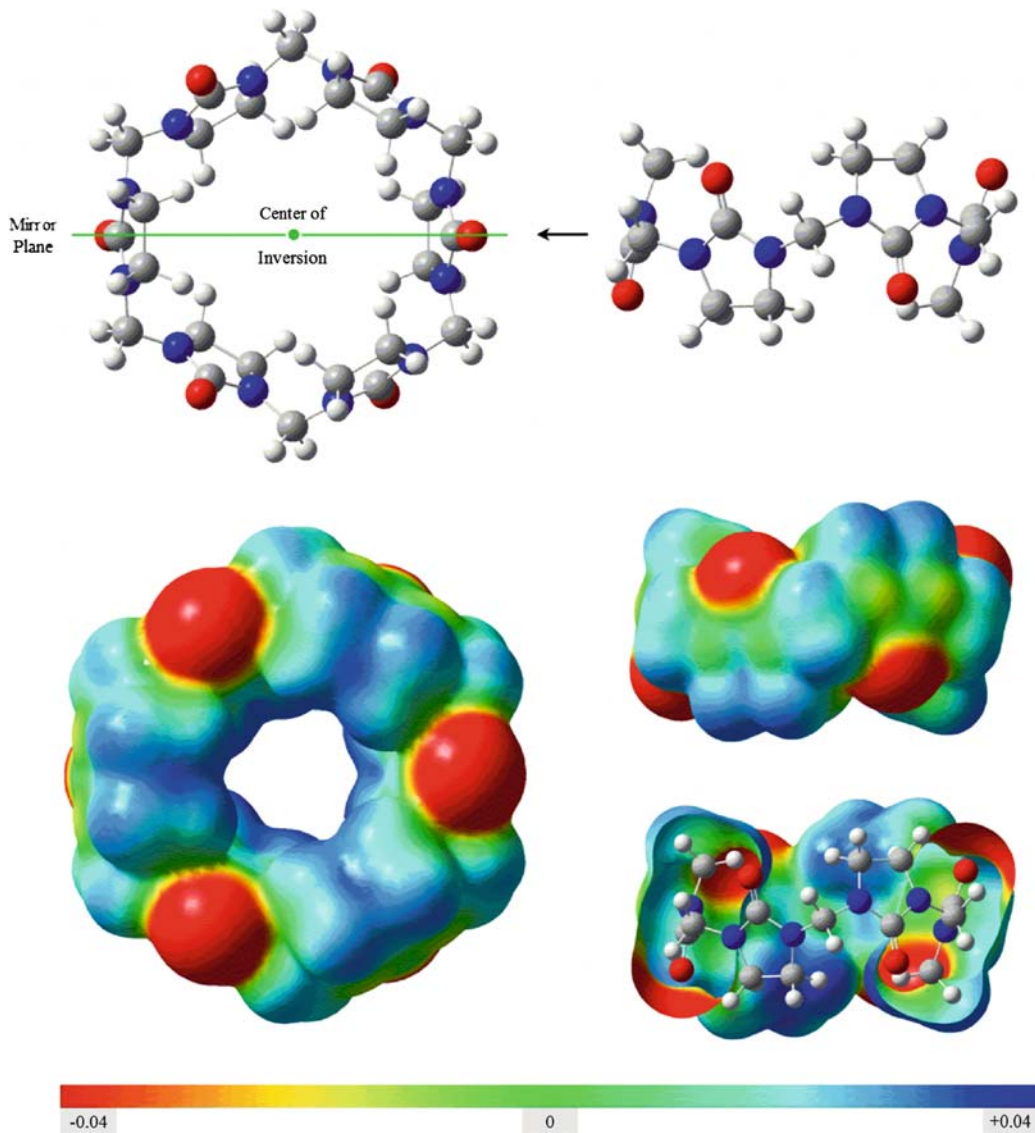


Figure 3. HmCuc6: Optimized geometry (by DFT B3LYP/6-31G(d) method) and electrostatic potential mapped on the molecular 'size surface' with electronic density isovalue of 0.002 a.u.

$$K = \frac{b}{1 - b \cdot [L]_{\text{sat}}} \quad (8)$$

If the solubility of the ligand is low than equation (9) is valid:

$$b \cdot [L]_{\text{sat}} \ll 1 \quad (9)$$

Respectively, from these assumptions the slope b will be identical with the stability constants. The activity coefficients were obtained from the extended Debye–Hückel expression.

Results and discussion

It is known that hmCuc6 does not form complexes with alkali, alkaline earth cations and an ammonium ion. However, this macrocyclic ligand has been shown to complex with some anions [13, 14]. This behaviour is best explained by the formation of an ‘alternate’ conformation of hmCuc6 in solution. This is supported by Density Functional Theory calculations (B3LYP/6-31G(d) model chemistry) [18], and geometry optimisation of the uncomplexed ligand, see Figure 3.

All the carbonyl groups locate outside the cavity. Thus, the formed cavity creates an electropositive inner

sphere enabling the complexation of anions. To form complexes with cations the carbonyl groups must orientate themselves to the centre of the cavity resulting in unfavourable energetic contributions due to the electrostatic repulsion between the partial negative charged carbonyl groups.

According to (3) the solubility of hmCuc6 increases due to the complex formation either with cations or anions. In cases that $c_L \equiv [L]_{\text{sat}}$ no or only extreme weak complexes have been formed in solution. If $c_L > [L]_{\text{sat}}$ a complex exists with the cation or anion or both present in solution. Only from the variation of the cation and anion a decision about the nature of the complex becomes possible. In Table 1 some values of the solubility of hemicucurbituril in 0.01 M solutions of different salts are given.

The measured solubilities clearly indicate a significant increase in solubility only for UO_2^{2+} , Ni^{2+} and Co^{2+} . No influence from the anions examined is detectable. According to equation (7) the stability constant of the formed complexes can be calculated from a plot of the experimental TOC values as a function of the total salt concentration.

Independent one obtains the stability constants summarized in Table 2. These results clearly demonstrate the ability of hmCuc6 to form complexes with some transition metal cations. Thus, hmCuc6 is able to act as a ligand for selected anions and cations. Without the knowledge of the reaction enthalpies and entropies for the complex formation no detailed discussion about the factors responsible for the complex formation with cations is possible. Due to the low solubility the synthesis of derivatives with higher solubilities in water or organic solvents is necessary for a fundamental understanding of the factors responsible for the formation of anion and cation complexes.

Table 1. Solubility of hemicucurbit[6]uril in aqueous solution in the presence of different salts (0.01 M) at 298 K

Salt	Solubility/M
–	$(3.8 \pm 0.2) \cdot 10^{-4}$
$\text{Co}(\text{NO}_3)_2$	$(5.5 \pm 0.2) \cdot 10^{-4}$
$\text{Co}(\text{ClO}_4)_2$	$(5.4 \pm 0.3) \cdot 10^{-4}$
$\text{Ni}(\text{NO}_3)_2$	$(6.2 \pm 0.2) \cdot 10^{-4}$
$\text{Ni}(\text{ClO}_4)_2$	$(5.8 \pm 0.3) \cdot 10^{-4}$
$\text{Cu}(\text{NO}_3)_2$	$(3.8 \pm 0.1) \cdot 10^{-4}$
AgNO_3	$(4.5 \pm 0.2) \cdot 10^{-4}$
$\text{Cd}(\text{NO}_3)_2$	$(4.0 \pm 0.3) \cdot 10^{-4}$
TlNO_3	$(4.0 \pm 0.2) \cdot 10^{-4}$
$\text{Pb}(\text{NO}_3)_2$	$(4.6 \pm 0.1) \cdot 10^{-4}$
CeCl_3	$(3.8 \pm 0.3) \cdot 10^{-4}$
TmCl_3	$(3.7 \pm 0.2) \cdot 10^{-4}$
LuCl_3	$(3.8 \pm 0.2) \cdot 10^{-4}$
$\text{UO}_2(\text{NO}_3)_2$	$(9.2 \pm 0.3) \cdot 10^{-4}$
UO_2Cl_2	$(9.1 \pm 0.2) \cdot 10^{-4}$

Table 2. Stability constants (log K, K in 1/mol) for the complexation of different cations by hemicucurbit[6]uril in water at 25 °C and an ionic strength of zero

Cation	log K
Co^{2+}	1.18 ± 0.02
Ni^{2+}	1.34 ± 0.04
UO_2^{2+}	1.78 ± 0.03

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