

Lower rim substituted *p*-*tert*-butyl calix[4]arene; Part 14. Synthesis, structures and binding studies of calix[4]arene thioamides

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Abstract A number of *p*-*tert*-butylcalix[4]arene thioamides were synthesized and characterized by ¹H-NMR and elemental analysis. Compounds **1–5** are *O*-substituted derivatives with –CH₂–C(=S)–N–X groups, where NX = morpholidyl, NEt₂, NHC₂H₄Ph, NHCH₂Ph and NHEt, respectively. The X-ray structures of the ligands **1**, **3**, **5** and of the complex **3**·Pb(ClO₄)₂, (compound **6**), are presented and their slightly distorted *cone* conformation is established. The influence of the nature of the thioamide functions (secondary or tertiary) on the extractability of some selected metal cations was investigated. Whereas all these calixarenes show the highest extraction level for Ag⁺, tertiary thioamides are more efficient extractants for Pb²⁺ than secondary thioamides.

Keywords *p*-*tert*-butylcalix[4]arene thioamides · Synthesis · Crystal structure · Liquid–liquid extraction

Introduction

High impact is put nowadays to control the level of toxic heavy metals, like lead, cadmium, copper or mercury, in natural waters, which may cause great risk to human health. Our objective in this work was to design ligands possessing the ability of binding these metal cations. Previous studies have shown that the versatile ionophoric properties of chemically modified calixarenes depend greatly on the nature of the different substituents attached to the calixarene scaffold [1–6]. The introduction of soft donor atoms such as phosphorus or sulphur atoms into calix[4]arene substituents has been shown to promote their complexing ability towards transition and heavy metal ions [7]. For example the replacement of the amide carbonyl oxygen atoms of amide groups by sulphur atoms leading to thioamides [8, 9]. The X-ray crystal structure of the lead complex of the *p*-*tert*-butylcalix[4]arene diethylthioamide (**2**) showed that Pb²⁺ was bound to the four ethereal oxygen and the four thiocarbonyl sulphur atoms of the ligand in the *cone* conformation.

This paper reports the synthesis and the characterization of new calix[4]arene ligands appended with tertiary (compound **1**) and secondary thioamide moieties (compounds **3–5**). The X-ray structures of the free ligands **1**, **3** and **5** and of the lead complex of **3** (compound **6**) are also presented. A first estimation of the binding properties of these compounds towards a selection of metal ions (Na⁺, Ca²⁺, Cu²⁺, Zn²⁺, Pb²⁺, Ag⁺ and Gd³⁺) has been investigated by liquid–liquid extraction of the corresponding metal picrates from water into dichloromethane. The results have been compared to those previously obtained with the *p*-*tert*-butylcalix[4]arene diethylthioamide (**2**) [8, 9], which was re-synthesized in this work.

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Experimental

General

$^1\text{H-NMR}$ spectra were recorded in CDCl_3 on a Varian spectrometer (200 MHz). Elemental analysis was done on Carlo Erba Instruments CHNS-O EA1108—Elemental Analyzer. They both confirmed the structure and purity of the compounds. The absorbances were measured on a Shimadzu UV-2101 spectrophotometer.

Chemicals

Organic reagents and solvents (dichloromethane, methanol and toluene) were reagent grade and were used without further purification. The starting materials, amides **A–E**, all in the *cone* conformation, were obtained with good yields (78–85%) and in some cases with excellent yields (91–98%) by the procedure described before [3, 6]. Lawesson's Reagent was purchased from Aldrich. The metal picrates were obtained according to the procedures described in the literature, starting from Na^+ hydroxide [10], Ca^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} and Gd^{3+} carbonates [11] and Pb^{2+} acetate [12]. Pb(II) perchlorate trihydrate, 98%, was from Sigma–Aldrich.

Synthesis

The thioamides **1–5** were prepared according to the reaction shown in Scheme 1, by the following procedure [13]:

The respective calix[4]arene amide (**A**, **B**, **C**, **D** or **E**), (0.3 mmol) and the Lawesson's Reagent (2.1 equiv.) dissolved in dry toluene were stirred overnight at 90°C under argon. After that time, the solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2

and then washed with water. The organic phase was dried over MgSO_4 and evaporated under reduced pressure. After solvent removal the thioamides **1–5** were obtained as pale brown or yellowish products after crystallization from the CH_2Cl_2 – MeOH mixture, or if necessary were purified by means of silica gel chromatography. In the case of **1**, **3** and **5** single crystals suitable for X-ray analysis were obtained after few weeks or months of slow solvent evaporation. The characteristics of the compounds **1–5** are presented below.

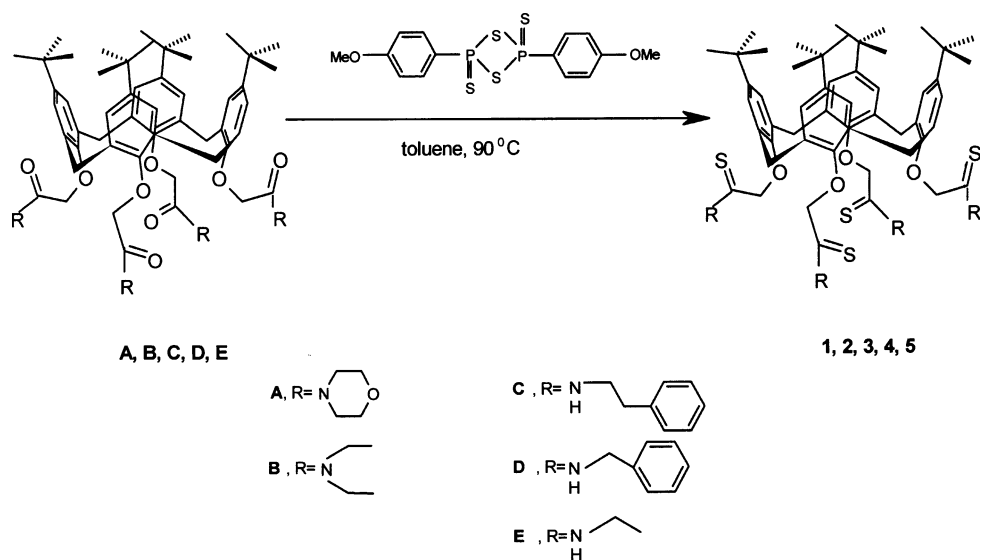
25, 26, 27, 28-Tetrakis(thiomorpholidylmethoxy)-*p*-tert-butylcalix[4]arene (**1**)

$\text{C}_{68}\text{H}_{92}\text{O}_8\text{N}_4\text{S}_4$ M.W. 1221.7, yield 59%, m.p. 240 – 245°C , $^1\text{H-NMR}$ (200 MHz, CDCl_3): *cone* conformation δ [ppm]: 1.08 (s, 36H, *t*-Bu); 3.16 (d, 4H, ArCH_2Ar , $J = 12.83$ Hz); 3.48 (bs, 8H, H_{morph}); 3.71–3.77 (m, 16H, H_{morph}); 4.34 (bs, 8H, H_{morph}); 4.88 (d, 4H, ArCH_2Ar , $J = 12.74$ Hz); 5.19 (s, 8H, OCH_2CO); 6.81 (s, 8H, ArH); Anal. calculated for $\text{C}_{68}\text{H}_{92}\text{O}_8\text{N}_4\text{S}_4$: C 66.79, H 7.58, N 4.58, S 10.47%; Found: C 66.91, H 7.70, N 3.56, S 9.79%.

25, 26, 27, 28-Tetrakis(diethylthiocarbamoylmethoxy)-*p*-tert-butylcalix[4]arene (**2**)

$\text{C}_{68}\text{H}_{100}\text{O}_4\text{N}_4\text{S}_4$, M.W. 1165.8, yield 68%, m.p. 212 – 218°C , $^1\text{H-NMR}$ (200 MHz, CDCl_3): *cone* conformation δ [ppm]: 1.08 (s, 36H, *t*-Bu); 1.24 (t, 12H, NCH_2CH_3); 1.32 (t, 12H, NCH_2CH_3); 3.17 (d, 4H, ArCH_2Ar , $J = 12.69$ Hz); 3.61 (q, 8H, NCH_2CH_3); 3.98 (q, 8H, NCH_2CH_3); 4.76 (d, 4H, ArCH_2Ar , $J = 12.21$ Hz); 5.09 (s, 8H, OCH_2CO); 6.79 (s, 8H, ArH); Anal. Calcd. for $\text{C}_{68}\text{H}_{100}\text{O}_4\text{N}_4\text{S}_4$: C 70.06, H 8.65, N 4.81, S 11.0%; Found: C 69.67, H 8.57, N 4.38, S 11.18%.

Scheme 1 The synthesis of thioamides **1–5**



25, 26, 27, 28-Tetrakis(*N*-phenylthiocarbamoylmethoxy)-*p*-tert-butylcalix[4]arene (3)

C₈₄H₁₀₀O₄N₄S₄, M.W. 1374.9, yield 64%, m.p. 233–235 °C, ¹H-NMR (200 MHz, CDCl₃): *cone* conformation δ[ppm]: 1.08 (s, 36H, *t*-Bu); 2.99 (t, 8H, HNCH₂CH₂Ar); 3.11 (d, 4H, ArCH₂Ar, *J* = 13.35 Hz); 4.06 (d, 4H, ArCH₂Ar, *J* = 13.56); 4.06 (m, 8H, HNCH₂CH₂Ar); 4.81 (s, 8H, OCH₂CO); 6.73 (s, 8H, ArH); 7.22–7.26 (m, 20H, ArH_{Benzyl}); 8.70 (t, 4H, NH); Anal. Calcd. for C₈₄H₁₀₀O₄N₄S₄: C 74.29, H 7.42, N 4.13, S 9.43%; Found: C 73.85, H 7.41, N 3.99, S 9.32%.

25, 26, 27, 28-Tetrakis(*N*-benzylthiocarbamoylmethoxy)-*p*-tert-butylcalix[4]arene (4)

C₈₀H₉₂O₄N₄S₄, M.W. 1301.9, yield 69%, m.p. 191–194 °C, ¹H-NMR (200 MHz, CDCl₃): *cone* conformation δ[ppm]: 1.06 (s, 36H, *t*-Bu); 3.00 and 4.17 (d, 4H, ArCH₂Ar, *J* = 13.18 Hz); 4.81 (s, 8H, OCH₂CO); 4.97 (d, 8H, HNCH₂Ar); 6.66 (s, 8H, ArH); 7.26–7.35 (m, 20H, ArH_{Benzyl}); 8.65 (t, 4H, NH); Anal. Calcd. for C₈₀H₉₂O₄N₄S₄: C 73.81, H 7.12, N 4.30, S 9.85%; Found: C 72.1, H 7.03, N 4.08, S 9.61%.

25, 26, 27, 28-Tetrakis(*N*-ethylthiocarbamoylmethoxy)-*p*-tert-butylcalix[4]arene (5)

C₆₀H₈₄O₄N₄S₄, M.W. 1053.6, yield 72%, m.p. 263–264 °C, ¹H-NMR (200 MHz, CDCl₃): *cone* conformation δ[ppm]: 1.09 (s, 36H, *t*-Bu); 1.24–1.33 (m, 12H, HNCH₂CH₃); 3.35 (d, 4H, ArCH₂Ar, *J* = 12.9 Hz); 3.83–3.89 (m, 8H, HNCH₂CH₃); 4.35 (d, 4H, ArCH₂Ar, *J* = 12.9 Hz); 4.91 (s, 8H, OCH₂CO); 6.82 (s, 8H, ArH); 8.60 (bs, 4H, NH); Anal. Calcd. for C₆₀H₈₄O₄N₄S₄: C 68.40, H 8.04, N 5.32, S 12.15%; Found: C 68.39, H 7.99, N 4.24, S 10.39%.

Synthesis of the complex (6)

Compound **3** (15 mg, 0.011 mmol) was dissolved in a minimum amount of methylene chloride. Subsequently, a solution of Pb(ClO₄)₂ trihydrate (0.044 mmol) in methanol was added. The resultant solution was stored at room temperature for several months yielding single crystals of **6** suitable for X-ray analysis; m.p. 273–274 °C.

X-ray structure analysis of compounds **1**, **3**, **5** and **6**

General remarks

Structures of **1**, **3**, **5** and **6** were solved by direct methods and all non-hydrogen atoms were refined with anisotropic thermal parameters by full-matrix least squares procedure based on *F*². All hydrogen atoms were refined using

isotropic model with *U*_{iso}(*H*) values fixed to be 1.5 times *U*_{eq} of C atoms for CH₃ or 1.2 times *U*_{eq} for CH₂ and CH groups. N–H were refined free with N–H distances fixed at 0.88 Å and *U*_{iso}(*H*) was refined free or fixed at 0.050. Solutions and refinements were carried out using the SHELX-97 program package [14].

Details of X-ray diffraction data determination

Experimental diffraction data were collected on KM4CCD kappa-geometry diffractometer, equipped with a Sapphire2 CCD detector. Enhanced X-ray MoK α radiation source with a graphite monochromator was used. Determination of the unit cells and data collection were carried out at 120 K. Data reduction, absorption correction, space group determination, solution and refinement were made using Crysalis software package (Oxford Diffraction, 2008) [15]. Single frame exposure time was adjusted to obtain reliable data for crystals of poor scattering power. Nevertheless, this parameter could not be set longer than 90 s due to serious ice-forming problems encountered.

Details related with structure determinations for specific samples are listed below.

Compound 1 One morpholine arm (starting from O1 atom) was found to be disordered over two positions, occupied with probabilities: 0.766(10)/0.234(10). The group was restrained to have identical C–C and C–N bond lengths in both parts. Additionally, *tert*-butyl group C68, C69, C70 was also found disordered over two positions with occupation factors of 0.515(16)/0.485(16). Solvating dichloromethane molecule was modeled as disordered over two positions with occupation probabilities of 0.768(6)/0.232(6). A second solvent molecule, present in the structure, was identified as methanol. Since it is disordered (0.63/0.37) and located close to the inversion centre, it was refined using isotropic displacement parameters and C–O distance restrained to *d*(C–O) = 1.435(1) Å. We decided not to attribute hydrogen atoms to the molecule as it would be very speculative.

Compound 3 The quality of the structure is not high due to the low diffracting power of the specimen (all were similar), but it is supported by similarity to the related structure of its lead perchlorate complex **6**. Most of the atoms but sulphur atoms were refined in isotropic model in order to keep the data to parameter ratio at reasonable level. Conformation of the calixarene portion of the molecule can be analyzed with rather good confidence. A single ethylphenyl group is disordered over two positions with occupancies 0.543(7)/0.457(7). This group was refined with both parts constrained to have the same bond lengths as the respective ordered groups. Additional restrains were applied to assure proper shape of the phenyl groups. One tertiary butyl group C59–C62 was modeled as disordered

over two positions 0.549(15)/0.451(15). A molecule of water was found in a position that generates a hydrogen bond of the N–H···O type.

Compound 5 One *tert*-butyl group C57–59 is disordered over two positions with probabilities 0.60(3)/0.40(3). The structure contains two solvent accessible voids of volume ca. 100 Å³. Program PLATON/SQUEEZE [16] revealed that each void is occupied by disordered molecules possessing ~17 e, probably methanol (see CIF file). The electron density is smeared so much, that no well defined position of a solvent could be found. The voids are placed between the calixarene molecule, outside the cone.

Compound 6 Relatively strong scattering power of **6** crystals allowed to collect diffraction data with shorter frame exposure times. It appeared necessary to apply numerical absorption correction. The structure contains voids (of volume ca. 38 Å³) at the calixarene cone. Search with PLATON routines revealed no solvent molecules trapped in the voids.

Extraction studies

Extraction studies were carried out according to the Pedersen procedure [17] as follows:

Five milliliter of the aqueous solution of each metal picrate and 5 mL of CH₂Cl₂ solution of respective calix[4]arene, each of the same concentration 2.5×10^{-4} mol/L, were introduced into tubes with stoppers. After 10 min of vigorous shaking, followed by 30 min of magnetic stirring in a thermostated water bath at 20 ± 0.1 °C, the tubes were left standing for at least 30 min without stirring, in order to complete phase separation. The percentage of cation extracted (%E) from water into dichloromethane was determined from the absorbance (A) of the picrate anion remaining in the aqueous phase after extraction at $\lambda_{\max} = 355$ nm and from the absorbance (A₀) of a blank experiment without ligand.

$$\%E = 100(A_0 - A)/A_0$$

Results and discussion

Synthesis

All the ligands studied were obtained with rather good yield (59–72%) in a one-step synthesis, shown in Scheme 1. This relatively easy synthetic route, using the Lawesson's Reagent, regarded as a convenient and efficient thionating agent, led to the desired compounds. Their *cone* conformation was confirmed by ¹H-NMR spectroscopy and, in the case of compounds **1**, **3** and **5**, by X-ray structural analysis.

X-ray diffraction data

Single crystals suitable for X-ray analysis were obtained for the ligands **1**, **3** and **5**. The corresponding X-ray molecular structures are presented in Figs. 1, 2, 3 and 4, respectively. For calixarene **3** we managed to obtain monocrystals of its complex with Pb(ClO₄)₂, which allowed to determine also the structure of **6**, presented in Fig. 5.

Up to now, only two X-ray structures of calixarenes substituted with thioamides were known. The first one corresponds to a bis-substituted calix[4]arene with two distal –CH₂–C(=S)–NEt₂ groups at the oxygen atoms of the lower rim [18]. The authors noted that, in this structure, the thioamide groups “are oriented in a divergent fashion”. The second structure is that of the complex of compound **2** with Pb(ClO₄)₂ [9]. The X-ray structure of the free (uncomplexed) ligand **2** still remains unknown, which hinders direct study on the conformational changes of the ligand upon complexation. Such a possibility emerges now in the case of the thioamide **3**, bearing –CH₂–C(=S)–NH–C₂H₄Ph arms, for which both structures—of the free ligand and of its lead perchlorate complex—are accessible.

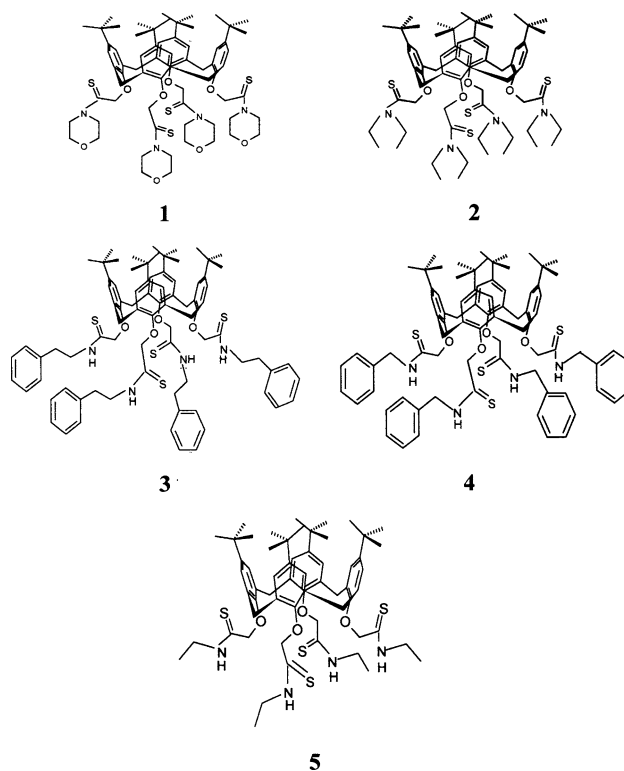


Fig. 1 Chemical structures of the studied ligands 1–5

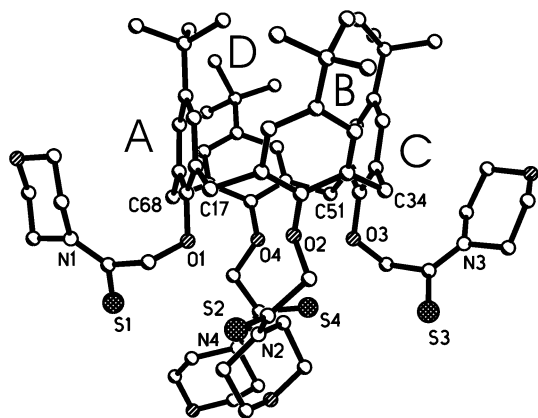


Fig. 2 Molecular structure of the compound **1** showing rings and atoms numbering scheme. Hydrogen atoms, solvent molecules and less-populated disorder parts are omitted

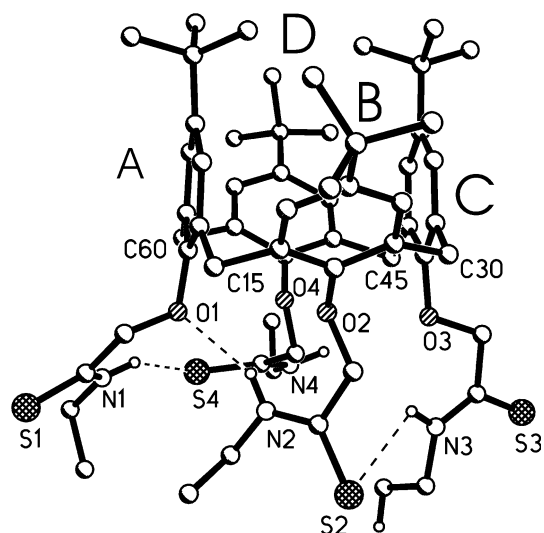


Fig. 4 Molecular structure of the compound **5** showing rings and atoms numbering scheme. Hydrocarbonic H atoms and less-populated disorder parts are omitted. Rings **A** and **C** are almost parallel—dihedral angle 3.77° , dihedral angle between **B** and **D**: 83.55° . Some intramolecular hydrogen bond of the N–H...O and N–H...S type can be found

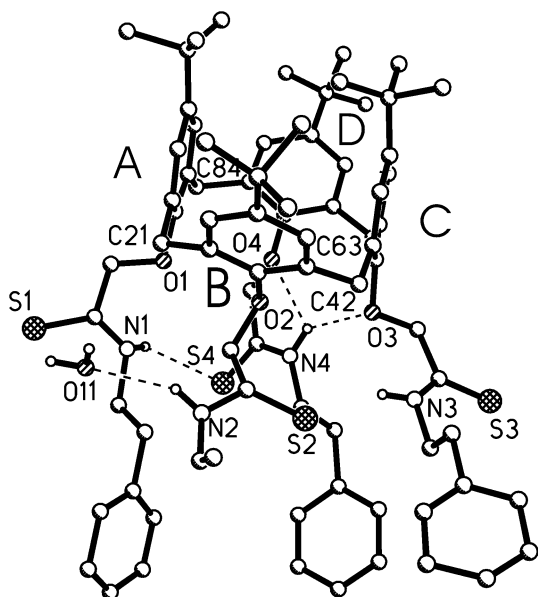


Fig. 3 Molecular structure of the compound **3**. A view showing its pinched cone conformation with two phenyl rings **B** and **D** almost parallel, and rings **A** and **C** almost perpendicular, one intramolecular N–H...S bond and two intramolecular N–H...O bond are presented. The water molecule is linked by N2–H2...O11 hydrogen bond. One phenyl ring was omitted for clarity

X-ray structure of **1**

X-ray structural analysis of single crystals proved that compound **1** adopts a pinched *cone* conformation, with *tert*-butyl groups pitched away from the open cavity. Conformation of the calixarene has been analyzed by calculation of dihedral angles of the rings **A–D** to a reference plane **R** passing through the methylene bridging carbon

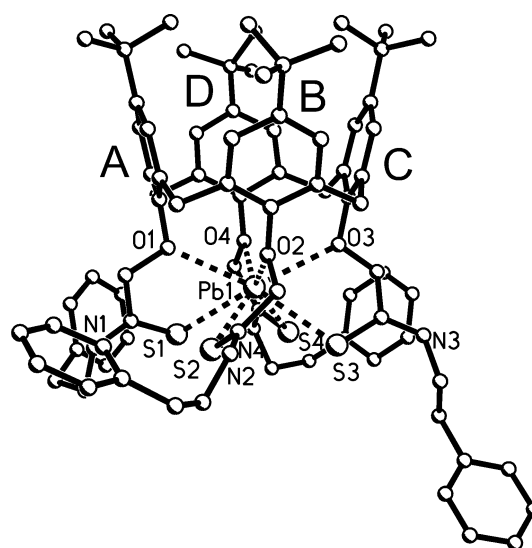


Fig. 5 Molecular structure of the compound **6** (side view)

atoms (see Table 3). Rings **A** and **C** can be regarded as almost parallel (dihedral angle between rings **A–C** is 9.76°), whereas the rings **B** and **D** are oriented at the angle of 74.62° (Fig. 2). No solvent molecule was found inside the cone. Strong hydrogen bonds are not found due to lack of a good hydrogen donor group. Thiocarbonyl groups are directed outside the center in positions optimal for weak dispersion intermolecular interactions such as C–H...S contacts. This is analogous to the conformation of the bis-substituted thioamide calix[4]arene [18].

X-ray structure of **3**

In the structure of compound **3**, phenyl rings **A** and **C** are practically parallel and ring **B** is almost perpendicular to ring **D**. The dihedral angle between rings **B** and **D** is equal to 89.47° and the angle between rings **A** and **C** is equal to 1.24° . Thiocarbonyl groups are directed outside the center in positions optimal for intermolecular interactions. Their spatial orientation arise mainly from intramolecular N–H...O and N–H...S hydrogen bonds. Hydrogen bonds formed in the structure are specified in Tables 1 and 2. It is evident, that the conformation of the free ligand (**3**) needs

to be re-adjusted for coordination of a cation, which is observed in the structure of **3**·Pb(ClO₄)₂, described later (see compound **6**).

X-ray structure of **5**

Rings **A** and **C** can be regarded as almost parallel (the dihedral angle between **A** and **C** is 3.77°), whereas the rings **B** and **D** form a dihedral angle of 83.55° (Fig. 4). The lower rim conformation is influenced by N2–H2...O1 and weaker N1–H1...S4 and N3–H3...S2 intramolecular hydrogen bonds (see Table 2). The solid may be regarded

Table 1 Crystal data and structure refinement details for compounds **1**, **3**, **5** and **6**

Compound	1	3	5	6
Empirical formula	C ₇₀ H ₉₈ Cl ₂ N ₄ O ₉ S ₄	C ₈₄ H ₁₀₁ N ₄ O ₅ S ₄	C ₆₀ H ₈₄ N ₄ O ₄ S ₄	C ₈₄ H ₁₀₀ Cl ₂ N ₄ O ₁₂ PbS ₄
Molecular weight	1338.7	1374.93	1053.6	1764.0
Temperature (K)	120(2)	120(2)	120(2)	120(2)
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
Crystal system	Triclinic	Triclinic	Triclinic	Monoclinic
Space group	<i>P</i> -1	<i>P</i> -1	<i>P</i> -1	<i>P</i> 2 ₁ / <i>c</i>
Unit cell dimensions (Å)	a = 14.2270(8) b = 14.2806(7) c = 20.2219(11) $\alpha = 72.653(5)^\circ$ $\beta = 78.609(5)^\circ$ $\gamma = 64.411(5)^\circ$	a = 13.6442(6) b = 18.6204(8) c = 18.7831(6) $\alpha = 117.550(4)^\circ$ $\beta = 98.043(3)^\circ$ $\gamma = 97.077(4)^\circ$	a = 13.3430(7) b = 13.3822(7) c = 18.3147(11) $\alpha = 75.389(5)^\circ$ $\beta = 82.708(5)^\circ$ $\gamma = 88.147(4)^\circ$	a = 17.7053(4) b = 15.2829(3) c = 31.3300(7) $\alpha = 90^\circ$ $\beta = 102.839(2)^\circ$ $\gamma = 90^\circ$
Volume (Å ³)	3525.7(3)	4092.2(3)	3138.9(3)	8265.6(3)
Z	2	2	2	4
Density (calculated, Mg/m ³)	1.261	1.116	1.115	1.418
Absorption coefficient (mm ⁻¹)	0.268	0.166	0.196	2.269
F(000)	1432	1474	1136	3632
Crystal size	0.43 × 0.32 × 0.26	0.36 × 0.23 × 0.12	0.36 × 0.28 × 0.14	0.42 × 0.37 × 0.08 mm ³
θ range for data collection	1.98–26.00°	2.01–23.50°	2.20–25.50°	1.97–27.0°
Index ranges	–17 ≤ h ≤ 17, –17 ≤ k ≤ 14, –24 ≤ l ≤ 24	–16 ≤ h ≤ 15, –21 ≤ k ≤ 22, –22 ≤ l ≤ 18	–14 ≤ h ≤ 16, –15 ≤ k ≤ 16, –22 ≤ l ≤ 22	–17 ≤ h ≤ 22, –11 ≤ k ≤ 19, –39 ≤ l ≤ 34
Reflections collected	26614	28507	21538	34963
Independent reflections	13818 [R(int) = 0.0621]	14391 [R(int) = 0.0853]	11574 [R(int) = 0.1040]	17768 [R(int) = 0.0386]
Completeness to theta (%)	26.00° 99.6	25.01° 99.7	25.50° 99.1	27.0° 98.4
Absorption correction	None	None	None	Empirical
Refinement method	Full-matrix least-squares on F ²	Full-matrix least-squares on F ²	Full-matrix least-squares on F ²	Full-matrix least-squares on F ²
Data/restraints/parameters	13818/22/871	14391/54/475	11574/6/708	17768/0/964
Goodness-of-fit on F ²	1.108	1.220	1.091	0.936
Final R indices [I > 2σ(I)]	R1 = 0.1044, wR2 = 0.2462	R1 = 0.1598, wR2 = 0.4013	R1 = 0.1091, wR2 = 0.295	R1 = 0.0377, wR2 = 0.0846
Frame exposure (s)	80	90	90	15
Largest diff. peak and hole (e·Å ⁻³)	0.788 and –0.590	1.239 and –0.673	0.787 and –0.698	1.684 and –1.250

Table 2 Geometry of hydrogen bonds (Å, °) in structures of **3**, **5** and **6** (D donor, A acceptor)

Compound	Atom labels	D–H	H···A	D···A	Angle (DHA)
3	N1–H1···S4	0.86(4)	2.81(4)	3.568(13)	147(4)
	N2–H2···O11	0.88(4)	2.30(7)	3.11(2)	151(11)
	N4–H4···O3	0.89(4)	2.27(6)	2.967(9)	134(6)
	N4–H4···O4	0.89(4)	2.18(6)	2.684(9)	115(5)
5	N2–H2···O1	0.89(3)	2.19(4)	3.006(6)	152(6)
	N1–H1···S4	0.85(3)	2.72(5)	3.368(6)	134(5)
	N3–H3···S2	0.87(3)	3.22(6)	3.726(7)	120(5)
6	N1–H1···O9	0.88(4)	2.47(4)	3.124(5)	131(3)
	N1–H1···O10	0.88(4)	2.33(4)	3.206(5)	171(3)
	N2–H2···O8#1	0.88(4)	2.06(4)	2.940(4)	177(4)
	N3–H3···O11#2	0.88(6)	2.29(6)	3.147(5)	165(5)
	N3–H3···O12#2	0.88(6)	2.37(6)	3.053(5)	135(5)
	N4–H4···O7	0.95(4)	1.98(4)	2.878(4)	157(3)

Symmetry codes: #1: x, y + 1, z; #2: x, -y + 3/2, z + 1/2

as a molecular crystal with no strong specific intermolecular interactions.

X-ray structure of **6**

This is the second example of the X-ray structure of a lead perchlorate complex with a calix[4]arene thioamide derivative. The Pb-complex of the calix[4]arene diethyl thioamide **2**, described in [9] contained (in average) half of a water molecule trapped in the cone void. Both structures show some similarities. The Pb²⁺ cation in **6** is bound to four ethereal oxygen atoms and four thiocarbonyl sulphur atoms. Coordination polyhedron can be regarded as distorted tetragonal (square) antiprism. The upper, oxygen “square” is twisted by angle of *ca* 32° in relation to the lower sulphur tetragon. As a measure of the twist we used the dihedral angle between the planes defined by O1–Pb1–O3 and S1–Pb1–S3. A similar twist angle (33°) was found in the structure of the complex described in [9]. The Pb–O bond lengths are in the range of 2.717(2)–2.751(2) Å with the average of 2.728(2) Å whereas the Pb–S lay in the range of 2.869(1)–

2.977(1) Å with the mean of Pb–S 2.933(1) Å. Pb–O bonds are slightly longer than in previously described Pb-complex of compound **2** [9]. Pb–S bonds in both complexes have similar lengths. Torsion angles O–C–C–S in the chelating fragments are more diverse in the present structure (–8.3(4); 43.3(4); 22.8(4); 9.1(4)° vs. 0(1); 17(1); 14(1); 2(1)° found in [9]. Torsions angles Pb–S–C–N are more consistent than found previously in the lead complex of **2** (–151.9(3); –176.9(3); –169.8(3); –158.4(3)° vs. 139(3); 147(4); 153(3), 147(3)°. Nevertheless, one must remember those are the angles which belong to different types of thioamides: secondary C(=S)NH–C₂H₄Ph (**6**) and tertiary C(=S)NET₂ (complex with **2**).

The conformation of **6** is more regular (less pinched) than that of the free ligand **3**. Notable difference in conformation between the complex **6** and the ligand **3** is the orientation of the aromatic rings **B** and **D** which in **6** are not orthogonal anymore (dihedral angle of 52.7(9)°, Fig. 5). The dihedral angles between the reference plane **R** and rings **A–D** are quite uniform and are in the range of 62.9–77.4° (see Table 3). In the related complex with **2** the corresponding angles vary from 65 to 71° (after rescaling as complement to 180°) [9]. Because the cone is less “pinched” small void of volume 38 Å³ is created inside the cone. In contrast to earlier structure in **6** this void is not occupied by solvent molecule. As expected, all the thiocarbonyl sulphur atoms are directed towards the lead atom. It follows that N–H groups, being hydrogen bond donors, are oriented outside. The perchlorate anions are located in positions optimal for intermolecular hydrogen bonding of the N–H···O type. Some of the bonds (NH1 and NH3 as donors) are bifurcated (see Fig. 6 and Table 2). Figure 6 also shows the clockwise twist of all four ethylphenyl residues around the calixarene core. Clearly, because the space group is centrosymmetric, both enantiomers are present in the crystal.

Extraction

Extraction data for thioamides **1–5** are given in Table 4. It is clear that the thioamides studied here are inefficient

Table 3 Conformation of the calix fragment for compounds **1**, **3**, **5** and **6**

	1	3	5	6
Reference plane	Defining atoms, r.m.s deviation from the mean plane [Å]			
R	C17–C34–C51–C68, 0.0326	C21–C42–C63–C64 0.0977	C15–C30–C45–C60, 0.1836	C21–C42–C63–C64, 0.0255
Defining rings	Dihedral angles between the planes [°]			
A–R	89.87 (0.12)	86.84(0.21)	88.88 (0.15)	77.38(0.09)
B–R	52.26 (0.10)	46.83 (0.23)	39.74 (0.20)	62.93(0.09)
C–R	80.22 (0.12)	85.14 (0.17)	87.56 (0.16)	76.37(0.08)
D–R	53.18 (0.13)	42.68(0.29)	43.81 (0.10)	64.35(0.09)

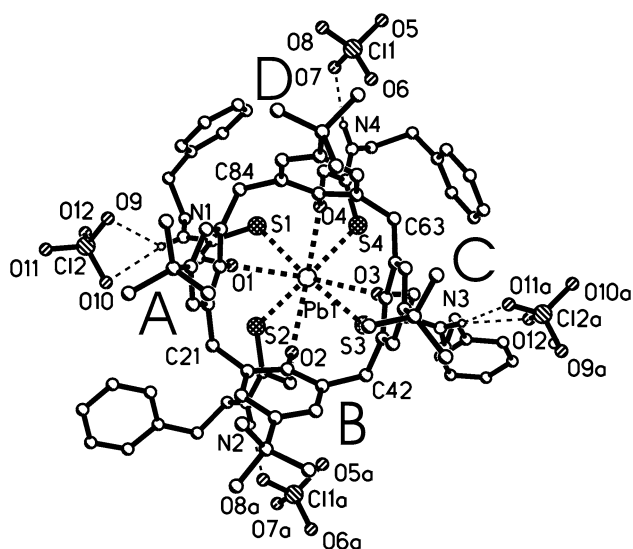


Fig. 6 Molecular structure of the compound **6** showing rings and atoms numbering scheme. Hydrocarbonic H atoms are not shown. In order to show hydrogen bonding network two neighbour symmetry equivalents of perchlorate anions are drawn. Detailed description of the bonds is given in Table 2

Table 4 Extraction (%E)^a of metal picrates ($C_M = 2.5 \times 10^{-4}$ M) with calix[4]arene-thioamides **1–5** ($C_L = 2.5 \times 10^{-4}$ M) from water into dichloromethane (organic to aqueous phase ratio $o/a = 1$, $T = 20$ °C)

M^{n+}	1	2	3	4	5
Na^+	6.3	7 ^b	≤1	2.0	≤1
Ca^{2+}	4.6	≤1	1.6	2.8	≤1
Cu^{2+}	14.5	19.0 ^b	2.3	2.9	1.9
Zn^{2+}	1.6	≤1	≤1	≤1	≤1
Gd^{3+}	4.8	≤1	≤1	1.6	≤1
Ag^+	99.2	80.0 ^b	98.0	85.5	92.1
Pb^{2+}	50.9	56.0 ^b	≤1	≤1	≤1

^a Values with uncertainties less than 5%

^b Data from [9]

extractants for alkali and alkaline earth metal ions and for lanthanide(III) cations (at least for Gd^{3+}). In contrast they all extract almost quantitatively Ag^+ (%E ≥ 80). The extraction level of Pb^{2+} depend strongly on the type of the thioamide function: %E values of 51 and 56 have been found with the tertiary thioamide derivatives **1** and **2**, whereas almost no extraction (%E ≤ 1) could be noticed with the secondary thioamide derivatives **3–5**. Among the transition metal ions, only Cu^{2+} is fairly extracted by the tertiary thioamide derivatives **1** and **2** (%E = 14.5 and 19.0, respectively). But again the secondary thioamide derivatives were found to be inefficient with this kind of cations. The influence of the amide type on the cation binding has already been noticed [5, 19]. It has been

reported that calix[4]arene derivatives based on secondary amide functions were inefficient in extraction of alkali and alkaline earth picrates probably due to intra- and intermolecular hydrogen bonding combined to the high hydrophilicity of the extracted complexes [19]. It has also been proved that intramolecular hydrogen bonding in calix[4]arenes bearing amino acids affected the extractability towards metal ions [20]. According to literature data, thioamides are weak hydrogen bond acceptors but strong hydrogen bond donors in comparison to amides due to the electronegativity of the sulphur atom [21]. Therefore, secondary thioamides should have a strong ability to form hydrogen bonds which is supported by the observation in the crystal structure of ligand **3** of several intramolecular hydrogen bonds (Table 2). In the structure of ligand **5** also hydrogen bonds, of the N–H···O and N–H···S type, are present. Tertiary thioamides have no N–H donor group, so these interactions are not possible. Moreover, secondary thioamides can interact with water molecules increasing the affinity of the ligand for the aqueous phase. This fact may explain, as with calix[4]arene amide derivatives, the very low effectiveness of ligands **3**, **4** and **5** for Pb^{2+} and other transition and heavy metal cations.

Conclusion

The extraction results show the low affinity of calix[4]thioamides for alkali and alkaline earth metal ions and lanthanide cations, contrary to most of the tertiary amides studied so far, which are good extracting agents for these metal ions. This is easily explained by the presence in thioamides, of soft sulphur atoms having a preference for soft cations like Ag^+ . The results also show that this affinity is strongly dependent (as it was previously shown in the amide series) on the nature of the thioamide attached to the calixarene framework. The dramatic drop in the extraction levels on going from the tertiary to the secondary thioamide derivatives is certainly due to the presence of donor N–H group enabling intramolecular hydrogen bonding in these ligands and intermolecular interactions with aqueous phase. The ionophoric properties of compounds **1–5** in ion selective PVC-membrane electrodes (ISEs) were also studied and are presented in a separate paper [22].

Supplementary material

Crystallographic data for the structures reported in this paper **1**, **3**, **5** and **6** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication No. CCDC 719145, CCDC 748376, CCDC 719144 and CCDC 748377, respectively. Copies of the data can be

obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: (+44) 1223-336-033; E-mail: deposit@ccdc.cam.ac.uk)

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