Synthesis and Complexive Abilities in Cone Conformation of Lower Rim Functionalized Calix[4]Arene with Alkali Metal Cations

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Abstract

The synthesis and complexive abilities of 5,11,17,23-tetra-*tert*-butyl-28,26-di(bromopropoxy)-25,27-dihydroxyca-lix[4]arene (**L1**) and 5,11,17,23-tetra-*tert*-butyl-25,27-dibenzoxy-26,28-di(phenoxy)propoxycalix[4]arene (**L2**) towards alkali metal cations Li$^+$, Na$^+$, K$^+$, Rb$^+$ and Cs$^+$ in methanol-chloroform mixture have been evaluated at 25 C, using UV-Vis spectrophotometric techniques. The results showed that the ligands are capable to complex with all the alkali cations by 1:1 metal to ligand ratios. Considering the formation constant values, the binding selectivities of the ligands towards alkali cations of the formed complexes are in the order Rb$^+$ ≈ K$^+$ > Cs$^+$ > Na$^+$ > Li$^+$ and Li$^+$ > Na$^+$ > K$^+$ ≈ Rb$^+$ ≈ Cs$^+$ for the ligands **L1** and **L2**, respectively.

Keywords: calix[4]arene, alkali cations, synthesis, complexation, formation constant

1. Introduction

Calix[*n*]arenes are cyclic oligomers obtained from condensation of formaldehyde with *para*-alkylphenols under alkaline conditions.[1] These compounds are built of *n* phenol units linked via alkylidene groups in such a way that large cavities of molecular dimensions are formed. Their bowl-like structure allows them to form complexes with a variety of species. The most accessible are the tetramers, the hexamers and the octamers, although all members of the series from *n* = 4 to 14 are known.[2] One essential characteristic of calixarenes is their great confor-

mational mobility, which increases with the degree of condensation. For example, tetramers can adopt four different conformations: the cone, partial cone, 1,2-alternate and finally 1,3-alternate conformations which differ by the respective orientation of the aromatic rings (Figure 1). Calix[*n*]arenes have been shown to complex alkali[3–7] and lanthanide cations.[8–10] However, the low solubility of these compounds in most organic solvents has severely limited the study of their complexing abilities.

Controlling the size of the molecule (by changing the value of *n*) and the introduction of various functional groups makes the calix[*n*]arenes useful for a variety of
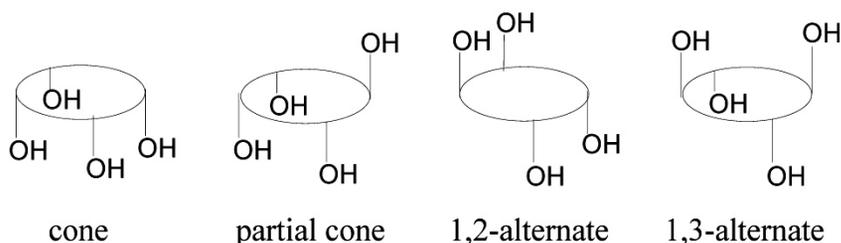

Figure 1: Chemical structure of calix[*n*]arenes and the four possible conformations of the tetrameric oligomer

applications, such as catalysts, ligands as molecular hosts, slow releasers of drugs, transporters across membranes, ion channels, for purification, chromatography etc.[12–16] Chiral calix[*n*]arenes have also been prepared.[17] Several calix[*n*]arene-metal ion complexes have been reported, most of them require that the hydroxyl groups of the calixarene are derivatized to esters or ethers due to the poor solubility of the *para-tert*-butylcalix[*n*]arenes.[18] The Cs+-*para-tert*-butylcalix[8]arene complex is used for the recovery of cesium from nuclear waste solutions[19] and as a lanthanide complexing agent under basic conditions.[20] Hexacid calixarene, also known as superuranophile, is a metal complex of derivatized calixarene used for the recovery of uranium.[21]

In our former research, various types of calix[4]arene molecules have been synthesized and tested as potential ligands for studies of complexation with alkali and alkali earth cations.[3–7] In the present work the synthesis of two new calix[4]arene derivatives 5,11,17,23-tetra-*tert*-butyl-28,26-di(bromopropoxy)-25,27-dihydroxycalix[4]arene (**L1**) and 5,11,17,23-tetra-*tert*-butyl-25,27-dibenzoxy-26,28-di(phenoxy)propoxycalix[4]arene (**L2**) recently prepared by our group and their complexation abilities towards alkali metal cations in a mixed solvent of methanol-chloroform is reported (Figure 2).
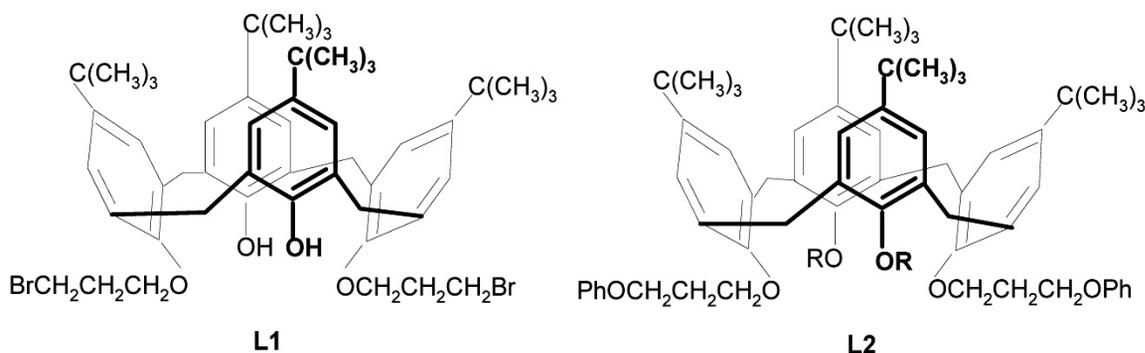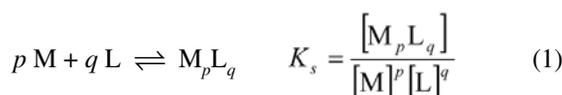
A, was measured by successive addition of an alkali metal ion solution to each ligand solution (see Experimental section). The absorption bands of the ligand decrease upon addition of the metal ion solution in all cases. Figure 3 shows typical spectrophotometric titration run of the ligands upon addition of an alkali cation solution. Treatment of the spectrophotometric data (260–300 nm with an interval of 1 nm) obtained during the titrations was conducted with the computer program Squad.[22]

The stoichiometric formation constants were computed from the data using the computer program. The number of experimental points were more than 30 (maximum 40) for each titration. In the computer program, if we designate *m* absorption spectra that will be measured at *n* wavelengths, the individual absorbance readings thus can be arranged in an $m \times n$ matrix **R**; the *m* spectra form the rows of **R** and the columns consist of the *n* response curves gathered at the different wavelengths. According to Beer's law, for a system with *N* absorbing components, **R** can be decomposed into the product of a concentration matrix **C** ($m \times N$) and a matrix of the molar absorptivities **S** ($N \times n$). However, because of the inherent noise in the measured data, the decomposition does not represent **R** exactly. The matrix **T** of the residuals is given by the difference between **CS** and **R**

Figure 2. The structure of **L1** and **L2**, where R is PhCH₂-

$$\mathbf{T} = \mathbf{CS} - \mathbf{R} \tag{2}$$

2. Results and Discussion

Assuming that the absorbance of each ligand would change upon complexation with an alkali cation, we performed spectrophotometric measurements. The complex M_pL_q formed is characterized by its stoichiometry, *p* and *q*, where M and L represent a metal ion and a ligand, respectively. To determine the formation constant of complexation, K_S, Eq. 1 is defined,

$$p\,\mathrm{M} + q\,\mathrm{L} \rightleftharpoons \mathrm{M}_p\mathrm{L}_q \qquad K_s = \frac{\left[\mathrm{M}_p\mathrm{L}_q\right]}{[\mathrm{M}]^p[\mathrm{L}]^q} \tag{1}$$

Determination of the formation constant was employed using the method mentioned before.[3–7] Absorbance,

In the fitting procedure, those matrices **C** and **S** are determined which best represent the original matrix **R**. The task of the fitting procedure is to optimize the matrix **T** of the residuals, Eq. 2, according to the least-squares criterion. In Eq. 3, *U* is the sum of the squares of all elements of **T**. It is the task of the nonlinear least-squares fitting to find the set of parameters that result in a minimum of *U*.

$$U = \sum_{i=1}^{m} \sum_{j=1}^{n} \mathbf{T}(i,j)^2 = \text{minimize} \tag{3}$$

All proposed species existing in significant concentration were checked over a reasonable range of data. As expected, polynuclear complexes were systematically re-
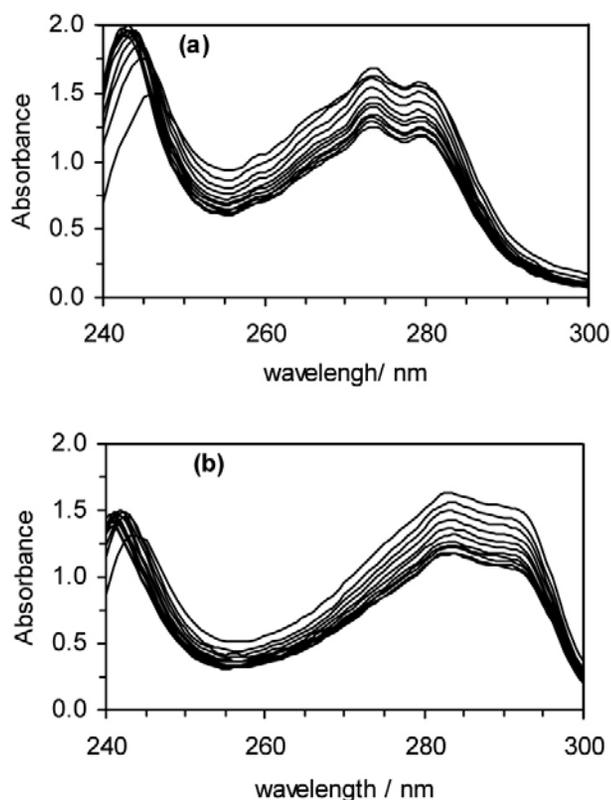
Figure 3. The variation of UV absorption spectrum of **L1** (a), and **L2** (b), upon successive addition of Rb+

jected by the computer program. Taking into account a binuclear complex alone or together with the mononuclear one does not improve the quality of the fit and even leads to the rejection of the model. The model finally chosen, formed by ML, resulted in a satisfactory numerical and graphical fitting for all systems. The average formation constant values of the 1:1 complex for species **L1** and **L2** with alkali cations at various wavelengths are listed in Table 1.

Table 1. Average values of $\log K_S$ at different wavelengths for the alkali cations and the ligands at 25 °C

metal ion	$\log K_S$ (L1)	$\log K_S$ (L2)
Li+	3.81 ± 0.01	4.82 ± 0.02
Na+	3.89 ± 0.02	4.23 ± 0.04
K+	4.58 ± 0.05	3.83 ± 0.05
Rb+	4.59 ± 0.03	3.82 ± 0.04
Cs+	4.06 ± 0.01	3.82 ± 0.03

The interesting curves resulting from the spectrophotometric titration of **L1** and **L2** with alkali cations are shown in Figure 4. The curves show a sharp break point when the ratio of the concentration of metal ion to the ligand reaches unity, indicating the formation of stable

complexes for K+, Rb+ and Cs+ with **L1** (Figure 4a) and Li+ and Na+ with **L2** (Figure 4b). However, the same titration for Na+ and Li+ with **L1**, as well as K+, Rb+ and Cs+ with **L2** shows the absorbance increases within a small and more continuous variation with concentration ratios in complexation curves (Figure 4), indicating low stability constant of formation. In these cases the extrapolating of the slopes at high and low metal to ligand ratios correspond to 1:1 complex stoichiometry in the point of intersections. This behavior is typical for complexes less stable than those found for the former species.
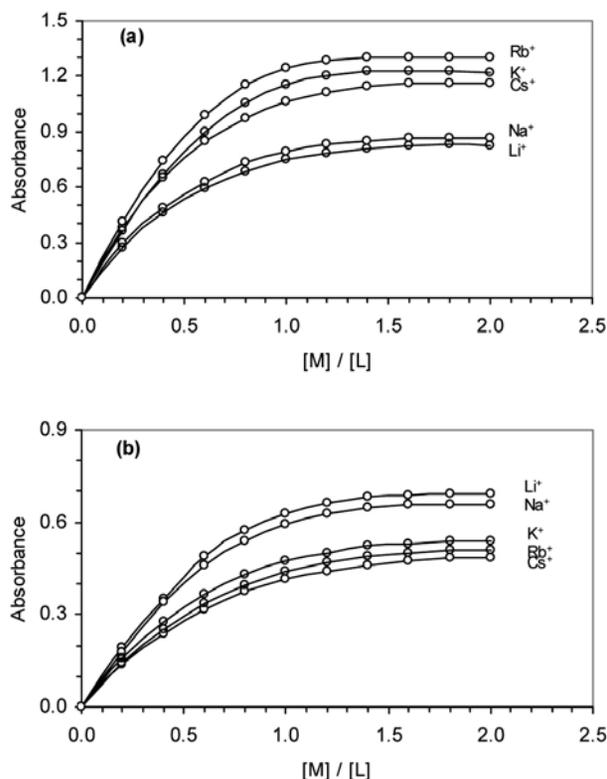

Figure 4. Spectrophotometric titration plots of the ligands **L1** (a), and **L2** (b), by the metal ions, Li+, Na+, K+, Rb+, and Cs+ at 25 °C and 280 nm, respectively

The two calix[4]arenes, **L1** and **L2**, form complexes with alkali metal ions, but show different affinities for the small and the large cations. Figure 5 shows the formation constant values of the species formed by the ligands and the alkali cations versus the ionic radius of the cations. **L1** appears to be more efficient for chelating with K+ and Rb+. The binding selectivity of **L1** towards alkali cations, based on the formation constant values of the formed species, is in the order of Rb+ ≈ K+ > Cs+ > Na+ > Li+. However, the substitution with four aryl groups at the lower rim of **L1** leads to an increase in the formation constant values of the complexes formed by the smaller cations, Li+ and Na+ in the case of **L2**. This could be described by the

introduction of the aryl groups that possibly makes **L2** to possess a smaller cavity which can better fit the small cations. Further, the electron donating tendency of the substituents located at the lower rim of **L2** is possibly more effective especially towards small cations. The results suggest that K^+, Rb^+ and Cs^+ are possibly located near the cavity of **L2** and hence are more shielded than the other ions which better fit the cavity size of the ligand. The fact that a more continuous variation of the absorbance with the concentration ratios of K^+, Rb^+ and Cs^+ were obtained in Figure 4b, should be due to the low complexation ability of these cations. The selectivity of binding tendency of alkali cations towards **L2** is in the order of $Li^+ > Na^+ > K^+ \approx Rb^+ \approx Cs^+$.
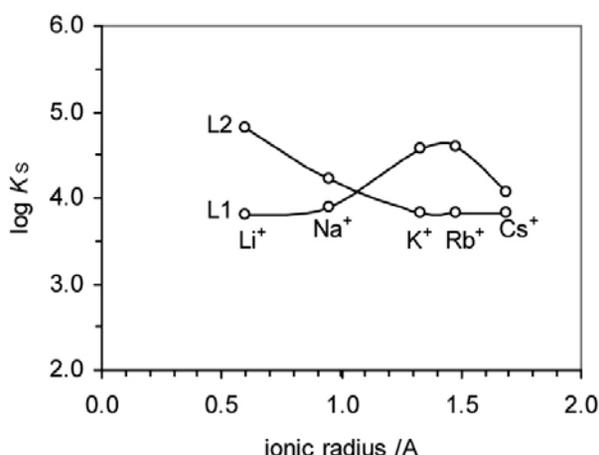

Figure 5. The plots of logK_S versus the ionic radii of the alkali cations at 25 °C

3. Experimental

Chemicals: Parent calix[4]arene was obtained from Aldrich and used without further purification. The ligands were synthesized following the procedure described below. The solvents, methanol and chloroform (Merck, p.a.), were used without further purification. LiCl (Merck, p.a.), NaCl (Merck, p.a.), KCl (Merck, p.a.), RbCl (Fluka, Purum), and CsCl (Merck, p.a.) as the alkali cations sources were dried under vacuum at room temperature for at least 72 h before use.

3. 1. Synthesis of L1 and L2

Synthesis of 5,11,17,23-tetra-*tert*-butyl-26,28-di(bromopropoxy)-25,27-dihydroxycalix[4]arene (**L1**): The ligand **L1** was synthesized by mixing 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene (1.7 g, 2.08 mmol) and a solution of 1,3-dibromopropane in acetonitrile (2.7 mL) with acetonitrile (45 mL). The solu-

tion was refluxed for 5 h in the presence of potassium carbonate (3.1 g, 22.3 mmol). The reaction mixture was then treated with a hydrochloric acid solution (5%) and extracted with dichloromethane. The organic layer was then separated, dried over magnesium sulfate, filtered, and evaporated to yield a white solid, which was crystallized from methanol, to give 61% of **L1**. Mp 169–173 °C, ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.77 (2H, s, OH), 7.07 (4H, s, ArH), 6.89 (4H, s, ArH), 4.28 (4H, d, J = 12.9 Hz, ArCH$_2$Ar), 4.14 (4H, t, CH$_2$), 4.07 (4H, t, CH$_2$), 3.37 (4H, d, J = 12.9 Hz, CH$_2$), 2.57 (4H, m, CH$_2$), 1.15 (18H, s, CH$_3$), 0.81 (18H, s, CH$_3$), ^{13}C NMR (CDCl$_3$, 125 MHz) δ 10.7, 12.4, 32.8, 34.0, 38.1, 57.5, 58.0, 73.8, 126.3, 127.1, 127.6, 132.8, 141.0, 146.2, 148.7, 150.9. IR (KBr, cm^{-1}) 3317, 2953, 1485, 1364, 1206.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-dibenzoxy-26,28-di(phenoxy)propoxycalix[4]arene (**L2**): The ligand **L2** was synthesized by dissolving phenol (0.35 g, 3.7 mmol) and sodium hydride (0.17 g, 7.08 mmol) in DMF (20 mL). The mixture was kept at 55 °C for 1.5 h while stirring vigorously. To above mixture was added 5,11,17,23-tetra-*tert*-butyl-26,28-dibenzoxy-25,27-di(3-bromopropoxy)calix[4]arene (0.2 g, 0.18 mmol) and it was then kept at 55 °C for 24 h while stirring vigorously. The reaction mixture was diluted with water (250 mL) and extracted with dichloromethane. The organic layer was then separated, dried over magnesium sulfate, filtered, and evaporated to give a viscose liquid, which crystallized from dichloromethane-methanol to give a 50% of **L2** (white solid). Mp 204.5–208.5 °C, ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.54 (4H, m, ArH), 7.34 (6H, m, ArH), 7.23 (4H, m, ArH), 7.18 (4H, s, ArH),7.01 (2H, t, ArH), 6.86 (4H, m, ArH), 6.56 (4H, s, ArH), 4.72 (4H, s, OCH$_2$Ph), 4.03 (4H, t, CH$_2$), 3.19, 4.49 (8H, 2d, J = 15 Hz, ArCH$_2$Ar), 3.56 (4H, t, CH$_2$), 2.25 (4H, m, CH$_2$), 1.40 (18H, s, C(CH$_3$)$_3$), 0.91 (18H, s, C(CH$_3$)$_3$), ^{13}C NMR (CDCl$_3$, 125 MHz) δ 30.2, 31.5, 32.1, 34.0, 34.5, 53.4, 65.6, 72.7, 78.6, 114.8, 120.7, 125.0, 125.8, 128.4, 128.7, 128.8, 130.3, 132.5, 135.9, 138.0, 144.8, 145.3, 152.5, 155.0, 159.7. IR (KBr, cm^{-1}) 2964, 1480, 1247, 1197, 752.

Measurements: Absorption spectra, 260–300 nm, were measured on Shimadzu 2100 UV-Vis scanning spectrophotometer with a Pentium IV computer using 10 mm quartz cells. The system was thermostated at 25 °C by circulating water from an isothermal bath. In all cases, the procedure was repeated at least three times and the resulting average values and corresponding standard deviations are shown in the text and Table 1.

Procedure: 2.0 mL solution of the ligands, 2.5–3.0 × 10^{-4} mol L^{-1}, were titrated with stepwise addition of an alkali cation solution (1.0 × 10^{-3} mol L^{-1}), all in the same solvent (methanol-chloroform 40 : 60 by volume). The UV-Vis spectra of the mixtures undergo small changes at 260–300 nm, but the measured absorbances were sufficient to allow the treatment of the data by the computer program.

4. References

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Povzetek

Predstavljamo sintezo in spospobnost kompleksiranja 5,11,17,23-tetra-*terc*-butil-28,26-di(bromopropoksi)-25,27-dihidroksikaliks[4]arena (**L1**) in 5,11,17,23-tetra-*tert*-butil-25,27-dibenzoksi-26,28-di(fenoksi)propoksikaliks[4]arena (**L2**) s kationi alkalijskih kovin (Li⁺, Na⁺, K⁺, Rb⁺ in Cs⁺) v zmeseh metanola in kloroforma pri 25 °C, ki smo jo raziskali z uporabo UV-Vis spektrofotometričnih tehnik. Rezultati kažejo, da sta se liganda sposobna kompleksirati z alkalijskimi kationi v razmerju kovina proti ligandu 1:1. Glede na konstante tvorbe, je selektivnost alkalijskih kationov proti ligandoma v naslednjem vrstnem redu: Rb⁺ ≈ K⁺ > Cs⁺ > Na⁺ > Li⁺ za **L1** in Li⁺ > Na⁺ > K⁺ ≈ Rb⁺ ≈ Cs⁺ za **L2**.