

Lower Rim Substituted *tert*-Butylcalix[4]arenes (Part VI). Synthesis and Ionophoric Properties of 5,11,17,23-Tetra-*tert*-Butyl-25,26,27,28-Tetrakis(3-Diethoxyphosphorylpropoxy)Calix[4]arene

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Abstract

New compound – 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(3-diethoxyphosphorylpropoxy)calix[4]arene was synthesized and its complexing properties were investigated using ion-selective membrane electrodes. The compound selectively recognizes lithium and calcium ions. Stability constants of the respective complexes formed within the membrane were determined.

Introduction

Calix[4]arene derivatives are of great interest as ionophores for chemical sensors: ion-selective electrodes (ISE) or optodes [1, 2]. The rather rigid and lipophilic macrocyclic structure of tetrakis-*tert*-butyl-calix[4]arenes, in which four hydroxy groups are arranged around the central cavity, can be modified by introducing a variety of electron donating substituents [2–4]. Among them synthetic ligands containing phosphoryl groups were so far relatively less studied [4–8, 16]. However, the receptors containing P=O groups are well known in nature. They represent excellent host molecules for not only metal ions but also for many classes of organic cations, for example amino acid arginine with guanidinium moiety [9].

In this paper we present the preparation and characterization of the new tetrasubstituted compound (**L**): 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(3-diethoxyphosphorylpropoxy)calix[4]arene and investigation of its ionophoric properties in ISE. The results are compared to those of the electrode based on calix[4]arene tetraphosphine oxide presented in [10].

Experimental

General

The ¹H, ¹³C and ³¹P NMR spectra were recorded on Varian 500 MHz spectrometer. The chemical shifts are reported in δ [ppm]. Mass spectra (MALDI TOF

techniques) were obtained on a Bruker BIFLEX 3 mass spectrometer. Both structure and purity of the compound were confirmed by NMR and mass spectra. Used organic reagents and solvents were reagent grade.

Synthesis

Compound **L** was synthesized as described and is shown in Figure 1.

A suspension of *p-tert*-butylcalix[4]arene (0.39 g, 0.6 mmol) and NaH (60% dispersion in mineral oil) (0.115 g, 4.8 mmol) in toluene (20 mL) was stirred at 80 °C for 3 h. Then diethyl(3-bromopropyl)phosphonate (0.95 g, 3.7 mmol) was added and the resultant reaction mixture was maintained at 80 °C for 6 days. An excess of NaH was decomposed with MeOH (10 mL) and the solvent was evaporated *in vacuo*. The residue was dissolved in CH₂Cl₂ (25 mL) and washed with 1 N HCl (15 mL), then with water (2 × 10 mL). The organic layer was dried over MgSO₄ and filtered. After evaporation of the solvent, the residue was purified via column chromatography on silica gel by eluting with CHCl₃/MeOH (50/1 v/v and then 20/1 v/v). Pure product 0.56 g, 68% was obtained in the *cone* conformation as a waxy semisolid.

$R_f = 0.3$, CHCl₃/MeOH (10/1 v/v).

C₇₂H₁₁₆O₁₆P₄ 1361.5, MS (MALDI TOF) M/z 1361.

¹H NMR (CDCl₃) δ (ppm): 1.07 (36H, s, (CH₃)₃C), 1.32 (24H, t, ³J_{H-H} = 6.8 Hz, CH₂CH₃), 1.80–1.90 (8H, m, CH₂), 2.14–2.24 (8H, m, CH₂), 3.14 (4H, d ²J_{HH} = 12.7 Hz, ArCH₂Ar-eq), 3.98 (8H, t, ³J_{HH} = 7 Hz, ArOCH₂), 4.10 (16H, m, POCH₂), 4.34 (4H, d, ²J_{H,H} = 12.7 Hz, ArCH₂Ar-ax), 6.76 (8H, s, ArH).

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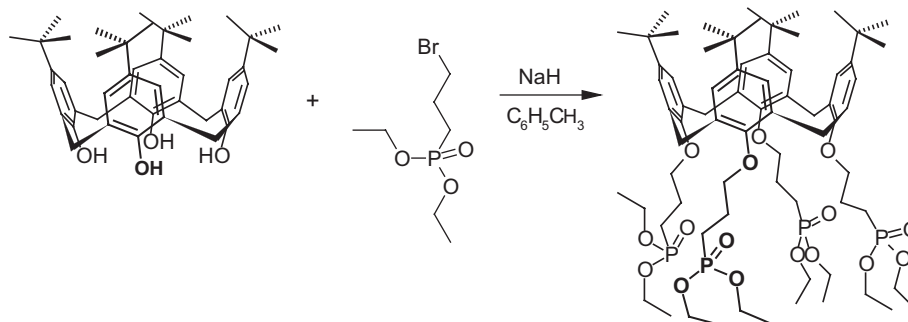


Figure 1. Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(3-diethoxyphosphorylpropoxy)calix[4]arene (**L**).

^{13}C NMR (CDCl_3) δ (ppm): 16.8 (d, $^3J_{\text{C,P}} = 5.3$ Hz, CH_2CH_3), 22.7 (d, $^1J_{\text{C,P}} = 141$ Hz, $\text{P}-\text{CH}_2$), 23.2 (d, $^2J_{\text{CP}} = 5.3$ Hz, $\text{P}-\text{CH}_2\text{CH}_2$), 31.6 ($(\text{CH}_3)_3\text{C}$), 34.0 ($\text{Ar}-\text{CH}_2-\text{Ar}$), 61.8 (d, $^2J_{\text{CP}} = 6.1$ Hz, POCH_2), 74.9 (d, $^3J_{\text{CP}} = 18.3$ Hz, $\text{Ar}-\text{O}-\text{CH}_2$), 125.3 ($\text{Ar}-\text{H}$), 133.7 ($\text{Ar}-\text{CH}_2$), 144.8 ($\text{Ar}-t\text{Bu}$), 153.2 ($\text{Ar}-\text{O}$).

^{31}P NMR (CDCl_3) δ (ppm): 33.2.

Membrane preparation and EMF measurements

General: Poly(vinyl chloride) high molecular (PVC), bis(2-ethylhexyl)sebacate (BEHS), tris(2-ethylhexyl)phosphate (TEHP) and potassium tetrakis(*p*-chlorophenyl)borate (KTCIPB) were from Fluka. Tetrahydrofuran (THF) p.a. from POCh, was dried and freshly distilled before use. All aqueous salt solutions were prepared with redistilled water (conductivity $< 1.8 \mu\text{S}/\text{cm}$). The salts LiCl , NaCl , KCl , NH_4Cl , MgCl_2 , SrCl_2 , BaCl_2 , NiCl_2 , CuCl_2 , ZnCl_2 , CdCl_2 , $\text{Pb}(\text{NO}_3)_2$ (POCh) and CaCl_2 , tetramethylammonium chloride (TMA^+Cl^-), guanidinium chloride (G^+Cl^-) (Fluka), RbCl and CsCl (Ubi-chem Ltd) were of p.a. grade.

The preparation of membrane for ISE was described in [16]. The membrane composition: 4 mg of ionophore, 60 mg of PVC, 120 mg of plasticizer and 0.5 mg of (KTpClPB), about 190 mg in total, were dissolved in 1.5 mL of dried and distilled THF and the solution was poured into a glass ring. The membranes of 7 mm diameter were incorporated into Ag/AgCl electrode bodies of IS 561 type (Philips). A double-junction reference Radelkis 0P0820P electrode was used with 1 M NH_4NO_3 solution in a bridge cell. The measure-

ments were carried out at 20°C using multimeter METROHM 654 and the cells of the type: $\text{Ag}|\text{AgCl}|1\text{ M KCl}|1\text{ M NH}_4\text{NO}_3|\text{sample}||\text{membrane}||0.01\text{ M KCl}|\text{AgCl}|\text{Ag}$. Measured salt solutions normally were prepared by successive dilution of initial 5×10^{-2} mol/ dm^3 stock solution. But for BaCl_2 , NiCl_2 , CuCl_2 , ZnCl_2 , CdCl_2 and $\text{Pb}(\text{NO}_3)_2$ the 0.1 M starting solutions were made at $\text{pH} = 4$ and the solutions were further diluted with 10^{-4} M HCl to maintained $\text{pH} = 4$ for the measurements. The samples were diluted until further dilution resulted in non-potential change.

Selectivity coefficients and electrode characteristics

Potentiometric selectivity coefficients ($\log K_{\text{Ca,J}}^{\text{pot}}$) were determined by the separate solution method [15] and were calculated (Equation 1), by using the EMF values for the highest measured ion activities at concentration 5×10^{-2} M. These results are presented in Table 2.

$$\log K_{\text{IJ}}^{\text{pot}} = \frac{(E_{\text{J}} - E_{\text{I}})z_{\text{I}}F}{2.303 \cdot RT} + \left(1 - \frac{z_{\text{I}}}{z_{\text{J}}}\right) \log a_{\text{I}} \quad (1)$$

The calculated selectivity coefficients for both membrane electrodes **1** and **2** containing ionophore **L** and optionally two plasticizers BEHS (bis((2-ethylhexyl)sebacate) and TEHP (tris(2-ethylhexyl)phosphate) and for the *blank* membrane electrodes **3** (IE) are presented in Table 2 (Figure 2). The characteristics of the studied electrodes **1–4** are shown in Table 1.

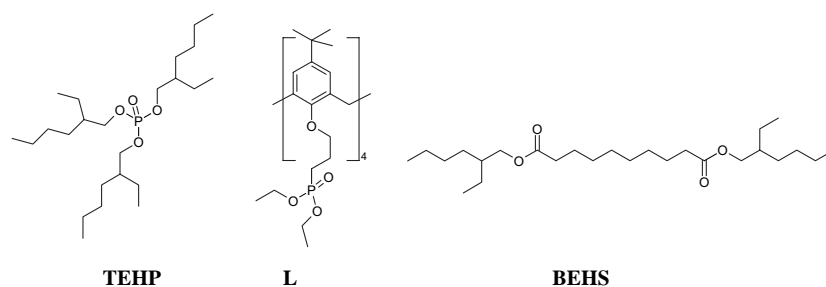


Figure 2. Ligand **L** and plasticizers used in this work.

Table 1. The characteristics of the studied electrodes 1–4

Electrode number	Ionophore	Plasticizer	Ion of preference I	S [mV]	Linear range $-\log a_I$
1	L	BEHS	Li ⁺	54.0(0.5)	1.0–3.4
			Ca ²⁺	31.2(0.3)	1.0–5.5
			G ⁺	50.6(0.6)	1.0–4.0
			Sr ²⁺	26.5(0.5)	1.0–4.0
2	L	TEHP	Li ⁺	50.4(0.3)	1.0–3.4
			Ca ²⁺	29.8(0.2)	1.0–5.5
			G ⁺	56.6(0.5)	1.0–5.5
			Sr ²⁺	25.6(0.8)	1.0–4.0
3	–	BEHS	TMA ⁺	51.8(0.6)	1.0–4.8
			G ⁺	60.6(0.7)	1.0–5.0
4	–	TEHP	G ⁺	60.0(0.5)	1.0–5.0
			Ca ²⁺	24.2(0.4)	1.0–3.5
			Li ⁺	46.3(0.7)	1.0–4.0

Determination of complex formation constants

The values of the complex formation constants β_{LM} for tetra-phosphorylated calixarene **L** with calcium, strontium, lithium and sodium were determined using the procedure proposed by Ceresa and Pretsch and Bakker [11] in PVC/BEHS membrane. Tetramethylammonium cation (TMA⁺) was used as a reference ion [11, 16]. The values of the complex formation constants are presented in Table 3.

Results and discussion

Phosphorus containing calix[4]arenes are promising compounds for the design of highly selective receptors of metal cations, anions or neutral organic molecules. The general method for the synthesis of the alkoxyphosphorylated calix[4]arene is based on alkylation of the phenolic groups with appropriate alkylating reagents [5, 16]. Our tetra phosphorylated compound **L** was prepared with good yield by the alkylation of *p*-tert-butylcalix[4]arene with diethyl(3-bromopropyl)phosphonate [12] in the presence of sodium hydride in toluene at 80 °C. Under the reaction condition tetra-

substitution was realised and compound **L** was obtained for the first time [5]. The ligand molecule **L** was obtained in the *cone* conformation which was proved by proton NMR and additionally by ¹³C and ³¹P NMR methods. The *cone* conformation is most suitable for complex formation.

Complexing behaviour of the compound towards alkali metal ions, alkali earth cations, some transition metal ions Ni²⁺, Cu²⁺, Zn²⁺, Cd²⁺, Pb²⁺ and tetramethylammonium (TMA⁺) ions were studied by applying ligand **L** in ISEs. Two different plasticizers: BEHS in the electrode **1** and TEHP in the electrode **2** were used. The electrodes generated very stable potentials. The characteristics of the studied electrodes and preferred ions are presented in Table 1. The ligand **L** is calcium selective, independently on the used plasticizer, with Nerstian characteristic (29 mV) and wide linear range response (10⁻¹–10^{-5.5} M). It also shows good lithium selectivity, but Nerstian response only in rather high lithium salt concentration (0.1–0.0008 M) in both electrode membranes **1** and **2**. The values of potentiometric selectivity coefficients for electrodes **1**–**3** are presented in Table 2. The selectivity is one of the most important and characteristic parameter of a sensor. The following selectivity pattern was observed: Li > Ca > Na > Sr > K, Rb, Cs > Mg, Ba.

Table 2. Comparison of the selectivity coefficients $\log K_{Ca,M}^{pot}$ of the membrane electrodes **1**, **2** and **3** ($M = \text{Li, Na, K, Rb, Cs, TMA, G, Mg, Ca, Sr, Ba, Zn, Cd, Ni, Cu, Pb}$)

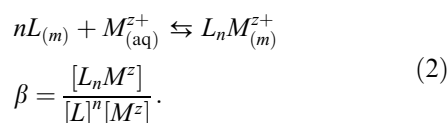
Electrode no.	$\log K_{i,j}^{pot}$								
	Ca ²⁺	Li ⁺	Na ⁺	K ⁺	Rb ⁺	Cs ⁺	TMA ⁺	G ⁺	
1	0	1.4	-1.2	-2.0	-2.1	-2.1	-2.5	0.2	
2	0	2.2	-0.2	-1.5	-1.6	-1.7	-1.7	3.8	
3	-4.2	-1.9	-1.6	-1.2	-1.2	-1.1	0	0.6	
	Mg ²⁺	Ca ²⁺	Sr ²⁺	Ba ²⁺	Zn ²⁺	Cd ²⁺	Ni ²⁺	Cu ²⁺	Pb ²⁺
1	-2.4	0	-1.6	-2.3	-0.6	-0.8	-2.6	-2.2	-0.8
2	-2.2	0	-1.5	-2.0	-1.3	-0.6	-2.3	-1.5	-0.7
3	-4.5	-4.2	-4.0	–	–	–	–	–	–

Table 3. The values of complex formation constants ($\log \beta$) for ligand **L** with studied cations in BEHS/PVC membrane

Electrode no	$\log \beta_{LM}$			
	Li	Na	Ca	Sr
1	5.3	4.2	8.7	6.9

The possibility of hydrogen bond formation between $P=O \cdots HN$ of the ligand and large, flat guanidinium cation (G^+) was the reason for guanidinium ion testing [9, 13, 16]. Guanidinium-ion-selectivity was higher in TEHP/PVC membrane **2**; blank membrane electrode **4** is also G^+ -selective. These suggest that the plasticizer: *tris*(2-ethylhexyl)phosphate might interact with guanidinium ion (G^+) similarly as ionophore **L**.

Presented values of selectivity coefficients for the electrodes **1** and **3** give the idea about the complexing ability of the studied tetra-phosphorylated compound **L**. The values of constants of the complex formation were determined for the complexes of the ligand **L** with calcium, strontium, lithium and sodium cations in BEHS/PVC membrane using the potentiometric procedure proposed by Pretsch [11], in accordance with Equation 2.



TMA^+ cation, used as a reference ion in the described procedure is not complexed in BEHS/PVC membrane. The calculated values of complex stability constants are presented in Table 3.

Conclusion

We have shown that in ISE the compound **L** selectively binds lithium cation among investigated alkali metal ions and calcium among alkali earth cations. Ligand **L** interacts with lithium and calcium ions in both electrode membranes: BEHS/PVC and TEHP/PVC. It was interesting to compare the properties of our calcium-selective electrode based on tetraphosphorylated calix[4]arene ligand to those reported by Diamond and others of Ca^{2+} -selective electrode based on calixarene tetraphosphine oxide, which shows similar selectivity pattern: $Ca > Li > Na > Mg > K$ [10]. The observed calcium selectivity of both compared electrodes may suggest that four $P=O$ groups and four ethereal oxygen atoms are taking part in complexation of Ca^{2+} .

Three carbon atoms bridge between coordination centers of ligand **L** might be the reason for observed lithium selectivity. From our observation the best known lithium ligands possess structure with 3-carbon bridge between coordination centers (see Fluka Catalogue: Li^+ – ionophores I, IV, VI, VII and VIII) [14].

New, functionalized at lower rim, 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(3-diethoxyphosphorylpropoxy)calix[4]arene **L** was synthesized with good yield and its structure and *cone* conformation were proved by 1H , ^{13}C and ^{31}P NMR methods. It belongs to a new series of calcium-selective ligands based on *tert*-butylcalix[4]arene platform.

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References

1. M.A. McKervey, M.-J. Schwing-Weill, and F. Arnaud-Neu: in J.L. Atwood, J.E.D. Davies, D. Macnicol and F. Vogtle (eds.), *Cation Binding by Calixarenes in Comprehensive Supramolecular Chemistry*, Vol. 1, Pergamon (1996).
2. F. Cadogan, K. Nolan, and D. Diamond: Sensor Applications, Chap. 34, in Z. Asfari, V. Bohmer, J. Harrowfield and J. Vicens (eds.), *Calixarenes 2001*, Kluwer Academic Publishers (2001).
3. C.D. Gutsche: *Calixarenes, Monographs in Supramolecular Chemistry*; The Royal Society of Chemistry (1989).
4. C.B. Dieleman, D. Matt, and P.G. Jones: *J. Organometal. Chem.* **545–546**, 461–471 (1997).
5. P. Jurečka, P. Vojtišek, K. Novotny, J. Rohovec, and I. Lukeš: *J. Chem. Soc., Perkin Trans.* **2**, 1370–1377 (2002).
6. S. Kunsagi-Mate, G. Nagy, P. Jurečka, and L. Kollar: *Tetrahedron* **58**, 5119–5124 (2002).
7. A. Solovyov, S. Cherenok, I. Tsymbal, S. Failla, G.A. Consiglio, P. Finocchiaro, and V. Kalchenko: *Heteroatom Chem.* **12**, 58 (2001).
8. C. Wieser-Jeunesse, D. Matt, M.R. Yaftian, M. Burgard, and J.M. Harrowfield: *C. R. Acad. Sci. Paris Serie IIC Chimie* 479–502 (1998).
9. T. Schrader: *J. Incl. Phenom.* **34**, 117 (1999).
10. T. McKittrick, D. Diamond, D.J. Marrs, P. O'Hagan, and M.A. McKervey: *Talanta* **43**, 1145 (1996).
11. A. Ceresa and E. Pretsch: *Anal. Chim. Acta* **395**, 41–52 (1999).
12. P. Bonhote, J.-E. Moser, R. Bumpfry-Baker, N. Vlachopoulos, and S.M. Zakeeruddin: *J. Am. Chem. Soc.* **121**, 1324–1336 (1999).
13. M. Bocheńska and J. Biernat: in E. Pungor (ed.), *Bioelectroanalysis, 2nd Bioelectroanalytical Symposium, Matrafured*, Akademiai Kiado, Budapest (1992).
14. FLUKA – CHEMICA: *Selectophore Catalogue* (1996).
15. Y. Umezawa, P. Buhlman, K. Umezawa, K. Tohda, and S. Amemiya: *Pure Appl. Chem.* **72**, 1851 (2000).
16. M. Hoffmann, A. Konitz, A. Sikorski, U. Lesińska, M. Bocheńska: *J. Incl. Phenom.* **47**, 137–142 (2003).