Lower rim substituted *p-tert*-butyl-calix[4]arene. Part 17. Synthesis, extractive and ionophoric properties of *p-tert*-butylcalix[4]arene appended with hydroxamic acid moieties

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ABSTRACT

The synthesis and characterization of four *p-tert*-butylcalix[4]arene-hydroxamic acids are reported. The dependence of the metal ion binding, assessed by liquid–liquid extraction of the metal nitrates from water into dichloromethane in individual and competitive experiments, on the ligand structure, is presented. The results showed that those ligands could be successfully used in separation process of transition and heavy metals often present together. Two of the ligands were used as active materials in Pb-ion-selective membrane electrodes. The characteristics of these electrodes, in particular their selectivity coefficients for Pb^{2+} over other metal ions, are discussed.

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1. Introduction

Naturally occurring compounds possessing hydroxamic acid moieties, known as siderophores, are produced by fungi and bacteria and act as sequestering agents for Fe^{3+} incorporation into microorganisms [1]. Their excellent binding properties found biomedical application in removal of Fe^{3+} and Al^{3+} from the body. It has been reported that siderophores show affinity also for other bivalent metal cations such as Pb^{2+}, Cu^{2+} or Ni^{2+} as well as UO_2^{2+} [1]. Calixarenes appended with hydroxamic acid groups could be regarded as synthetic siderophores and were mainly tested in solvent extraction experiments. They occurred to be excellent uranophiles [2–4], although they may efficiently extract transition and precious metal cations such as Fe^{3+}, Cu^{2+}, Zn^{2+}, Ni^{2+} and Pd^{2+} as well [5,6]. Solid-phase extraction of heavy metal ions using immobilized calix[4]arene-hydroxamic acids was also reported [7,8].

Heavy metals such as lead, cadmium, copper, nickel, cobalt, zinc or others, are present in our environment, mainly in wastewaters coming from various industries. These metals are easily accumulated in the human body, causing serious health disorders such as kidney and liver dysfunction, respiratory problems and bone disease. Therefore, the level of these toxic metals in natural and wastewaters needs to be monitored and controlled. However, the direct determination of their concentration level is frequently not sufficiently sensitive and the removal and separation of metal ions from their mixture is necessary.

Removal and separation of toxic heavy metals reduces the environmental impact and if they can be recovered in an economical way, it may generate some revenue for the industries. Therefore, the separation of metal ions, often present together, like Pb(II) and Cd(II) or Cu(II), Zn(II) and Ni(II), is a very important and challenging task and requires more and more selective ligands [9–11].

In this paper, we present the synthesis, characterization, extractive and ionophoric properties of four *p-tert*-butylcalix[4]arene hydroxamic acid derivatives (Fig. 1), among which, ligand **1** is reported here for the first time. These ligands differ by the number of functional groups attached to the calixarene framework (three or four arms) and by the substituents on the nitrogen atoms (R = H for **1** and **3**, R = CH$_3$ for **2** and **4**). Such structural changes are expected to influence binding properties of these compounds. Extraction experiments were carried out in individual and competitive conditions to evaluate the ability of these compounds to selectively separate heavy metal ions.

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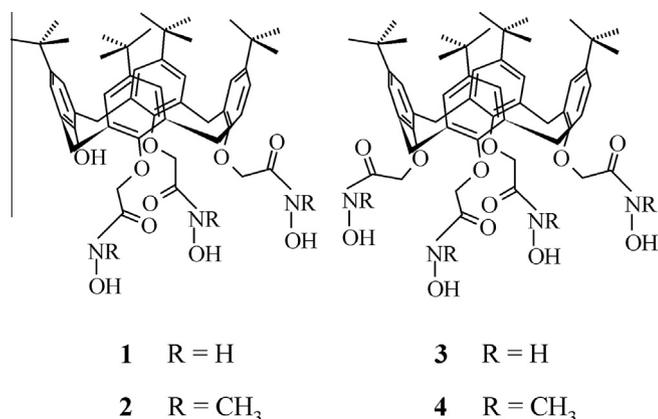
Fig. 1. Chemical structures of the *p-tert*-butylcalix[4]arene hydroxamic acids synthesized and studied in this work.

Functionalized calixarenes play an important role as ionophores in the field of chemical sensors [12–14]. In the previous paper, ligands **2** and **4** were preliminary tested as Pb-ionophores in ion-selective membrane electrodes (ISEs) showing promising properties [15]. In this work, the results of the continued studies in this field are presented.

2. Experimental

2.1. General

TLC was performed on silica gel plates Merck 60 F$_{254}$. Melting points were measured and are uncorrected. ^{1}H NMR spectra were recorded in DMSO on a Varian instrument (200 or 500 MHz). IR spectra were obtained on a Mattson Genesis II spectrometer. Elemental analyses were performed on a Carlo Erba Instrument CHNS EA 1108-Elemental analyzer. The absorbances were measured by atomic absorption spectrometry with an air-acetylene flame (Varian-55).

The calibration curves were obtained by measuring the absorbance of several samples of known metal cation concentration under the same conditions as the unknown. Therefore, the metal concentration of the unknown sample could be calculated.

The EMF measurements were done on a 16 – channel LAWSON LAB potentiometer (16 EMF, USA).

2.2. Chemicals

p-tert-Butylcalix[4]arene, ethylbromoacetate, ethylchloroformate, triethylamine, DMSO, BaO, Ba(OH)$_2$.8H$_2$O, *N*-hydroxylamine hydrochloride (NH$_2$OH.HCl), *N*-methylhydroxylamine hydrochloride (CH$_3$NHOH·HCl) were purchased from Aldrich; CH$_3$COOH and CH$_3$COONa were purchased from Prolabo and Merck, respectively.

For extraction experiments, the metal salts: Ni(NO$_3$)$_2$·6H$_2$O, Zn(NO$_3$)$_2$·6H$_2$O (Fluka, purum), Pb(NO$_3$)$_2$, Cd(NO$_3$)$_2$·4H$_2$O, Fe(NO$_3$)$_3$·H$_2$O (Merck, p.a.), Cu(NO$_3$)$_2$·3H$_2$O (Prolabo) and Co(NO$_3$)$_2$·6H$_2$O (Strem Chemicals) (analytical grade) were dried under vacuum at room temperature before use.

Poly(vinylchloride) (PVC, high molecular fraction), *o*-nitrophenyloctyl ether (NPOE) and the lipophilic salt, potassium tetrakis(*p*-chlorophenyl)borate (KT*p*ClPB), were purchased from Fluka (Selectophore). All aqueous salt solutions used for ISE studies: NaCl, KCl, CaCl$_2$, ZnCl$_2$, CdCl$_2$ (POCh all p.a. grade) and Pb(NO$_3$)$_2$ and Cu(NO$_3$)$_2$ (Aldrich) were prepared using ultrapure water from a Hydro-lab (RO) station (conductivity below 0.1 μS cm^{-1}).

The reagent grade organic solvents, dichloromethane (Fluka Analytical), ethyl ether (Fluka Analytical), acetone (Riedel-de-Haën), ethyl alcohol (Carlo Erba) were used without further purification. Tetrahydrofuran (THF) p.a. (from POCh) was dried and freshly distilled before use. Dimethylformamide (DMF) (from POCh) used in reactions was dried before use.

2.3. Synthesis

The four calix[4]arene-hydroxamic acids were prepared *via* the so-called mixed anhydrides method [16]. The intermediate compounds **I–IV** (Schemes 1 and 2) were synthesized according to the known procedures [17–19].

The tris-substituted calix[4]arene-hydroxamic acids (**1** and **2**) were prepared as follows (Scheme 1): calix[4]arene-triscarboxylic acid (**II**) was dissolved in dry CH$_2$Cl$_2$ (10 mL) and the solution was stirred and cooled to −10 °C. Subsequently, 3.2 equivalents of NEt$_3$ and 3.2 equivalents of ethyl chloroformate were added. The solution was stirred at −10 °C for 30 min. and then 18 equivalents of an appropriate hydroxylamine hydrochloride (NH$_2$OH.HCl or CH$_3$NHOH.HCl, respectively) in 5 mL of CH$_2$Cl$_2$ were added. Before introducing amine hydrochloride to the reaction mixture, it was released from its hydrochloride form by adding the same equivalent of NEt$_3$. After 1 h, the mixture was diluted with CH$_2$Cl$_2$ (15 mL), washed with water (15 mL), then with 0.1 mol L^{-1} HCl (15 mL) and again with water (15 mL). The water phase was extracted twice with CH$_2$Cl$_2$ (30 mL). The combined organic layers were dried over MgSO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was crystallized from CH$_2$Cl$_2$/Et$_2$O mixture to give the pure products.

The tetrakis-substituted compounds (**3** and **4**) were prepared similarly by reacting calix[4]arene-tetra-carboxylic acid (**IV**) with 4.2 equivalents of ethyl chloroformate and 4.2 equivalents of triethyl amine. Subsequently, 24 equivalents of an appropriate hydroxylamine hydrochloride (NH$_2$OH.HCl or CH$_3$NHOH.HCl, respectively) were added (Scheme 2).

2.3.1. 25-hydroxy-26, 27, 28-tris(N-hydroxycarbamoylmethoxy)-p-tert-butylcalix[4]arene (1)

C$_{50}$H$_{65}$O$_{10}$N$_3$; M.W. = 868.2 g/mol; m.p. = 188–190 °C; yield: 76%; IR ν_{max} (C=O) 1645 cm^{-1}; ^{1}H NMR (500 MHz, DMSO): *cone* conformation, δ [ppm]: 0.96 (s, 18H, C–(CH$_3$)$_3$); 1.20 (s, 9H, C–(CH$_3$)$_3$); 1.22 (s, 9H, C–(CH$_3$)$_3$); 3.30 (d, 2H, Ar–CH$_2$–Ar, J = 13.67 Hz); 4.26 (d, 2H, Ar–CH$_2$–Ar, J = 13.67 Hz); 4.40 (d, 2H, Ar–CH$_2$–Ar, J = 13.19 Hz); 4.45 (d, 2H, Ar–CH$_2$–Ar, J = 13.19 Hz); 4.22 (s, 2H, –O–CH$_2$–CO); 4.41 (s, 4H, –O–CH$_2$–CO); 6.78 (s, 2H, Ar–H); 6.91 (s, 2H, Ar–H); 7.07 (s, 2H, Ar–H); 7.20 (s, 2H, Ar–H); 7.10 (s, 1H, N–H); 7.24 (s, 2H, N–H); 9.09 (s, 1H, O–H); 10.53 (s, 1H, O–H); 10.83 (s, 2H, O–H).

Experimental *Anal.* Calc. for C$_{50}$H$_{65}$O$_{10}$N$_3$·2H$_2$O: C, 66.36; H, 7.63; N, 4.64. Found: C, 66.81; H, 7.45; N, 3.34%.

2.3.2. 25-Hydroxy-26,27,28-tris(N-methyl, N-hydroxycarbamoylmethoxy)-p-tert-butylcalix[4]arene (2)

C$_{53}$H$_{71}$O$_{10}$N$_3$; M.W. = 910.2 g/mol; m.p. = 217–221 °C; yield: 79%; IR ν_{max} (C=O) 1650 cm^{-1}; ^{1}H NMR (500 MHz, DMSO): *cone* conformation, δ [ppm]: 0.94 (s, 18H, C–(CH$_3$)$_3$); 1.17 (s, 18H, C–(CH$_3$)$_3$); 3.14 (s, 9H, –N–CH$_3$); 3.18 (d, 2H, Ar–CH$_2$–Ar, J = 12.7 Hz); 3.22 (d, 2H, Ar–CH$_2$–Ar, J = 12.7 Hz); 4.37 (d, 2H, Ar–CH$_2$–Ar, J = 12.7 Hz); 4.54 (d, 2H, Ar–CH$_2$–Ar, J = 12.7 Hz); 4.95 (s, 6H, –O–CH$_2$–CO); 6.70 (s, 2H, Ar–H); 6.81 (s, 2H, Ar–H); 6.94 (s, 2H, Ar–H); 7.02 (s, 2H, Ar–H); 9.70 (s, 1H, O–H); 9.84 (s, 3H, O–H).

Experimental *Anal.* Calc. for C$_{53}$H$_{71}$O$_{10}$N$_3$·2H$_2$O: C, 67.22; H, 7.93; N, 4.44. Found: C, 67.72; H, 7.70; N, 4.48%.
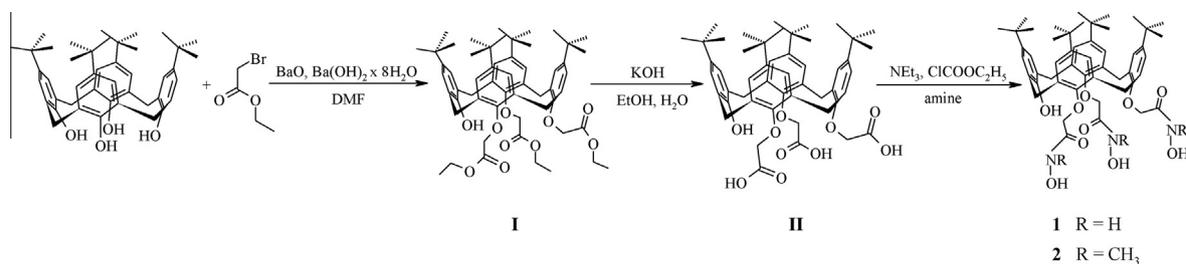
Scheme 1. Synthesis of tris-substituted calix[4]arene-hydroxamic acids (**1** and **2**).
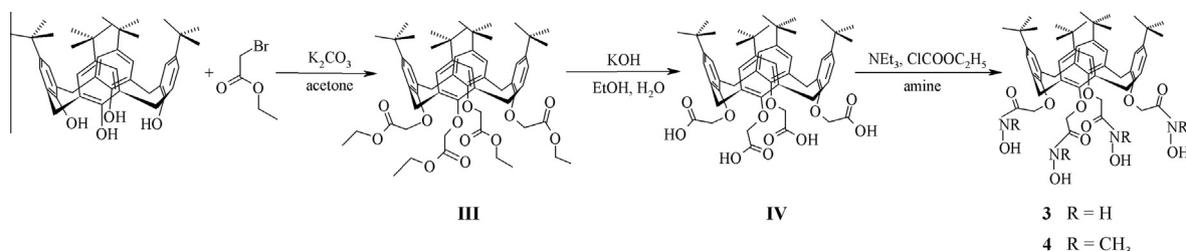
Scheme 2. Synthesis of tetrakis-substituted calix[4]arene-hydroxamic acids (**3** and **4**).

2.3.3. 25,26,27,28-Tetrakis(N-hydroxycarbamoylmethoxy)-p-tert-butylcalix[4]arene (3)

$C_{52}H_{68}O_{12}N_4$; M.W. = 940.1 g/mol; m.p. = 220–222 °C; yield: 82%; IR v_{max} (C=O) 1640 cm^{-1}; ^{1}H NMR (500 MHz, DMSO): *cone* conformation, δ [ppm]: 0.91–1.24 (bs, 36H, C–(CH_3)$_3$); 3.23 (d, 4H, Ar–CH_2–Ar, J = 13.18 Hz); 4.11–4.87 (m, 16H, –O–CH_2–CO + Ar–CH_2–Ar, J = 13.18 Hz); 6.68–7.13 (m, 8H, Ar–H).

Experimental *Anal.* Calc. for $C_{52}H_{68}O_{12}N_4\cdot2H_2O$: C, 63.93; H, 7.38; N, 5.73. Found: C, 64.18; H, 7.41; N, 3.79%.

2.3.4. 25,26,27,28-Tetrakis(N-methyl,N-hydroxycarbamoylmethoxy)-p-tert-butylcalix[4]arene (4)

$C_{56}H_{76}O_{12}N_4$; M.W. = 996.2 g/mol; m.p. = 214–215 °C; yield: 60%; IR v_{max} (C=O) 1646 cm^{-1}; ^{1}H NMR (500 MHz, DMSO): *cone* conformation, δ [ppm]: 1.04 (bs, 36H, C–(CH_3)$_3$); 3.14 (m, 16H, –N–CH_3 + Ar–CH_2–Ar, J = 12.7 Hz); 4.76 (d, 4H, Ar–CH_2–Ar, J = 12.7 Hz); 4.88 (s, 8H, –O–CH_2–CO); 6.78 (s, 4H, Ar–H); 9.72 (s, 4H, –O–H).

Experimental *Anal.* Calc. for $C_{56}H_{76}O_{12}N_4$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.24; H, 7.61; N, 5.62%.

2.4. Extraction studies

The organic solutions were made by dissolving a weighted amount of the ligand in CH_2Cl_2. The aqueous solutions containing the metal cation as nitrate were buffered to pH 5.4 with 0.01 mol L^{-1} acetate buffer (8.2×10^{-3} mol L^{-1} CH_3COONa and 1.8×10^{-3} mol L^{-1} CH_3COOH) for Co^{2+}, Ni^{2+}, Zn^{2+}, Cu^{2+}, Pb^{2+} and Cd^{2+} solutions or adjusted to pH 2.2 with HNO$_3$ in the case of Fe^{3+}. The ionic strength was settled as constant at I = 0.1 mol L^{-1} using KCl.

The extractive properties of the ligands studied were investigated following the procedure described in [5,20]: 25 mL of an 1.06×10^{-4} mol L^{-1} aqueous metal ion solution and 5 mL of the 5.3×10^{-4} mol L^{-1} ligand solution in CH_2Cl_2 were mechanically shaken in a stoppered glass tube immersed in a thermostated water bath at 30 °C for about 12 h. After that time the two phases were separated and the aqueous layer was analyzed by atomic absorption spectrometry and the absorbance A was measured. The absorbance A_0 of a blank experiment performed in the absence of the ligand (aqueous phase extracted with pure dichloromethane) was measured in the same conditions. The percentages of cations extracted from water into dichloromethane were calculated from the equation: %E = $100(A_0 - A)/A_0$.

For the competitive metal ion extraction, two solutions of metal salts mixture were prepared; one containing Pb^{2+} and Cd^{2+} and the other with Cu^{2+}, Zn^{2+} and Ni^{2+} metal salts. The concentration of each metal ion was 1.06×10^{-4} mol L^{-1}. The experimental conditions were the same as for the individual extraction experiments.

2.5. Ion-selective electrode studies

2.5.1. Membrane preparation and EMF measurements

The membrane components (2.25 wt.% of ionophore, 32.5 wt.% PVC, 65 wt.% o-nitrophenyl-octylether (NPOE) or bis(1-butylpentyl)adipate (BBPA), 0.25 wt.% potassium tetrakis(4-chlorophenylborate) (KTpClPB)), a total cocktail mass of about 185 mg, were dissolved in 1.5 mL of dried and freshly distilled THF. The solution was poured into a glass ring (diameter d = 24 mm). After overnight slow solvent evaporation, the membranes could be used to prepare the electrodes. Several small membranes of d = 7 mm were cut from the mother membrane and incorporated into Ag/AgCl electrode bodies of IS 561 type (Moeller S.A., Zurich, Switzerland). The electrode body was filled up with an internal filling solution (Pb(NO$_3$)$_2$ 10^{-3} mol L^{-1}, Na$_2$EDTA 10^{-3} mol L^{-1}). A double-junction reference electrode Eurosensor EAgClK – 312 was used with 1 mol L^{-1} KNO$_3$ solution in the bridge cell. The measurements were carried out at 23 °C, using the following cell:

Ag|AgCl|internal electrolyte|membrane|sample|KNO$_3$ 1 mol L^{-1}|KCl 1 mol L^{-1}|AgCl|Ag and a 16 – channel LAWSON LAB potentiometer (16 EMF USA).

2.5.2. Electrode characteristics and selectivity coefficients

The potentiometric measurements of heavy and transition metal ions were performed at pH 4, adjusted with HNO$_3$. Activity coefficients were estimated using the semi-empirical Pitzer's model which is able to describe the non-ideal behavior of the electrolytes up to high concentrations [21–24]. The single ion activities were calculated using PHREEQC software version 2.17 [25]. The ion activity was calculated by taking into account the complexation with Cl$^-$, NO$_3^-$ and OH$^-$ (hydrolysis). The selectivity coefficients were determined by the Separate Solution Method (SSM) according

to the procedure described by Bakker et al. and were calculated according to the following equation [26,27].

$$\log K_{Pb,M}^{pot} = \frac{E_M^0 - E_{Pb^0}}{S_{Pb}}$$

where E_M^0 and E_{Pb}^0 are the potentials corresponding to the interfering metal cation and Pb^{2+}, respectively; S is the experimental value of the slope of the electrode for Pb^{2+}.

In order to obtain unbiased values of the selectivity coefficients, the calibration of the electrodes was performed starting preferably from the most discriminating cation.

3. Results and discussion

3.1. Synthesis

Ligands **1**–**4** were obtained with good yields (60–82%) *via* the mixed anhydrides method. The *cone* conformation of the synthesized calixarene-derivatives were confirmed by the caracteristic splitting pattern of the methylene bridge prótons in the 3.2–4.9 ppm region in their ^1H NMR spectra with the coupling constant around J_{H-H} = 13 Hz. Those patterns are similar to that observed in the literature for tetrakis- and tris-substituted derivatives of calix[4]arene [28–30].

The purity of compounds was proved by ^1H NMR spectroscopy and elemental analysis.

3.2. Liquid–liquid extraction studies

3.2.1. Individual extraction

The extractive properties of calix[4]arene-hydroxamic acids (**1**–**4**) were studied using the nitrate extraction method at pH 5.4 except for iron, as precipitation occurred above pH 4. In this case, the pH was lowered to 2.2 with HNO_3. Data of the individual extraction experiments are presented in Table 1. Literature data concerning the extraction properties of ligand **3** from water into chloroform are also shown [5]. It can be seen that for ligand **3**, the percentage extraction of Co^{2+} and Zn^{2+} from water into dicloromethane and from water to chloroform at the same pH 5.4, are similar and the values are 89.0 and 90, for Cu^{2+}, whereas for Zn^{2+} are 60% and 63%, respectively. The bigger difference in percentage extraction might be observed for Co^{2+} ($\Delta\%E$ = 8.2) which is slightly better extracted into chloroform than into dichloromethane in the same experimental conditions. On the other hand, Ni^{2+} is much less extracted into chloroform (17%) than into dichloromethane (54.2%) also in the same experimental conditions. The percentage extraction for Fe^{3+} was compared with the literature data for the experiments conducted at the same value of pH 2.2. The slightly better Fe^{3+} extraction was achieved from H_2O into CH_2Cl_2 with $\%E$ = 59.8 compared to $\%E$ = 54 for $H_2O/CHCl_3$ system.

As expected for siderophore-like compounds, they are all good extractants for Fe^{3+} ($\%E \geqslant 59.8$) at low pH (2.2). In particular, ligand **4** extracts almost quantitatively this cation ($\%E$ = 89.3%). Some experiments were performed at pH 2.2 with the rest of cations but no significant extraction was observed which is in agreement with the results obtained by Shinkai and co-workers [5]. On the other hand, at pH 5.4 most of the cations were fairly extracted.

A remarkable result is the almost quantitative extraction of Cu^{2+} ($\%E \geqslant 88$) with all ligands. The other divalent cations Co^{2+}, Ni^{2+}, Zn^{2+}, Pb^{2+} and Cd^{2+} are in most cases fairly extracted, however less than Cu^{2+}. No clear cut effect of extraction percentage is observed when an additional functional group is present in the calixarene molecule. Actually, the extractive properties depend on the substitution of the nitrogen atoms in the hydroxamic acid moiety. With unsubstituted compounds **1** and **3**, $\%E$ values are similar except for Pb^{2+} and Cu^{2+} which are better extracted by **1** than by **3**. With the methylated compounds **2** and **4** Co^{2+}, Ni^{2+}, Pb^{2+} and especially Cu^{2+} are better extracted by **4** than by **2**. For both tris and tetrakis compounds the unsubstituted **1** and **3** are always much more efficient than the methylated compounds **2** and **4**, except for Cu^{2+} which is better extracted by **4** ($\%E$ = 98) than by **3** ($\%E$ = 89). This is globally in agreement with the results of Dasaradhi et al. [31] who observed that compounds bearing secondary hydroxamate functions were more efficient extractants than those with tertiary hydroxamate substituents.

3.2.2. Competitive extraction

Competitive metal ion extraction experiments were performed in order to determine the potential of the synthesized ligands as selective extractive agents for Pb^{2+} in the presence of Cd^{2+} and for Cu^{2+} in the presence of Zn^{2+} and Ni^{2+}, cations which are usually present together.

The results of the competitive extraction experiments are given in Table 2 together with those of the individual extraction experiments, recalled in brackets.

With ligand **1** the percentages of Pb^{2+} and Cd^{2+} extraction decrease when the two cations are present together in the solution. Nevertheless, Pb^{2+} is still extracted at almost 70% demonstrating a quite good selectivity over Cd^{2+}. Interesting results were obtained with ligand **3** for Pb^{2+} extraction in the presence of Cd^{2+}. In this case, Pb^{2+} is almost quantitatively extracted, showing higher percentage extraction than in individual experiments. In contrary, the percentage of Cd^{2+} extraction decreases as compared to the individual extraction. Thus, a very high selectivity for Pb^{2+} over Cd^{2+} can be observed. It is evident that the presence of Cd^{2+} tends to increase the percentage extraction of Pb^{2+}. Although a synergic effect is generally ascribed to the situation where two extractants are present together, it can be assumed, in a way, that similar effect occurred in this case. A salting effect present due to an excess of nitrate could also explain these observations. This result is very important for the removal of Pb^{2+} and its separation from other toxic metal ions like Cd^{2+} in this particular pH conditions.

In the case of ligands **2** and **4**, the competitive extraction confirmed the low $\%E$ values of Cd^{2+} and Pb^{2+}.

It can be seen from the Table 2 that in all cases Cu^{2+} is still almost quantitatively extracted in the presence of Zn^{2+} and Ni^{2+} cations. A significant decrease of extraction percentages of Zn^{2+} and Ni^{2+} can be observed in all cases. Ligands **2** and **4** show the best selectivity for Cu^{2+} over Zn^{2+} and Ni^{2+} and, therefore, they could be successfully used in separation processes.

3.3. Potentiometric response and membrane selectivity

Compounds **1** and **3**, unsubstituted on the nitrogen atoms, were poorly soluble in THF what precluded the possibility of their application as ionophores in ion-selective membrane electrodes.

Table 1
Percentage extraction ($\%E$) of metal nitrates (C_M = 1.06 × 10^{-4} mol L^{-1}) with ligands **1**–**4** (C_L = 5.3 × 10^{-4} mol L^{-1}) from water into dichloromethane (Organic to aqueous phase ratio o/a = 5, T = 30 °C, pH 5.4 or 2.2 in the case of Fe^{3+}).

Ligand/cation	Fe^{3+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
1	70.7	48.1	52.1	97.7	62.4	32.1	85.4
2	63.1	2.1	15.4	88.5	⩽1	5.5	2.6
3	59.8	45.8	54.2	89.0	60	32.7	61.6
3[a]	54	54	17	88	63	nd	nd
4	89.3	6.2	41.9	98.0	1.6	5.5	8.5

"nd" – not determined.
Values with uncertainties less than 5%.
[a] Extraction H_2O–$CHCl_3$, data from Ref. [5] (C_M = 1.06 × 10^{-4} mol L^{-1}; C_L = 5.3 × 10^{-4} mol L^{-1}; T = 30 °C, pH 5.4 or 2.2 in the case of Fe^{3+}).

Table 2
Percentage of competitive extraction (%E) from water into dichloromethane of mixtures: Pb^{2+}/Cd^{2+} and $Cu^{2+}/Zn^{2+}/Ni^{2+}$ ($C_M = 1.06 \times 10^{-4}$ mol L^{-1} of each metal) with ligands **1–4** ($C_L = 5.3 \times 10^{-4}$ mol L^{-1}) (Organic to aqueous phase ratio o/a = 5, $T = 30$ °C, pH 5.4). In brackets, percentage of individual extraction.

Ligand/metal	Cd^{2+}	Pb^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
1	12.8 (32.1)	69.6 (85.4)	21.0 (52.1)	98.6 (97.7)	20.0 (62.4)
2	2.6 (5.5)	1.7 (2.6)	2.6 (15.4)	89.9 (88.5)	2.2 (⩽1)
3	7.7 (32.7)	95.5 (61.6)	15.8 (54.2)	99.5 (89.0)	23.3 (60.0)
4	2.6 (5.5)	5.2 (8.5)	5.3 (41.9)	99.1 (98.0)	⩽1 (1.6)

Therefore, only ligands **2** and **4** were tested as ionophores in the membrane of ISEs. The ligands differ by the number of substituents, three for ligand **2**, four for ligand **4**. Two plasticizers BBPA and NPOE of different dielectric constant (5.6 and 24, respectively) were used. The exemples of characteristics of the ion selective electrode based on 2/BBPA and 4/NPOE membranes for Pb^{2+}, Na^+ and Ca^{2+} cations are illustrated in Fig. 2 and 3. The full characteristic parameters of the electrodes studied are presented in Table 3.

The results showed that the studied calix[4]arene-hydroxamic acids (**2** and **4**) act as Pb^{2+}-selective ionophores. The electrodes showed good response for Pb^{2+} in both membranes, PVC/NPOE and PVC/BBPA.

The electrode based on ionophore **4** showed close to Nernstian slope value in Pb^{2+} solution (≈ 30 mV/dec) within a linear range 10^{-2}–10^{-5} mol L^{-1} in both plasticizers. For Na^+ and K^+ cations, the electrodes showed still acceptable but less good parameters especially with NPOE as plasticizer (sub-nernstian slope and narrow linear range).

The electrodes based on ligand **2** present a similar behavior towards Na^+ and Ca^{2+} cations. However, for Pb^{2+} the slope is typical for monovalent cations. Preliminary results on the behavior of electrodes incorporating the ionophore **4** showed close to Nernstian response in Pb^{2+} solution, whereas those based on ionophore **2** presented a typical monovalent cations slope ($S_{Pb} = 58.9$ mV/dec) [15]. In this work we confirmed those results. Such a behavior has already been reported by Lindner et al. and was interpreted as a sensitivity towards PbX^+ species (where X: OH^-, Cl^-, NO_3^-, CH_{3}-COO^-) [32]. These authors suggested that the contribution to the electrode potential is divided among the monovalent form of the lead complex as well as the free Pb^{2+} cations. On the other hand, it has been later shown that the monovalent, divalent or even mixed response is depending on the molar ratio between ionic sites and ionophore [33]. Suzuki et al. suggested that during complexation process one proton is dissociated and released from the
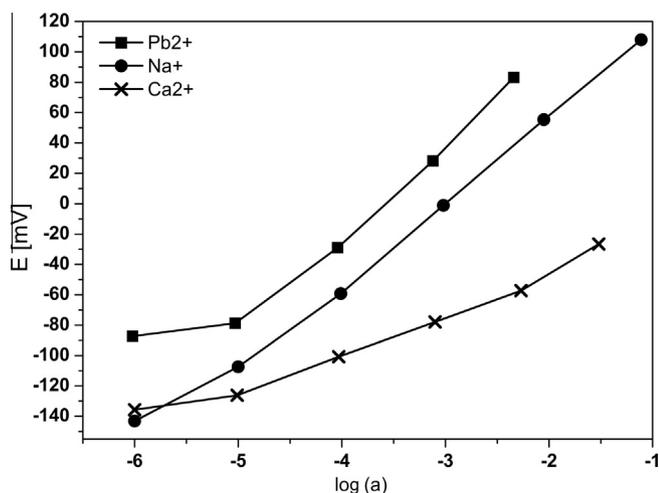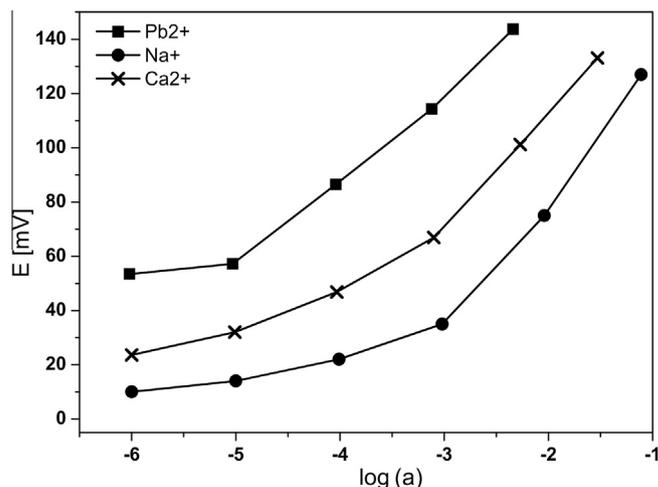
Fig. 3. Response of the ion selective electrode based on **4**/NPOE membrane for Pb^{2+}, Na^+ and Ca^{2+} cations.

membrane which results in monovalent behavior of the divalent selective electrodes [34]. Later, theoretical consideration showed that double nernstian slope is possible if ionophore has acid/base properties which result in various slope depending on the pH of the sample and ionophore pK [35].

The response for Cu^{2+} and Cd^{2+} cations of the electrodes based on ligand 2 or 4 were in all cases of sub-nernstian slope within narrow linear range which might indicate weak interaction between ionophores and those cations in the membrane.

The potentiometric selectivity coefficients, determined by the Separate Solution Method (SSM), are presented in Table 4 and Fig. 4.

These results proved that the electrodes are selective for the Pb^{2+} cations.

It can be seen that generally better selectivity coefficients were obtained with PVC/NPOE membranes than with PVC/BBPA membranes, which is in agreement with the results reported earlier showing that NPOE is preferred for Pb-sensors (and other divalent cations), whereas BBPA seems to be the best plasticizer for Na^+ or Li^+ sensors [36]. These results may be explained by the strong Pb^{2+} cation/ionophore interaction in the membrane containing NPOE due to the high dielectric constant of this plasticizer [37].

Exceptionally, better Pb^{2+}/Cd^{2+} selectivity coefficients were obtained in PVC/BBPA membrane which suggests stronger affinity of Cd^{2+} for NPOE than for BBPA plasticizer.

The best selectivity was obtained using the **2**/NPOE membrane. Selectivity coefficients over Na^+ and Cu^{2+} are particularly good ($\log K^{pot}_{Pb,Na} = -5.67$, $\log K^{pot}_{Pb,Cu} = -5.53$, respectively), whereas Ca^{2+} is the most interfering ions with $\log K^{pot}_{Pb,Ca} = -2.76$.

The electrode with the membrane **2**/BBPA is less selective and the most interfering cation is Na^+ ($\log K^{pot}_{Pb,Ca} = -1.02$). A similar situation occurs with the membrane containing **4**, where better selectivity was obtained using NPOE. In both membranes with **4**, the most interfering cation is Ca^{2+} ($\log K^{pot}_{Pb,Ca} = -1.13$ with BBPA

Fig. 2. Response of the ion selective electrode based on **2**/BBPA membrane for Pb^{2+}, Na^+ and Ca^{2+} cations.

Table 3
Characteristics of the studied ion-selective electrodes with ionophores **2** and **4**.

Ion of preference	2/BBPA		2/NPOE		4/BBPA		4/NPOE	
	$S \pm \sigma^*$ (mV/dec)	LR $-\log a$	$S \pm \sigma^*$ (mV/dec)	LR $-\log a$	$S \pm \sigma^*$ (mV/dec)	LR $-\log a$	$S \pm \sigma^*$ [mV/dec]	LR $-\log a$
Pb^{2+}	60.3 ± 1.8	2–5	59.0 ± 2.6	2–5	31.2 ± 1.3	2–5	29.2 ± 0.7	2–5
Ca^{2+}	27.3 ± 1.7	1–5	29.5 ± 0.6	1–5	32.1 ± 0.9	2–5	27.5 ± 1.5	2–3
Na^+	57.8 ± 0.2	1–5	43.1 ± 0.9	1–3	49.9 ± 0.5	1–3	47.5 ± 1.5	1–2
K^+	54.5 ± 0.5	1–3	48.7 ± 0.8	1–2	43.4 ± 0.8	1–3	48.9 ± 1.6	1–2
Cd^{2+}	21.2 ± 1.1	2–3	19.5 ± 1.2	2–3	20.8 ± 1.1	2–3	22.3 ± 0.9	2–3
Cu^{2+}	20.7 ± 2.8	2–3	18.9 ± 2.6	2–3	19.9 ± 0.9	2–3	20.2 ± 1.7	2–3

* Standard deviation of five independent measurements.

Table 4
Potentiometric selectivity coefficients ($\log K_{Pb,M}^{pot} \pm \sigma^*$) of the electrodes based on ionophores **2** and **4**.

Ion	**2**/BBPA	**2**/NPOE	**4**/BBPA	**4**/NPOE
Pb^{2+}	0.00	0.00	0.00	0.00
Na^+	−1.02 ± 0.21	−5.67 ± 0.21	−2.46 ± 0.26	−3.85 ± 0.11
K^+	−2.02 ± 0.21	−3.97 ± 0.08	−2.89 ± 0.28	−3.55 ± 0.06
Cd^{2+}	−4.82 ± 0.29	−3.46 ± 0.05	−4.24 ± 0.06	−3.36 ± 0.17
Cu^{2+}	−1.10 ± 0.15	−5.53 ± 0.23	−3.11 ± 0.32	−4.72 ± 0.39
Ca^{2+}	−3.74 ± 0.29	−2.76 ± 0.06	−1.13 ± 0.03	−2.11 ± 0.02

* Standard deviation of five independent measurements.
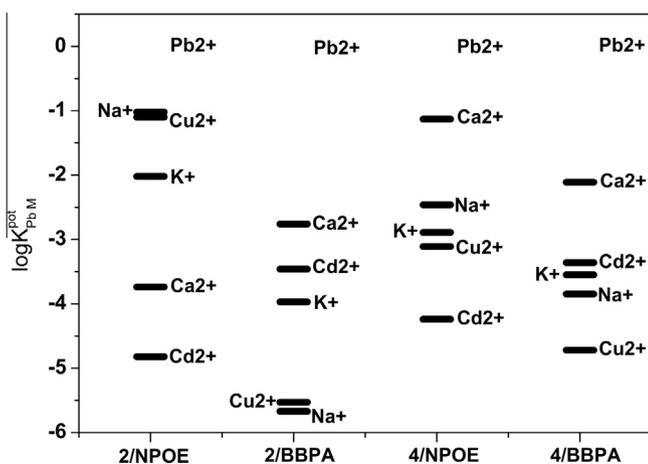
Fig. 4. Potentiometric selectivity coefficients ($\log K_{Pb,M}^{pot}$) for the electrodes based on ligands **2** and **4**.

and $\log K_{Pb,Ca}^{pot} = -2.11$ with NPOE). It should be noted that for Cu^{2+} and Cd^{2+} cations, sub-nernstian slopes (about 20 mV/dec for both cations) were obtained which may underestimate the selectivity over those cations. It must be noted that direct comparison of the selectivity coeffcients of ligands **2** and **4** is difficult since the electrodes with ligand **2** showed monovalent slope for Pb^{2+}. Nevertheless, the previous studies of ligand **4** in Pb^{2+}-transport experiments through polymeric inclusion membrane revealed very good selectivity for Pb^{2+} over i.e. Cd^{2+}. Two different solutions: one containing a mixture of Pb^{2+}, Zn^{2+} and Cd^{2+} cations and the second consisting of Co^{2+}, Ni^{2+} and Pb^{2+} cations at equimolar concentration were prepared. It occurred that only Pb^{2+} was transported across the membrane, whereas transport of Zn^{2+} was less than 3% and the rest of the cations remained in the source phase [38].

The electrode with **2**/NPOE membrane could be used to determine Pb^{2+} in real samples because of its high selectivity. However, it must be noted that the Ca^{2+} ions might interfere when present in a 1000-fold excess. On the other hand, the "double" sensitivity may be useful in analytical applications and in the absence of Pb^{2+}

cations, the electrode **2**/NPOE could be successfully used to determine the concentration of Ca^{2+} ions in real samples.

4. Conclusions

In this paper, *p-tert*-butylcalix[4]arene appended with hydroxamic acid moieties were prepared, among which, the ligand **1** is reported here for the first time.

The ligands studied here were shown to be efficient extractants of Fe^{3+} and Cu^{2+}. For the rest of the cations tested, better extraction was observed in the case of ligands **1** and **3**, unsubstituted on nitrogen atoms, with particularly high Pb^{2+} extraction level.

Competitive extraction experiments revealed that for ligand **3**, the extraction of Pb^{2+} in the presence of Cd^{2+} was almost quantitative and higher than for individual experiments, whereas the percentage of Cd^{2+} extraction was lower compared to the individual extraction. It is very important in the context of the removal and separation of Pb^{2+} from other toxic metal ions such as Cd^{2+}. In addition, it was shown that ligands **2** and **4** possess the best selectivity for Cu^{2+} over Zn^{2+} and Ni^{2+} and could be successfully used in separation processes of Cu^{2+} from Zn^{2+} and Ni^{2+}, often present together.

Despite weak Pb^{2+} extraction, ligands **2** and **4** act as Pb^{2+}-selective ionophores. The studies in ion-selective electrodes showed that a particularly good selectivity was found with **2**/NPOE membranes for Pb^{2+} over Na^+, Cd^{2+} and Cu^{2+} and the electrodes based on ionophore **2** might be useful in analytical application.

Acknowledgements

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