Cucurbituril as a ligand for the complexation of cations in aqueous solutions

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Abstract

The complex formation of the ligand cucurbituril with alkaline cations and other cations have been studied by means of solubility measurements in the presence of the salts in aqueous solutions at 25 °C. Due to the stronger interactions of carbonyl donor atoms with cations compared with ether oxygen donor atoms, cucurbituril forms stronger complexes compared to the crown ether 18-crown-6.

Introduction

It is well known that crown ethers, cryptands and naturally occurring ionophores are able to form complexes with alkali, alkaline earth and other cations [1, 2]. The number of already synthesized macrocyclic and macrobicyclic ligands is very high [3].

Some years ago the structure of a condensation product of urea, glyoxal and formaldehyde was examined [4]. The synthesis of this compound has been known since 1905 [5]. The interactions of this molecule with cations were indirectly described. The authors mentioned that the synthesized molecule can be recrystallized from acidic solution simply by dilution with water. This procedure failed in the presence of salts.

The molecule is rather rigid with an internal cavity of approximately 5.5 Å diameter. This cavity is accessible by two portals with 4 Å diameter [6]. Due to the cumbersome correct name of this substance, Freeman *et al.* suggested the trivial name cucurbituril. The encapsulation of alkylammonium and alkyldiammonium ions was studied by NMR and UV spectroscopy [7, 8]. The influence of salts and different diamines on the dissociation kinetics of the complex with 4-methylbenzylamine hs been reported [9]. The reactions with dyes have also been studied [10–13]. In most cases they form insoluble complexes with this ligand.

All known results indicate that this ligand interacts with cations. Few crown ethers are known which incorporate urea or carbonyl groups [3, 14, 15]. No data for the complexation of cations have been published. Naturally occurring ionophores also contain carbonyl groups and other donor atoms as binding sites for ions [16]. Some stability constants are available for these ligands [2]. Up to now, no results for the reaction of cucurbituril with alkali and alkaline earth cations have been published. The cations may interact with the carbonyl atoms at the portals. Thus in contrast to the cryptands, the ions are not encapsulated into the cavity due to their hydrophobic nature but they are located at the portals. Due to the strong interactions of the carbonyl oxygen donor atoms with cations stable complexes will be formed. The present work was done to get some quantitative data for the complex formation of cucurbituril with alkali and alkaline earth cations in aqueous solution.

Experimental

The macrocyclic cavitand cucurbituril, see Fig. 1, was synthesized according to procedures given in the literature [5, 17]. After recrystallization several times from acidic solution the pure ligand is obtained.

The molecular weight of cucurbituril (996.84) was experimentally determined to be 997.51 using fast-atom bombardment mass spectral analysis. This is in accordance with the protonated ligand. No evidence for the formation of smaller or larger rings was found [18]. The elemental analysis of the ligand gives the following results: C, 36.3; H, 4.45; N, 28.1. The results indicate that the ligand contains 10 water molecules. The estimated values are in agreement with those already reported: C, 40.92; H, 4.17; N, 30.17, [6]; C, 36.66; H, 4.53; N, 30.08 [6]; C, 35.16; H, 4.51; N, 27.45 [17]. The differences in all elemental analyses are explained by changes in the number of water molecules in the crystals [17].

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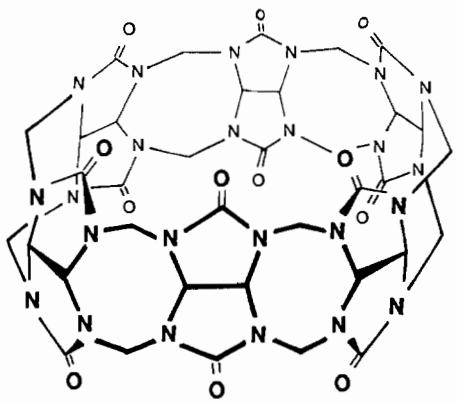

Fig. 1. Chemical structure of cucurbituril.

A 200 MHz ^{1}H NMR spectrum in D_2O/DCl contains only three signals of equal intensity: δ 5.75, δ 5.70 and δ 4.46 (d, $|J|_{gem} = 15.4$ Hz). Three signals are also observed when measuring the ^{13}C NMR resonances at 50 MHz with sodium trimethylsilylpropanesulfonate as internal standard: δ 53.70, δ 72.36 and δ 158.52. From a DEPT edited ^{13}C NMR spectra the signals at δ 158.52 can be attributed to the carbonyl groups, at δ 72.36 to the CH_2 group and at δ 53.70 to the CH group. Both in the proton and ^{13}C NMR spectra other resonances indicating impurities of the ligand cucurbituril could not be observed.

All salts used were chlorides and of the highest purity available. Double distilled water was used as solvent.

All attempts to estimate directly the concentration of cucurbituril in saturated aqueous solutions failed due to the low solubility of the ligand. Cucurbituril shows a strong absorption band in the UV region between 190 and 220 nm. Thus it was possible to measure the absorbance E_0 of saturated aqueous solutions of cucurbituril at 25 °C. The values of E_0 were obtained from at least five independent measurements.

The addition of salts (1×10^{-5} to 5×10^{-4} M) to solutions with solid cucurbituril results in an increase of the absorbance between 190 and 220 nm. To ensure that the dissolution of cucurbituril had reached the solution equilibrium all solutions were thermostated for several weeks at 25 °C. Spectra were recorded every week. If no spectral changes were observed within two weeks the equilibrium obviously had been reached. The complex of cucurbituril with Ba^{2+} is not soluble in water. No increase of the absorbance was found in the presence of barium ions. The addition of different barium salts to solutions of cucurbituril with alkali ions resulted in the precipitation of a white solid.

Results and discussion

In Fig. 2 the increase in the absorbance of aqueous solutions containing cucurbituril for different potassium chloride concentrations is shown. Due to the complex formation with cations the concentration of cucurbituril in solution increases.

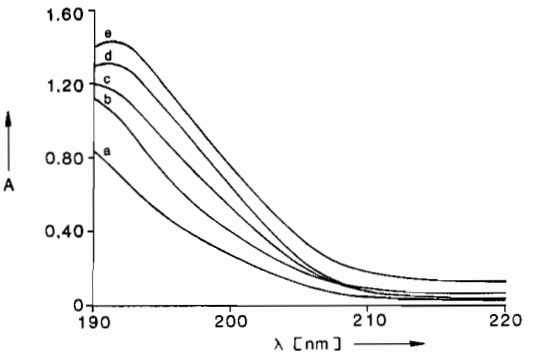

Fig. 2. Adsorption spectra of solutions containing potassium chloride at different concentrations: a, 2×10^{-5} M; b, 1×10^{-4} M; c, 2.5×10^{-4} M; d, 3.5×10^{-4} M; e, 4×10^{-4} M; saturated with cucurbituril at 25 °C.

Cucurbituril possesses two portals with carbonyl groups which are able to complex cations. The formation constant for a 1:2 complex (ratio of ligand to complexed cations) is given by

$$\beta = \frac{[M_2L^{2n+}]}{[M^{n+}]^2[L]} \quad (1)$$

The concentration of 1:1 complexes in solution is expected to be very low due to the fact that in the solution the salt concentration is always much higher than the ligand concentration. On the other hand the solubility of 1:1 complexes with cations is lower compared with the solubility of the 2:1 complexes because only the complexation of the ligand is responsible for the increase in solubility.

If no other species absorb at a given wavelength the experimentally measured absorbance E can be expressed by a linear superposition:

$$E = \epsilon_1[L] + \epsilon_2[M_2L] \quad (2)$$

Since the ligand is quite insoluble the concentration of the uncomplexed ligand in solution is equal the concentration of a saturated ligand solution [L_{sat}]:

$$[L] = [L_{sat}]$$

Therefore, the first term of eqn. (2) is constant and the observed variation is only caused by the increase of the concentration of the formed complex.

Taking into account all species present in solution and using eqn. (1) it is possible to get an expression for [M_2L]:

$$[M_2L] = (1 + 4\beta[L_{sat}][c_M] + (1 + 8\beta[L_{sat}][c_M])^{1/2})/(8\beta[L_{sat}]) \quad (3)$$

with $[c_M]$ as total concentration of the metal cation in solution. The combination of eqns. (2) and (3) gives:

$$E - E_0 = \epsilon_2 c_M/2 + \epsilon_2/(8\beta[L_{sat}]) \times (1 + (1 + 8\beta[L_{sat}]c_M)^{1/2}) \quad (4)$$

Substituting $[L_{sat}]$ by E_0/ϵ_1 we obtain

$$E - E_0 = t(1 + s[c_M]/2 + (1 + s[c_M])^{1/2}) \quad (5)$$

where s and t are given by

$s = 8\beta E_0/\epsilon_1$ and

$t = \epsilon_1\epsilon_2/(8\beta E_0) = \epsilon_2/s$

The parameters s and t are constants for a given system and can be fitted to the experimental data. In Fig. 3 the experimentally measured absorbances are shown as a function of the concentration of the salts RbCl and NH_4Cl together with the calculated curves. For all other cations examined the curves look identical with the exception of CsCl, see Fig. 4. From these data the stability constants β of the complexes formed can be obtained using eqn. (6):

$$\beta = \epsilon_1 t s^2/(8E_0\epsilon_2) \quad (6)$$

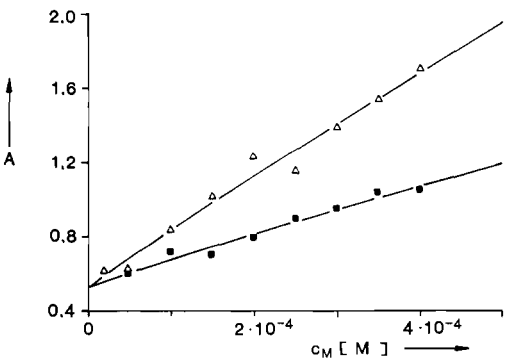

Fig. 3. Change of the absorbance of a saturated solution with cucurbituril for a given wavelength as a function of the concentration c_M of RbCl (△) and NH_4Cl (■) at 25 °C.

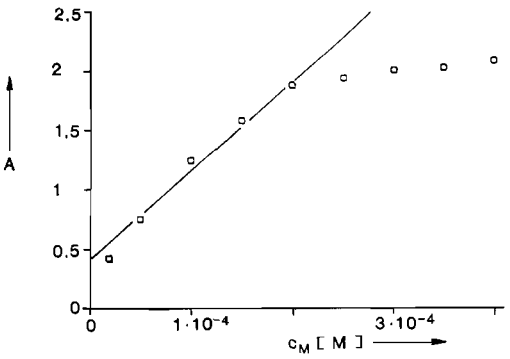

Fig. 4. Change of the absorbance of a saturated solution with cucurbituril for a given wavelength as a function of the concentration c_M of CsCl at 25 °C.

All attempts failed to determine the solubility of cucurbituril in aqueous solutions. However, it is still possible to calculate stability constants under the assumption that ϵ_1 and ϵ_2 are nearly equal. The values of s and t together with the calculated stability constants are given in Table 1.

Using eqn. (6) the influence of the ratio ϵ_1 to ϵ_2 can be estimated. In the case that they differ by a factor of 2 the stability constant for example of the sodium complex would be $\log \beta = 7.38 \pm 0.30$. This error is double of that found for the 1:1 complexation of dibenzo-18-crown-6 with K^+ from solubility measurements [19]. Thus the calculated values of the stability constants are reliable even without knowing the exact absorption coefficients.

In Figure 4 the absorbance of saturated solutions with cucurbituril is shown as a function of the concentration of CsCl. At higher concentrations of Cs^+ ions the experimental data cannot be fitted by the model suggested. However, the data taken at lower salt concentrations can be interpreted in terms of the formation of 1:2 complexes. The deviation at higher salt concentrations may be due to the formation of complexes with other stoichiometry. This is already known for the solid complex with Ca^{2+} [4].

The overall stability constant β for the formation of 1:2 complexes is the product of the stability constants K_1 and K_2 for each separate complex formation:

$$\log \beta = \log K_1 + \log K_2$$

Since both ligand sites of cucurbituril which form complexes with cations are separated by the rigid and

TABLE 1. Experimentally measured absorbances E_0 of saturated solutions of cucurbituril (the wavelength (nm) is given in parentheses), the fitted parameters s and t and the calculated stability constants ($\log \beta$, β in $dm^6\ mol^{-2}$) in aqueous solutions at 25 °C

Cation	E_0	s	t	$\log \beta$
Na^+	0.4961 (192)	37507	0.06761	7.38 ± 0.23
K^+	0.4961 (192)	105679	0.029	7.91 ± 0.25
Rb^+	0.4982 (194)	511388	0.0101	8.82 ± 0.24
Cs^+	0.3937 (200)	1147250	0.0106	9.64 ± 0.25
Ca^{2+}	0.4842 (196)	718516	0.0102	9.13 ± 0.26
NH_4^+	0.4961 (192)	157505	0.0142	7.94 ± 0.22
H^+	0.4961 (192)	7167	0.08467	6.04 ± 0.17

TABLE 2. Stability constants (log K, K in M^{-1}) for the complexation of cations by different ligands in aqueous solution at 25 °C

Cation	r [Å]	Cucurbituril (r=2.0 [Å])[d]	18-Crown-6 (r=1.4 [Å])[e]	Cryptand (222) (r=1.4 [Å])[f]
Na^+	1.02[a]	3.69	0.8[g]	3.98[l]
K^+	1.38[a]	3.96	2.03[g]	5.47[l]
Rb^+	1.49[a]	4.41	1.56[g]	4.24[l]
Cs^+	1.70[a]	4.82	0.99[g]	1.47[l]
Ca^{2+}	1.00[a]	4.57	0.48[h]	4.5[l]
NH_4^+	1.70[b]	3.97	1.23[g]	
H^+	1.38[c]	3.02	1.28[i] 0.40[k]	9.71[m]

[a]From ref. 22. [b]From ref. 23. [c]From ref. 24. [d]From ref. 6. [e]From ref. 25. [f]From ref. 26. [g]From ref. 27. [h]From ref. 28. [i]From ref. 29. [k]From ref. 30. [l]From ref. 31. [m]From ref. 32.

hydrophobic cavity the first cation complexed should not influence the binding of the second one. Therefore K_1 and K_2 can be assumed to be equal. The values of the stability constants for the 1:1 complex formation together with values for other ligands are summarized in Table 2.

Because all donor atoms interacting with one complexed cation are located in a plane, cucurbituril behaves like a macrocyclic ligand. Compared with the crown ether 18-crown-6 the stability constants of the cucurbituril complexes are several orders of magnitude higher. Both ligands have the same number of donor atoms and the dimensions of the cavity of 18-crown-6 should favour the complexation of the examined cations, because ionic radii and cavity radius are quite similar. The crown ether is even more flexible and can achieve optimum interactions with the complexed cation by structural changes. This is impossible for the rigid ligand cucurbituril. However, the crown ether has to change its conformation during the complex formation [20]. No conformational changes of the ligand cucurbituril during the complex formation are possible. Due to the rigid structure of this ligand all donor atoms are preorganized and located inside the cavity. A second advantage of this ligand is the higher electric charge of its donor atoms compared with crown ethers. The dipole moment of dipropylether in Debye units is 1.32 and of acetone it is 2.69 [21]. As a result stronger interactions between carbonyl groups and positively charged ions take place between ether oxygen atoms and the same ions.

The bicyclic structure of the cryptands is able to compensate the weaker interactions. On the other hand the size of the cavity becomes important for the strength of the complexes formed. In the case of the potassium ion the cavity and ionic dimensions are nearly identical. Thus, this ion forms the most stable complex of the alkaline cations with the cryptand (222). For all other cations the complexes of cucurbituril are of the same order of magnitude or even stronger than that of the bicyclic ligand (222). Only in the case of the complexation of protons does the cryptand form a much more stable complex because this ligand contains nitrogen donor atoms for the interactions with protons.

Cucurbituril as a monocyclic ligand forms the most stable complexes with cations in comparison with other monocyclic ligands. The stability constants with other ions will be reported in a forthcoming article.

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