



## Cation Binding Properties by Ligands Deriving from *p*-*tert*-butylcalix[4]arene O-substituted by Diethyl Malonate Functions

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### Abstract

The complexing properties of four dimalonate and one diester calix[4]arene derivatives toward alkali and alkaline earth cations have been investigated in acetonitrile by means of UV spectrophotometry. Mononuclear complexes have been detected for all the complexes except in the case of ligands **4** and **5** with Na<sup>+</sup> and Ca<sup>2+</sup> where a biligand species (ML<sub>2</sub>) is present. This later stoichiometry was also confirmed by <sup>1</sup>H-NMR and FAB<sup>+</sup> MS methods. In the case of ligand **3** and Sr<sup>2+</sup> we observed the formation of both mono and binuclear species (ML, M<sub>2</sub>L). Particular selectivities have to be noted from the unique complexation of Na<sup>+</sup> and Ba<sup>2+</sup> by ligand **2** and Rb<sup>+</sup> by ligand **3** toward the two series of cations. The complexation is predominantly dependent on the bulkiness of the cavity and the cation size.

### Introduction

The importance of the class of calixarenes in the family of host macrocycles is now well established [1–3]. This could be explained by the fact that they are considered to be attractive host molecules on which additional binding sites for target guest species are added, thanks to their unique upper and lower rim topologies [2]. In this context much work has been devoted to the synthesis of calixarenes chemically modified on the upper [2–4] and lower rims [1–10]. Several functions have been introduced in the lower rim such as ethers [5], amides [6], thioamides [7], ketones [8], carboxylic acids [9] and esters [8, 10]. Some of these derivatives have a high potential of encapsulation for metal cations and some selectivities have been reported, for example, *p*-*tert*-butylcalix[4]arene O-substituted by ethyl ester functions show a high affinity for sodium and potassium in methanol [11]. The crystal structure of the mononuclear complex of potassium with the tetraethylamide *p*-*tert*-butylcalix[4]arene indicates that K<sup>+</sup> is coordinated by 8 oxygen atoms (4 phenolic oxygen atoms and 4 carbonyl oxygen atoms) [12]. Up to now only four carbonyl groups have been introduced simultaneously on a calix[4]arene [11].

In order to observe the influence of the disposition and the number of carbonyl sites on the strength of metal cation complexes, we carried out the study of complexation properties toward alkali and alkaline-earth cations of a series of calix[4]arenes bearing ethyl ester and diethyl malonate functions. We present thermodynamical studies of the complexation of alkali and alkaline-earth metal cations by ligands **1–5**. 1,3-Diethyl ester **1** (this work) and the tetraester calix[4]arene **6** [13] will be considered as references in order

to evaluate the binding ability of the malonate derivatives **2–5**. We have been able to show the role of the number of ethyl ester functions and the role of the substitution of the hydrogen on the malonate by a methyl group.

In a previous paper [10] we have already reported the synthesis of the 1,3-O-diethyl malonate (**2, 3**) and diethyl ester-diethyl malonate calix[4]arenes (**4, 5**). Preliminary <sup>1</sup>H-NMR experiments showed [10] a very low extractability of solid alkali picrates to deuteriated chloroform containing ligands **2** to **5**. Only Li<sup>+</sup> and Na<sup>+</sup> metal cations have been extracted by ligands **4** and **5** with a significant change in the <sup>1</sup>H-NMR spectrum indicating the formation of 1:1 species for Li<sup>+</sup>: **4**, Na<sup>+</sup>: **4** and Li<sup>+</sup>: **5** and a particular stoichiometry 1:2 for Na<sup>+</sup>: [**5**]<sub>2</sub> [10].

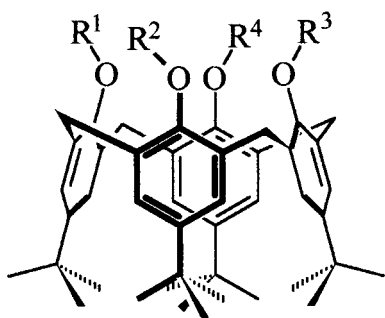
### Experimental

#### Materials

Acetonitrile (BAKER, Analytical grade) was used without any further purification. The supporting electrolyte used in the stability constant determinations was Et<sub>4</sub>NClO<sub>4</sub> (Acros). The metal salts were used as perchlorates (Fluka purum) except for cesium, the salt used was the CsNO<sub>3</sub> (Merck p.a.). Calixarene ligands **1–5** have been prepared as already published [10].

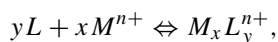
#### Stability constant measurements

The stability constants  $\beta_{xy}$  being the concentration ratio  $[M_x L_y^{n+}]/[M^{n+}]^x [L]^y$  and corresponding to the general equilibrium:



- |   |                          |                                 |
|---|--------------------------|---------------------------------|
| 1 | $R^1 = R^3 = H$          | $R^2 = R^4 = CH_2CO_2Et$        |
| 2 | $R^1 = R^3 = H$          | $R^2 = R^4 = CH(CO_2Et)_2$      |
| 3 | $R^1 = R^3 = H$          | $R^2 = R^4 = C(CH_3)(CO_2Et)_2$ |
| 4 | $R^1 = R^3 = CH_2CO_2Et$ | $R^2 = R^4 = CH(CO_2Et)_2$      |
| 5 | $R^1 = R^3 = CH_2CO_2Et$ | $R^2 = R^4 = C(CH_3)(CO_2Et)_2$ |
| 6 | $R^1 = R^3 = CH_2CO_2Et$ | $R^2 = R^4 = CH_2CO_2Et$        |

Figure 1. Studied compounds.



(where  $M^{n+}$  = metal cation,  $L$  = ligand) have been determined in acetonitrile by UV spectrophotometry at 25 °C and the ionic strength was maintained at 0.01 mol L<sup>-1</sup> by Et<sub>4</sub>NClO<sub>4</sub>, according to the procedure already described [14].

The spectra of solutions of different ligands, with concentrations ranging between 10<sup>-4</sup> to 2.0 × 10<sup>-4</sup> mol L<sup>-1</sup>, and increasing concentration of metal ion, were recorded between 250 nm and 320 nm, Figures 2 and 3 illustrate the complexation of Na<sup>+</sup> and Ca<sup>2+</sup> by ligand 4. Generally the metal to ligand ratio  $R$ , does not exceed 20 and the equilibrium was quasi-instantaneous for all the systems. Addition of the metal ion to the ligand undergoes, in general, enough changes in the spectra to allow for the analysis of the resultant data using the program “Letagrop” [15]. The log  $\beta_{xy}$  values, given in Tables 1 and 2, correspond to the arithmetic means of at least three independent experiments.

## Results and discussion

Data listed in Tables 1 and 2 correspond to stability constants (log  $\beta_{xy}$ ) of alkali and alkaline earth complexes limited to acetonitrile because of low solubility in methanol and ethanol.

### Alkali metal cations

Inspection of Table 1 shows that compared to the tetraethyl ester **6** [13] derivative, the calixarenes **1–5** have no affinity for Cs<sup>+</sup> indicating that the cavity delineated by four phenolic and four carbonyl oxygen atoms of the tetraethyl ester is suitable for cesium inclusion. The diethyl ester **1** forms mononuclear complexes with the smallest alkali cations Li<sup>+</sup>,

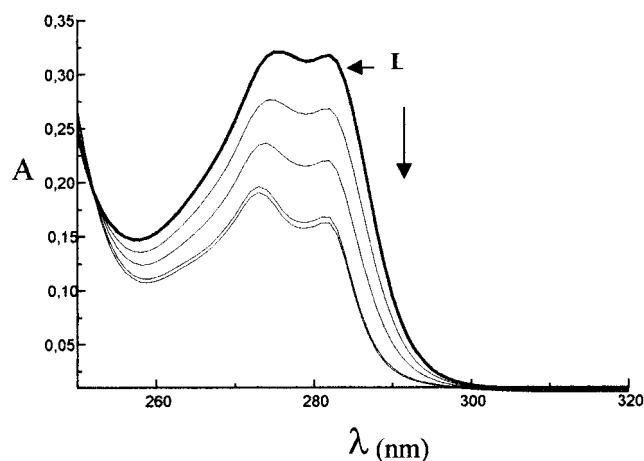


Figure 2. Changes in the UV/visible absorption spectrum of ligand 4 upon addition of Na(ClO<sub>4</sub>) in acetonitrile ( $C_L = 2.0 \times 10^{-4}$  M,  $0 \leq R_{M/L} \leq 1$ ; NEt<sub>4</sub>ClO<sub>4</sub> = 0.01 M).

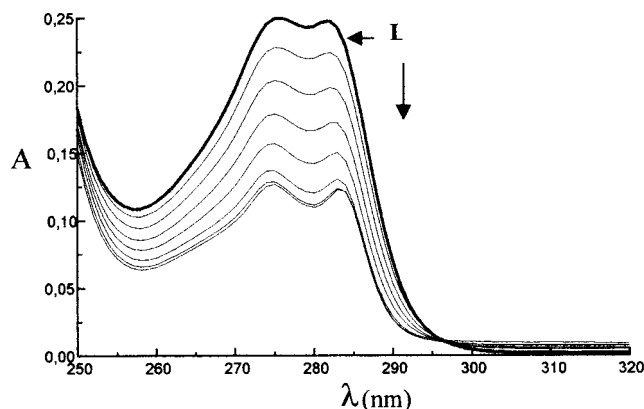


Figure 3. Changes in the UV/visible absorption spectrum of ligand 4 upon addition of Ca(ClO<sub>4</sub>)<sub>2</sub> in acetonitrile ( $C_L = 2.0 \times 10^{-4}$  M,  $0 \leq R_{M/L} \leq 1$ ; NEt<sub>4</sub>ClO<sub>4</sub> = 0.01 M).

Na<sup>+</sup> and K<sup>+</sup>, with a slight selectivity for Na<sup>+</sup> in contrast to the tetraethyl ester with its affinity for Li<sup>+</sup> in acetonitrile [13]. The complexing power of ligand **1** remains weak comparing to ligand **6** actually due to a lower number of carbonyl oxygen donor atoms.

In acetonitrile, compound **2** complexes only Na<sup>+</sup> while compound **3** complexes only Rb<sup>+</sup> with 1:1 stoichiometry and approximately with the same stability order (log  $\beta \sim 3.2$ ). No complexation was detected with the other cations since no significant spectral changes were observed during the titration. These complexation selectivities can be explained by a rigidity of the cavities due to the hydrogen bonds between the phenolic protons and carbonyl groups. However the complexation of Na<sup>+</sup> by **2** and Rb<sup>+</sup> by **3** can be related to the steric effect of the methyl group in ligand **3** inducing a spreading of the ethyl ester of the malonate functions making a larger cavity or rather a cavity surface than in ligand **2**.

In contrast to 1,3-substituted derivatives **2** and **3**, the tetrasubstituted ligands **4** and **5** complex Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup> and Rb<sup>+</sup>. Mononuclear complexes have been identified in all cases except Na<sup>+</sup>. With this latter cation unexpected biligand species were determined. The 1:2 (M:L) stoichiometry

Table 1. Stability constants ( $\log \beta_{ij}$ ) for alkali cation complexes in acetonitrile ( $T = 25^\circ\text{C}$ ,  $I = 10^{-2}\text{M}$ )

Compounds	M:L	Log $\beta$				
		Li <sup>+</sup>	Na <sup>+</sup>	K <sup>+</sup>	Rb <sup>+</sup>	Cs <sup>+</sup>
<b>1</b>	1:1	3.97 ± 0.05	4.12 ± 0.01	3.42 ± 0.01	a	a
<b>2</b>	1:1	a	3.18 ± 0.02	a	a	a
<b>3</b>	1:1	a	a	a	3.24 ± 0.05	a
<b>4</b>	1:1	4.64 ± 0.02		3.59 ± 0.03	3.38 ± 0.02	
	1:2		9.44 ± 0.08			a
<b>5</b>	1:1	4.30 ± 0.01		3.90 ± 0.03	3.47 ± 0.07	a
	1:2		8.99 ± 0.02			
<b>6<sup>b</sup></b>	1:1	6.4	5.8	4.5	1.9	2.8

<sup>a</sup>Small spectral variation.

<sup>b</sup>See reference 13.

Table 2. Stability constants ( $\log \beta_{ij}$ ) for alkaline earth cation complexes in acetonitrile ( $T = 25^\circ\text{C}$ ,  $I = 10^{-2}\text{M}$ )

Compounds	M:L	Log $\beta$			
		Mg <sup>2+</sup>	Ca <sup>2+</sup>	Sr <sup>2+</sup>	Ba <sup>2+</sup>
<b>1</b>	1:1	a	5.21 ± 0.02	3.30 ± 0.10	3.34 ± 0.06
<b>2</b>	1:1	a	a	a	3.31 ± 0.09
<b>3</b>	1:1	a	a	a	a
<b>4</b>	1:1	2.96 ± 0.02		4.96 ± 0.04	4.32 ± 0.02
	1:2		8.68 ± 0.05		
	2:1			8.90 ± 0.10	
<b>5</b>	1:1	3.31 ± 0.02		3.48 ± 0.03	5.13 ± 0.10
	1:2		8.50 ± 0.50		

<sup>a</sup>Small spectral variation.

is supported for **5** by NMR study [10] and for **4** by FAB<sup>+</sup> MS for which two signals were found at  $m/z$ : 2294,3 (1:2 species ( $\text{Na}^+:[\mathbf{4}]_2$ ), and at  $m/z$ : 1159,8 (1:1 species ( $\text{Na}^+:[\mathbf{4}]$ ), (Figure 4). In reality the stoichiometry 1:2 was already observed when  $\text{Na}^+$  is complexed by a diglycol-diethyl ester calix[4]arene in acetonitrile [16] or by a tetraethyl ester calix[4]arene (**6**) in a 1:1 mixture of  $\text{CDCl}_3 : \text{CD}_3\text{CN}$  [17]. For the first case the stoichiometry  $\text{ML}_2$  was identified by UV titration in acetonitrile and by NMR titration in a 1:1 mixture of  $\text{CDCl}_3 : \text{CD}_3\text{CN}$  [16]. For the second case the 1:2 complex was evidenced by <sup>23</sup>Na NMR and visualized as an outer-sphere association of the hydrophilic part of a second calixarene molecule with sodium encaged in the 1:1 complex. Probably the same feature could be assumed for the 1:2 species ( $\text{Na}^+:[\mathbf{4}]_2$ ) and ( $\text{Na}^+:[\mathbf{5}]_2$ ).

The stability of the 1:1 complexes decreases with the increase of the cation size suggesting a size match between the ligand cavity and the cation. The spreading of the cavity due to the methyl group as observed with ligands **2** and **3** can also be argued with **4** and **5**. In fact the presence of methyl in **5** disadvantages  $\text{Li}^+$  complexation and favors  $\text{K}^+$  and  $\text{Rb}^+$  (cations with higher ionic radius) complex formation. This effect is well reflected by stability constants where the lithium complex is more stable with **4** while potassium and rubidium complexes are more stable with **5**. A similar effect is highlighted by the biligand sodium complexes where the

stability with ligand **4** is higher than with **5** ( $\log \beta = 9.44$ ,  $\log \beta = 8.99$  respectively)

#### Alkaline-earth metal cations

The study of alkaline-earth complexation in acetonitrile shows that ligands **2** and **3** are inefficient towards the alkaline earth series except for ligand **2** with  $\text{Ba}^{2+}$  which forms a mononuclear complex with  $\log \beta = 3.31$  (Table 2). The diethyl ester **1** complexes  $\text{Ca}^{2+}$ ,  $\text{Sr}^{2+}$  and  $\text{Ba}^{2+}$  with a pronounced affinity for  $\text{Ca}^{2+}$  indicating that the cavity of the 1,3-diethyl ester compound **1** is appropriate for complexing  $\text{Ca}^{2+}$  ( $\log \beta = 5.21$ ) resulting in  $\text{Ca}^{2+}/\text{Sr}^{2+}$  and  $\text{Ca}^{2+}/\text{Ba}^{2+}$  selectivities of about 100.

Ligands **4** and **5** form mononuclear complexes with  $\text{Mg}^{2+}$ ,  $\text{Sr}^{2+}$  and  $\text{Ba}^{2+}$  with a preference for  $\text{Sr}^{2+}$  and  $\text{Ba}^{2+}$  versus  $\text{Mg}^{2+}$ . The complex of  $\text{Sr}^{2+}$  with **4** is 100 times more stable than the complex of  $\text{Mg}^{2+}$ . The same observation is made for ligand **5** for which the complex of  $\text{Ba}^{2+}$  is about 100 times more stable than the  $\text{Mg}^{2+}$  and  $\text{Sr}^{2+}$  complexes. As previously observed in the alkaline series, it appears that the selectivity depends strongly on the shape (surface of complexation) of the cavity: the diethyl ester **1** is selective for  $\text{Ca}^{2+}$ , followed by the diethyl ester dimalonate **4** (substituted with a hydrogen) which is selective for  $\text{Sr}^{2+}$  and then the diethyl ester dimalonate **5** (substituted with methyl) for which the selectivity is in favor of  $\text{Ba}^{2+}$  probably due to an

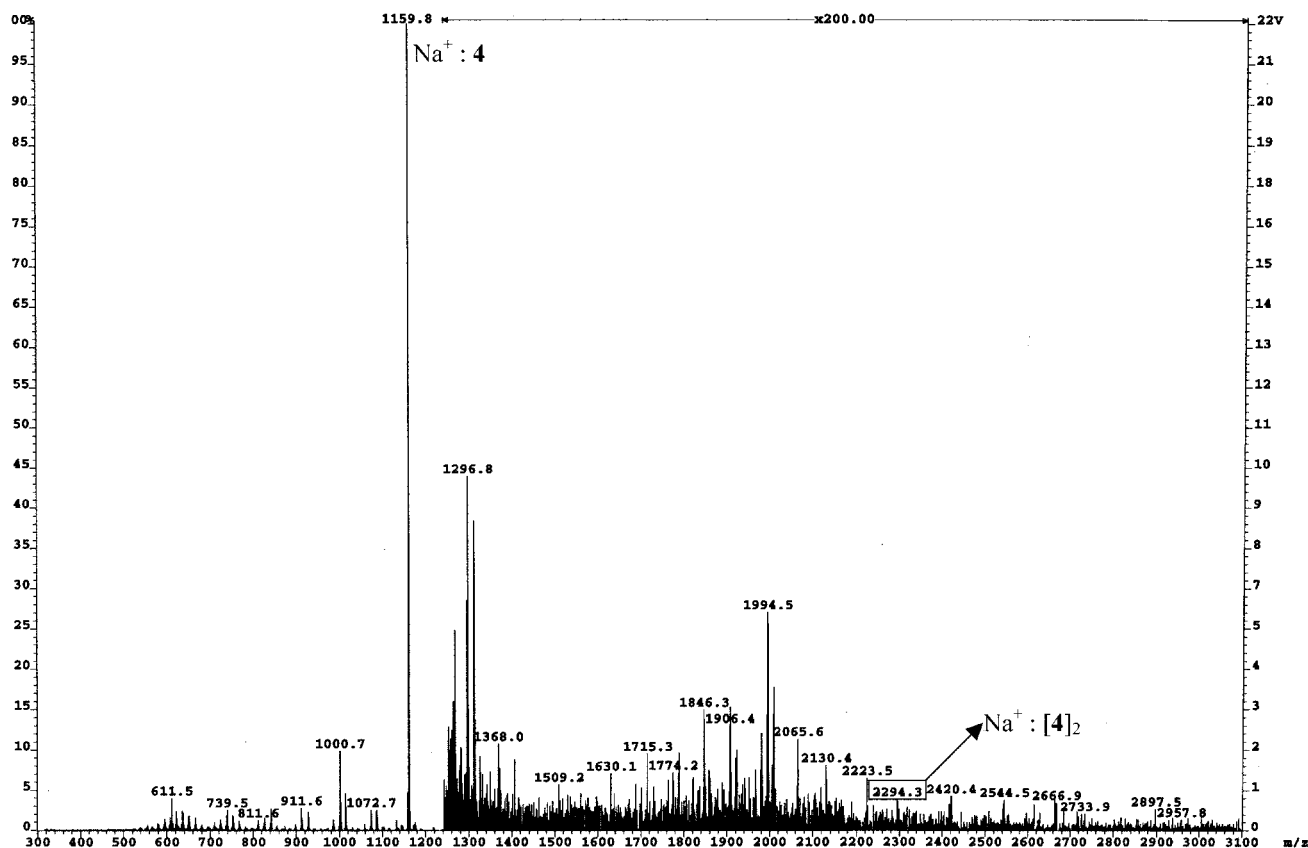


Figure 4. FAB<sup>+</sup> MS Spectrum of the sodium complex with ligand 4.

opening of the cavity because of the bulkiness of the methyl group.

On the other hand the combination of ester and malonate functions in **4** and **5** induces the complexation of Mg<sup>2+</sup> not observed with diester **1**. Ligands **4** and **5** form ML<sub>2</sub> species with Ca<sup>2+</sup>. We find here the peculiar behavior already observed with Na<sup>+</sup>. It is known [18, 19] that the common property of these two cations is their size indicating that the binding property of **4** and **5** is cation size dependent. Moreover an unexpected result appears during the complexation of Sr<sup>2+</sup> by ligand **4**: the coexistence of binuclear species with the mononuclear complex. The stability of the ML<sub>2</sub> complexes formed with Ca<sup>2+</sup> and ligands **4** and **5** are comparable with log β ~ 8.6. Those 1:2 complexes remain less stable than those with sodium. In general we notice that the stability of alkaline earth complexes with malonate derivatives reach lowest and highest values (log β<sub>Mg/4</sub> = 2.96 and log β<sub>Ba/5</sub> = 5.13) through both series of cations.

The most interesting results from this study are:

1. An increase in the cavity dimension with an increase of the number of ester groups when we go through diethyl ester to dimalonate and to diethyl ester-dimalonate derivatives.
2. The more bulky the substituent on the malonate, the more the ligand shows an opened cavity adequate for the largest cations.
3. The results obtained from alkaline complexation show that the substitution of an ethyl ester group by an ethyl

ester malonate gives some selectivities but does not generally improve the stability of complexes.

4. Significant complexation selectivities are observed for the dimalonate ligands **2** for Na<sup>+</sup> and Ba<sup>2+</sup>, and for ligand **3** for Rb<sup>+</sup> in the alkaline series. Slightly less important selectivity can be noticed for the ligand **3** and Sr<sup>2+</sup> system.
5. In acetonitrile it seems that, in a general way, ester derivatives are able to form biligand species particularly with Na<sup>+</sup> and Ca<sup>2+</sup>.

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