Complex Formation between Cucurbit[n]urils and Alkali, Alkaline Earth and Ammonium Ions in Aqueous Solution

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Abstract

The complex formation between cucurbit[5]uril, decamethylcucurbit[5]uril and cucurbit[6]uril and alkali, alkaline earth and ammonium cations is examined. The solubility of these ligands is rather small in aqueous solution. In the presence of salts the solubility normally increases due to the formation of complexes. The total concentration of the ligands can be easily measured from the total organic carbon content of the salt solutions saturated with the ligand. From these results it is possible to calculate the stability constants of the complexes formed even without the knowledge of the exact solubility of the ligand.

Introduction

Compared with other macrocyclic and macrobicyclic ligands relatively little is known about the complexation behaviour of the macrocyclic ligand cucurbit[6]uril (Figure 1). This ligand was first synthesized in 1905 [1]. The authors reported experimental observations about the remarkable behaviour of this ligand without any knowledge of its structure. This situation lasted until 1981 when the structure of cucurbit[6]uril was reported [2, 3]. Due to solubility problems the complexation behaviour of cucurbit[6]uril has been studied in 40% formic acid. Cucurbit[6]uril forms stable complexes with different ammonium, diammonium ions [4–7], alkaline, alkaline earth cations [8–10] and some other organic molecules [11, 12].

The synthesis of decamethylcucurbit[5]uril was reported some years ago [13, 14]. It was mentioned that this ligand does not form complexes [14]. Very recently the synthesis of mixtures containing cucurbit[n]urils (*n* = 5–8) and the procedure for the separation and characterization has been described [15]. The synthesis of pure cucurbit[5]uril has also been reported [16]. Up to now, only very few results about the complexation behaviour of decamethylcucurbit[5]uril have been reported [17].

Unfortunately all known derivatives of cucurbituril are sparingly soluble in aqueous solution. Thus, it is difficult to study the complex formation of these macrocyclic ligands using conventional techniques. Recently an experimental method has been produced to measure stability constants for complex formation with nearly insoluble ligands from the increase in solubility due to complex formation [18, 19]. This effect has been measured by a spectrophotometric method [18–20] or by the estimation of the total organic carbon content (TOC) of the resulting solutions [21].

The same experimental method is used to study the complex formation of cucurbit[5]uril, decamethylcucurbit[5]uril and cucurbit[6]uril in pure aqueous solution.

Experimental

The macrocyclic ligands cucurbit[5]uril, decamethylcucurbit[5]uril and cucurbit[6]uril were synthesized and characterized according to published procedures [16]. Their chemical structures are given in Figure 1.

The salts NaCl (Fluka), NaNO$_3$ (Fluka), NaClO$_4$ (Ventron), KCl (Merck), RbCl (Fluka), CsCl (Merck), NH$_4$Cl (Fluka), CaCl$_2$ (Fluka), Ca(NO$_3$)$_2$ (BDH), SrCl$_2$ (Fluka), BaCl$_2$ (Fluka), Ba(NO$_3$)$_2$ (Fluka) and Ba(ClO$_4$)$_2$ (Merck) were of the highest purity commercially available. C$_6$H$_{13}$NH$_3$Cl was prepared from hexylamine (Fluka). Double distilled water was used as solvent.

The solutions with the ligands were prepared by the addition of solid cucurbiturils to solutions containing different concentrations of the salts ($2 \times 10^{-3} - 2 \times 10^{-2}$ mol/l). The amount of the solid ligand is high enough to ensure the formation of salt solutions saturated with the ligands. The solutions were stirred for at least two weeks. Samples of the solutions were analysed after one and two weeks. Prior to the measurements of the total organic carbon content (TOC) of the solutions they were passed through a membrane filter (polycarbonate, 0.4 μm) to remove the undissolved ligands. In the case of hexylamine hydrochloride the TOC-values of the pure salt solutions were used to correct the TOC-values of the solutions saturated with the ligands. All solutions were thermostated at 25 °C. The resulting solutions were analysed

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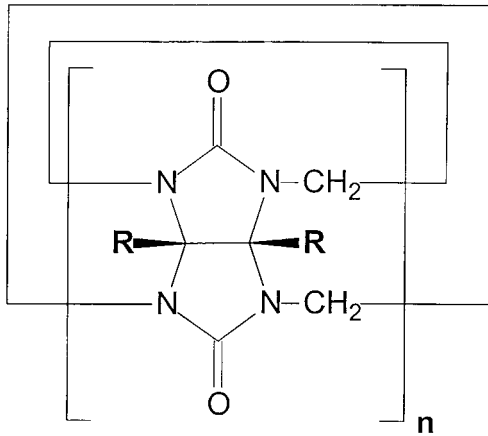
| R = H | n = 6 | Cucurbit[6]uril | **Cuc[6]** |
| R = CH$_3$ | n = 5 | Decamethylcucurbit[5]uril | **DMCuc[5]** |
| R = H | n = 5 | Cucurbit[5]uril | **Cuc[5]** |

Figure 1. Chemical structures of the cucurbituril derivatives used in this work.

by the measurement of the total organic carbon content TOC (TOC-5050, Shimadzu).

Results and discussion

Treatment of the experimental data

The 1 : 1 complex formation between a ligand L and a cation M^{n+} is given by:
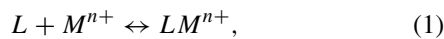
$$L + M^{n+} \leftrightarrow LM^{n+}, \qquad (1)$$

with the stability constant K:

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

The mass balances for the total ligand c_L and total salt c_{salt} concentration are:

$$c_L = [L] + [LM^{n+}] \qquad (3)$$

and

$$c_{salt} = [M^{n+}] + [LM^{n+}]. \qquad (4)$$

In the absence of any salt the TOC value of the solution saturated with the ligand is given by:

$$TOC_0 = f_1[L]_{sat}, \qquad (5)$$

with a proportionality factor f_1.

The TOC-value of the salt solution saturated with the ligand is:

$$TOC = f_i[L]_{sat} + f_2[LM^{n+}]. \qquad (6)$$

Due to complex formation the total concentration of the ligand in solution increases.

Using Equations (2)–(6) one gets

$$\frac{TOC}{TOC_0} - 1 = \frac{f_2}{f_1} \frac{K}{1 + K \cdot [L]_{sat}} c_{salt} = b c_{salt}. \qquad (7)$$

The proportionality factors f_1 and f_2 are identical for the pure ligand and the complex formed. The salt present in solution does not influence the measured TOC-values. Plotting $\left(\frac{TOC}{TOC_0} - 1 \right)$ as a function of the total salt concentration c_{salt} one expects a straight line with a slope b (Figure 2). From this slope, the stability constant of the complex formed can be calculated:

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

If the solubility of the ligand is low then Equation (9) is valid:

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

With this assumption the slope b is identical with the stability constant. The solubilities of the cucurbituril derivatives are low enough to ensure the use of this assumption [10, 16]. Thus it becomes possible to calculate the complex stabilities without exact knowledge of the solubilities.

In the case of cucurbit[n]uril also the formation of 2 : 1 complexes between the ligand L and a cation M^{n+} is possible. This reaction is shown in Equation (10):

$$L + 2M^{n+} \leftrightarrow LM_2^{2n+}. \qquad (10)$$
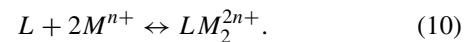
The overall stability constant β is given by:

$$\beta = K_1 K_2 = \frac{[LM_2^{2n+}]}{[L][M^{n+}]}. \qquad (11)$$

The same procedure as described in detail for the formation of the 1 : 1-complexes results in the following equation for the TOC-values in the case of the formation of 2 : 1 complexes:

$$\sqrt{TOC - TOC_0}$$
$$= \frac{f}{4} \left[\sqrt{\frac{f}{TOC_0 * \beta} + 8c_{salt}} - \sqrt{\frac{f}{TOC_0 * \beta}} \right], \qquad (12)$$

with the proportionality factor f which is identical for the ligand and the complex.

Equation (12) can only be solved by numerical methods. Using a nonlinear regression analysis it is possible to minimize the error square sum with respect to the overall stability constant β.

No salts are known to achieve constant ionic strength without possible interactions with cucurbit[n]urils or any contributions to the TOC-values of the solutions. Thus no inert salts could be used during these measurements. For the calculation of the stability constants activities are therefore used. The activity coefficients are calculated using the Debye–Hückel expression.
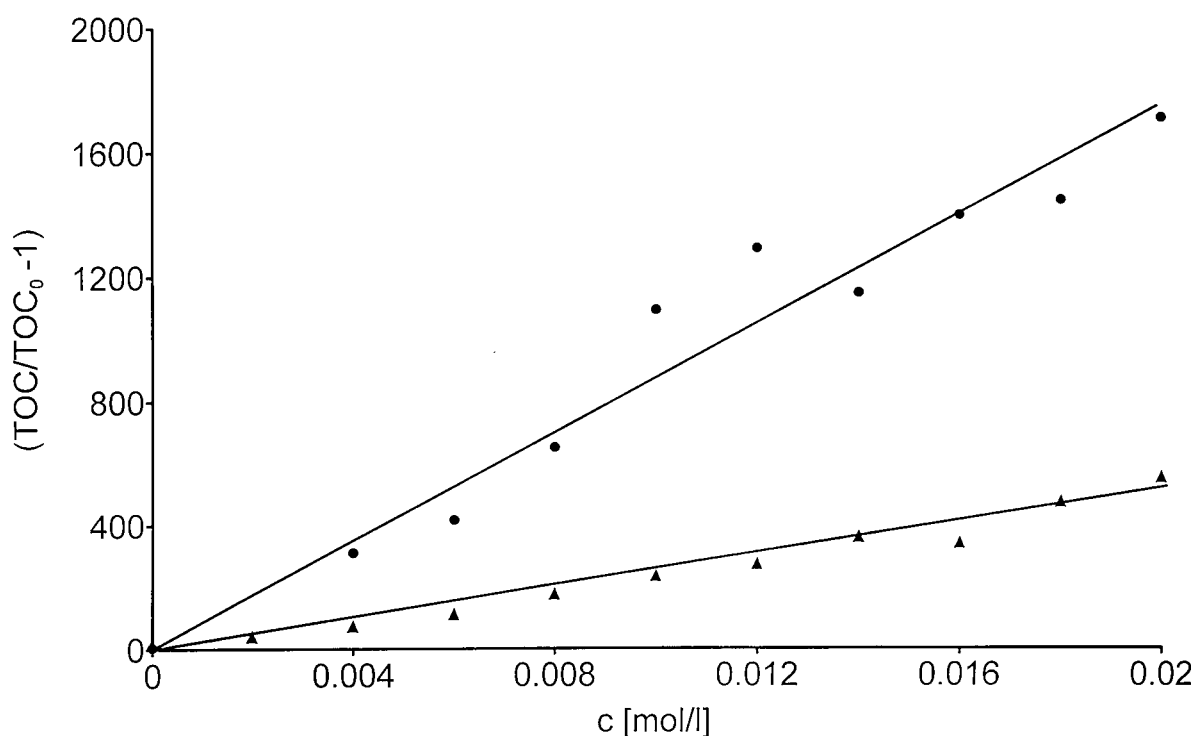
Figure 2. $\left(\frac{TOC}{TOC_0} - 1\right)$ of solutions saturated with cucurbit[6]uril as a function of the concentration of $CaCl_2$ (●) and KCl (▲).

Stabilities of the cucurbituril complexes

The treatment of the experimental TOC values under the assumption of a 1 : 1- or 2 : 1-complex formation leads to completely different results.

The stability constants for the formation of 1 : 1-complexes of alkali, alkaline earth and ammonium ions with Cuc[5], DMCuc[5] and Cuc[6] in aqueous solutions are summarized in Table 1. In the presence of some salts the TOC-values of the solutions saturated with the ligands decreased. Obviously the solubilities of these complexes are lower than the solubilities of the pure ligands. In all other cases examined the TOC-values of the solution increased. Up to now no explanation can be given for the different solubility behaviour of the complexes formed.

The stabilities of the complexes formed with Cuc[5] and DMCuc[5] are very similar. The portals of these ligands formed by the carbonyl groups are too small to give optimal interactions between all carbonyl groups and the complexed cations. The diameter of the portals of Cuc[6] at 4 Å is large enough to accommodate some of the cations examined. Thus all cations are complexed much stronger compared with the smaller cucurbiturils. However, with the exception of the complexation of Ba^{2+} with cucurbit[6]uril the stabilities of the complexes formed do not depend significantly upon the radii of the cations.

Using Equation (12) for the calculations of the overall stability constants β gives values of β smaller than 1. These values are not comparable with results obtained in aqueous formic acid, see Table 1. Under the experimental conditions the formation of 2 : 1-complexes obviously has only a minor influence on the measured TOC-values.

Table 1. Stability constants ($\log K$, K in l/mol) for the complexation of alkali, alkaline earth and ammonium cations by different cucurbit[n]urils in water at 25 °C

Salt	Ligand	Cuc[5]	DMCuc[5]	Cuc[6]
Na^+		1.85 ± 0.05	$-^a$	3.49 ± 0.04
				3.47^d
				3.16^e
K^+		1.31 ± 0.07	1.11 ± 0.05	2.85 ± 0.02
				2.75^e
Rb^+		1.01 ± 0.32	0.92 ± 0.09	2.98 ± 0.03
				2.61^e
Cs^+		0.90 ± 0.34	$-^b$	2.52 ± 0.04
Ca^{2+}		1.73 ± 0.07	1.61 ± 0.09^c	3.61 ± 0.03
Sr^{2+}		1.50 ± 0.13	1.59 ± 0.05	2.90 ± 0.03
Ba^{2+}		1.32 ± 0.16	1.32 ± 0.10	$-^f$
				5.23^d
NH_4^+		1.32 ± 0.12	1.10 ± 0.28	2.84 ± 0.01
$C_6H_{13}NH_3^+$		1.27 ± 0.14	0.67 ± 0.29	3.33 ± 0.02
				3.36^g

[a] Negative slopes in the presence of NaCl, $NaNO_3$ and $NaClO_4$.
[b] Negative slope in the presence of CsCl.
[c] Positive slope in the presence of $Ca(NO_3)_2$, negative slope in the presence of $CaCl_2$.
[d] Ref. [10], in H_2O.
[e] Ref. [10], in formic acid (40%).
[f] Negative slopes in the presence of $BaCl_2$, $BaNO_3$ and $Ba(ClO_4)_2$.
[g] Ref. [13], in formic acid (40%).

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Conclusions

The measurement of the TOC-values of salt solutions saturated with nearly insoluble ligands is an easy-to-handle technique for the determination of stability constants. A further advantage is that only very small samples of the ligands are used. The TOC values are also not affected by the complex formation with salts.

Spectrophotometric measurements of salt solutions containing cucurbit[6]uril [8] are less accurate compared with the results reported here. The maximum of absorption of this ligand is below 220 nm. Thus the absorbance could only be measured at wavelengths higher than the maximum. Therefore it is not possible to detect any shifts in the maximum of the absorbance of the complexes compared with the pure ligand.

Acknowledgement

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