



The Synthesis of Nitrogen-Containing Calixarene Derivatives and their Interactions with Lead Ions

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Abstract

Several new nitrogen-containing calixarene derivatives have been synthesized and their ion-binding properties investigated by UV spectroscopy and solvent extraction. These derivatives include 5,11,17,23-tetra-*t*-butyl-25,26,27,28-tetrakis(piperidinocarbonylmethoxy)calix[4]arene (**5**), 5,11,17,23,29,35,41,47-octa-*t*-butyl-49,50,51,52,53,54,55,56-octa(piperidinocarbonylmethoxy)calix[8]arene (**6**) and 5,11,17,23,29,35,41,47-octa-*t*-butyl-49,50,51,52,53,54,55,56-octa(*N,N*-diethylcarbamoylmethoxy)calix[8]arene (**7**). The UV spectra of **6** and **7** revealed they had an ability to transform tight lead picrate ion pairs into separated ones by complexation with Pb^{2+} in tetrahydrofuran. Both derivatives give 1 : 1 complexes with Pb^{2+} . Extraction studies showed that these derivatives could efficiently extract Pb^{2+} (as picrate salts) from the aqueous phase into chloroform. The extractability of these derivatives were also compared with that of the oxygen-containing ester derivative calix[8]arene **2** and the other two nitrogen-containing compounds **8** and **9**.

Introduction

Calixarenes are versatile building blocks for molecules with different properties. During the last two decades, they have attracted much attention as a kind of key receptors in supramolecular chemistry [1, 2]. The increasing interest in these compounds is stimulated by the simple large-scale synthesis of the calixarenes and the different ways in which they can be selectively functionalized at the lower (phenolic groups) or at the upper rim (aromatic nuclei). Recent developments in the synthesis of functionalized calixarenes have indeed led to some novel receptors suitable for complexation and separation of ions [3, 4]. From an environmental and economic viewpoint, there remains a need to discover more selective and effective extractants for the toxic heavy metals. The importance of controlling the levels of environmental pollutants has also generated increasing interest in the development of novel sensors such as calixarene-based ion-selective electrodes or chemically modified field effect transistors for the detection of the heavy metals [5–8]. In this point, lately more and more attention was paid on the calixarene derivatives with functional groups containing nitrogen, sulfur or phosphorus donor atoms because of their strong affinity for these metals such as Pb(II), Hg(II), Pd(II), Ag(I) [9–14].

The association of lead ions with the crown ether type of macrocyclic ligands has been extensively investigated and well documented [15–21]. However, only a few cases relate to calixarenes. Ohto and his co-workers reported the

adsorptive behavior of lead ions on the calix[4]arene tetracarboxylic acid immobilized resin [22]. Thioamide functionalized calixarenes [11, 23] and phosphine oxide derivatised calixarenes [12] have also been investigated as their potential application to ISEs or CHEMFET for lead ions. Among those calixarenes studied, most are devoted to calix[4]arene or its derivatives [24–27], and there are relatively fewer reports about the hexamers and the octamers of this kind of macrocyclic ligands. We report herein the synthesis and characterization of new nitrogen-containing calixarene derivatives **5**, **6** and **7** (shown in Figure 1). To study the ion-binding properties of these nitrogen-containing derivatives, the solvent extraction of Pb^{2+} with them as extractants and their complexation with Pb^{2+} in THF were investigated.

Experimental

Instrumentation and materials

^1H NMR and ^{13}C NMR spectra were recorded at 500 MHz using an AM500 spectrometer in CDCl_3 with TMS as an internal standard. IR spectra were recorded on a Nicolet FT-IR170SX spectrometer. UV-Visible spectra were obtained using a Perkin Elmer Lambda Bio40 spectrometer. Elemental analysis was performed on a Perkin Elmer 240 instrument.

Dichloromethane was distilled over P_2O_5 . THF and diethylamine were distilled and stored over sodium pellets. Triethylamine was dried by distilling over $(\text{CH}_3\text{CO}_2)_2\text{O}$. Piperidine was dried over KOH pellets. Water used here

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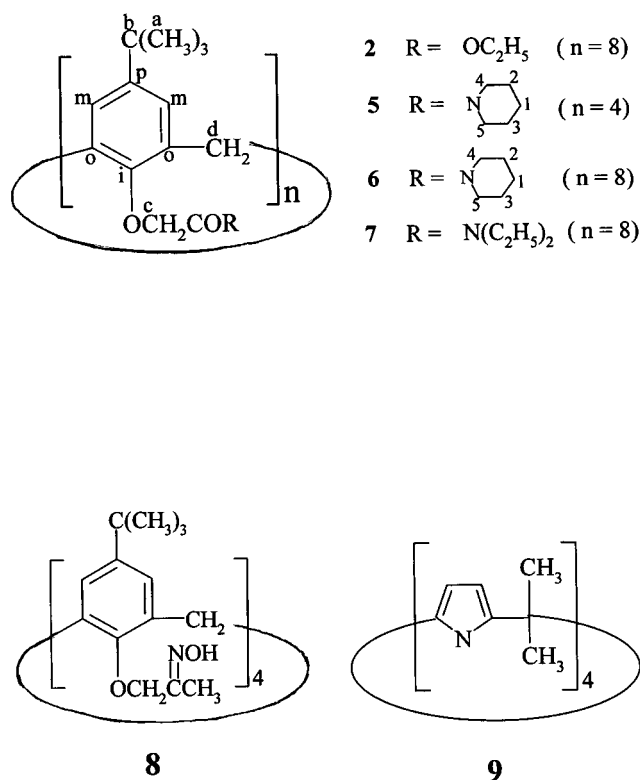
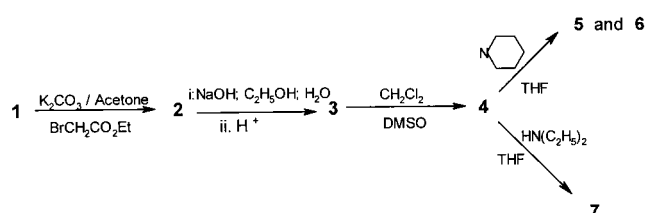


Figure 1. The structural formula of the derivatives **2**, **5**, **6** and **7** and the other two compounds **8** and **9**.



Scheme 1.

was de-ionized (with the conductivity of $1 \times 10^{-6} \text{ s} \sim 1 \times 10^{-7} \text{ s}$). All the other chemicals were of A.R. grade and were used without further purification.

Syntheses and characterization

The synthetic route is described in Scheme 1. Parent calix[n]arene **1** [28], the ester derivative **2** [29], the acid derivative **3** [29], the oximido derivative **8** [30] and the acetonepyrrole **9** [31] were prepared according to the literature methods. Acid derivative **3** was treated with thionyl chloride to afford the acid chloride derivative **4**, which without purification was treated with piperidine in THF to furnish the piperidine derivatives **5** and **6**, and with *N,N*-diethylamine in THF to furnish the diethylamide derivatives **7**.

The general procedure for synthesis is as follows:

Thionyl chloride (6 mL) was added dropwise to a solution of compound **3** (0.8 mmol) in dichloromethane (21 mL) under stirring. The reaction mixture was refluxed under N₂ atmosphere for 12 h. Solvent was then removed under vacuum to give a light yellow residue (derivative **4**). The dried THF (10 mL) was added to the residue. Then the mixture of

triethylamine (4 mL) and piperidine (4 mL) for **5** and **6** or diethylamine (4 mL) for **7** was added dropwise to the solution under stirring. After 24 h, all volatile components were removed under vacuum. Water was added. The insoluble material was collected by filtration and washed with water. Recrystallization from CH₂Cl₂/methanol gave the product in an analytical pure state.

For **5**, **11**, **17**, **23-tetra-*t*-butyl-25**, **26**, **27**, **28-tetrakis(piperidinocarbonylmethoxy)calix[4]arene (5)**: m.p. 284–286 °C. IR (KBr, ν^{-1} , cm^{-1}) 1658 (C=O stretching), 1356 ($-\text{C}(\text{CH}_3)_3$). ¹H NMR (CDCl₃, in ppm) 1.0 (36 H, s, $-\text{C}(\text{CH}_3)_3$), 1.45–1.54 (24 H, m, $-(\text{CH}_2)_3-$), 3.11 (4 H, d, *exo*-Ar-CH₂-Ar), 3.35–3.44 (16 H, m, N-CH₂), 4.92 (8 H, s, O-CH₂-CO), 5.01 (4 H, d, *endo*-Ar-CH₂-Ar), 6.71 (8 H, s, ArH). ¹³C NMR (CDCl₃) 24.69 (C¹), 25.63 (C²), 26.32 (C³), 31.41 (C^a), 32.13 (C^d), 33.705 (C^b), 42.47 (C⁴), 45.68 (C⁵), 71.73 (C^c), 125.26 (C^m), 133.56 (C^o), 144.34 (C^p), 153.76 (Cⁱ), 168.41 (C=O). Anal.: Calcd. for C₇₂H₁₀₀N₄O₈: C, 75.26; H, 8.71, N, 4.88. Found: C, 75.32; H, 8.66; N, 5.06.

For **5**, **11**, **17**, **23**, **29**, **35**, **41**, **47-octa-*t*-butyl-49**, **50**, **51**, **52**, **53**, **54**, **55**, **56-octa(piperidinocarbonylmethoxy)calix[8]arene (6)**: IR (KBr, ν , cm^{-1}) 1658 (C=O stretching), 1356 ($-\text{C}(\text{CH}_3)_3$). ¹H NMR (CDCl₃ in ppm) 1.01 (72 H, s, $-\text{C}(\text{CH}_3)_3$), 1.35 (48 H, m, $-(\text{CH}_2)_3$), 3.42 (48 H, m, N-CH₂) and Ar-CH₂-Ar), 4.16 (16 H, s, O-CH₂-CO), 6.84 (16 H, s, ArH). ¹³C NMR (CDCl₃) 24.21 (C¹), 25.43 (C²), 26.22 (C³), 29.87 (C^d), 31.45 (C^a), 34.17 (C^b), 42.49 (C⁴), 45.88 (C⁵), 71.74 (C^c), 126.02 (C^m), 132.60 (C^o), 146.10 (C^p), 153.55 (Cⁱ), 166.12 (C=O); Anal.: Calcd. for C₁₄₄H₂₀₀N₈O₁₆: C, 75.26; H, 8.71; N, 4.88. Found: C, 74.70; H, 8.22; N, 5.60.

For **5**, **11**, **17**, **23**, **29**, **35**, **41**, **47-octa-*t*-butyl-49**, **50**, **51**, **52**, **53**, **54**, **55**, **56-octa(*N,N*-diethylcarbamoylmethoxy)calix[8]arene (7)**: m.p. 281–282 °C. IR (KBr, ν , cm^{-1}) 1652 (C=O stretching), 1356 ($-\text{C}(\text{CH}_3)_3$). ¹H NMR (CDCl₃, ν^{-1} , ppm) 1.10–1.25 (120 H, m, $-\text{CH}_2$) 2.50–3.36 (48 H, m, Ar-CH₂-Ar and N-CH₂) 4.30 (16 H, s, O-CH₂-CO) 6.90 (16 H, m, ArH) Anal.: Calcd. for C₁₃₆H₂₀₀O₁₆N₈: C, 74.18; H, 9.09; N, 5.09. Found: C, 73.63; H, 8.86; N, 5.54.

UV - visible spectroscopy study

From a stock solution (10^{-4} mol/L) of tested compound in THF, aliquots of the solution were withdrawn and added to 5 mL THF solution (10^{-4} mol/L) of lead picrate. THF was then added and made up to a volume of 10 mL. The absorbance of the solutions were recorded in the range 250–500 nm at 25 °C.

Method for extraction

The extraction experiments were performed according to the following procedure: 5 mL solution (5.0×10^{-4} mol/L) of extractant in CHCl₃ and 5 mL aqueous solution (2.4×10^{-4} mol/L) of lead picrate with buffer (adjusting pH) and KNO₃ (adjusting ionic strength I = 0.1) were vigorously agitated in a stoppered glass tube with a mechanical

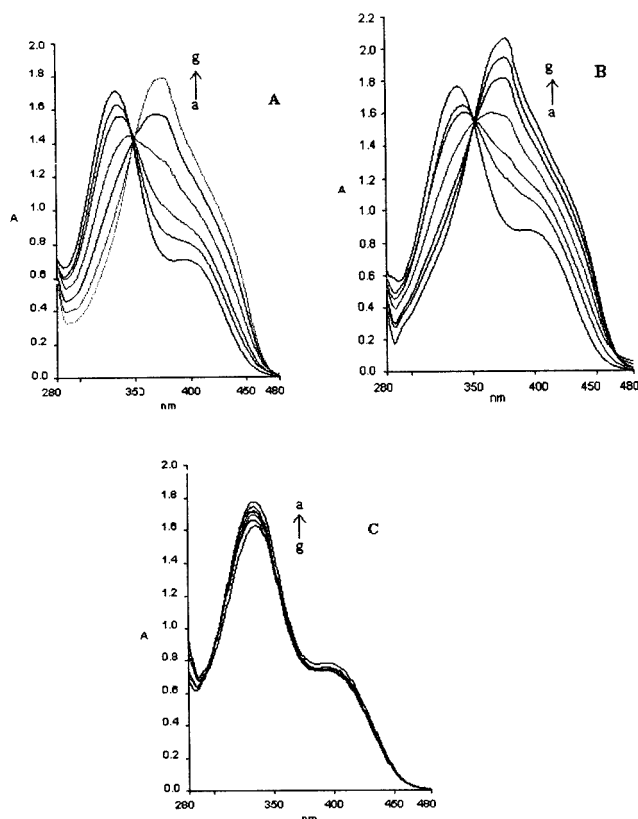


Figure 2. Absorption spectra of lead picrate in the absence and the presence of various amounts of **6** (A), **7** (B) and **2** (C); molar ratio of ligand (L) to lead picrate: a: 0; b: 0.2; c: 0.4; d: 0.5; e: 0.6; f: 0.8; g: 1.0.

shaker for 30 minutes under 30 °C. After the two phases were allowed to settle for 30 minutes, the concentration of Pb^{2+} retained in the aqueous phase was measured by means of the UV-Vis spectrometric analysis using 0.1% PAR as chromogenic agent. The extraction percentage of Pb^{2+} was calculated according to the difference between the initial and final concentration of Pb^{2+} in the aqueous phase. The pH value of the aqueous phase was also measured before and after the extraction.

At each extraction experiment, a blank experiment without extractant in the organic phase was conducted. All results reported here are the net results, after deducting the corresponding blank values and are the averages of more than three parallel extraction results.

Results and discussion

UV spectroscopies of derivative **2**, **6** and **7**

In order to demonstrate the suitability of these derivatives for Pb^{2+} complexation, the UV spectra of lead picrate ion pairs in THF were measured in the presence of different ligand/metal ratios. Similar behaviors were observed for compound **6** and **7**. As illustrated in Figures 2A and B, both present an isosbestic point at 350 nm, which indicates an equilibrium involving at least two absorbing species in solution.

Above 10^{-5} mol/L, the picrate salts are present in the form of tight ion pairs [32]. The absorption maximum λ_{max} of tight $\text{Pb}(\text{Pic})_2$ ion pairs (“Pic” stands for picrate anion) is 335 nm. For both derivatives, a common absorption maximum was observed at 378 nm, which is the λ_{max} of the free picrate anion. The bathochromic shifts of absorption maximum were caused by the addition of variable amounts of derivative **6** or **7** into the THF solution of lead picrate. This indicates that upon complexation full separation between Pb^{2+} and picrate has taken place. Taking the bathochromic shifts as reference, one can conclude that at least the bathochromic shift is to be related to the encapsulation of the Pb^{2+} in the ionophoric cavity of **6** and **7**.

The results suggested that these derivatives exhibited excellent complexation abilities for Pb^{2+} . For the ester derivatised calix[8]arene **2**, no shift in the absorption maximum was observed under similar conditions although a small absorbance decrease at 335 nm was found (see Figure 2C), which implies complex formation for compound **2** with Pb^{2+} is not significant enough to separate the Pb^{2+} and picrate anion fully and change the absorption spectrum of the lead picrate in THF.

Further studies revealed the formation of a 1 : 1 complex for both **6** and **7** with Pb^{2+} . The stoichiometry of the complex was determined by means of Job’s method, shown in Figure 3. The absorbance were measured at the λ_{max} 378 nm. The stability constants were calculated to be 2.36×10^5 for **6** and 2.84×10^5 for **7**. The molar absorptivities of the separated ion pair complexes of lead picrate with **6** and **7** were found at 378 nm to be 4.01×10^4 and 4.20×10^4 respectively.

Extraction studies

Extraction experiments were performed using these derivatives (**5**, **6** and **7**) as extractants with a series of pH values of the aqueous phase. To give a comparison, the same experiments were conducted with the oxygen-containing calix[8]arene derivative **2** and the other two nitrogen-containing compounds **8** and **9**. The extraction percentages for **8** and **9** were both found to be no more than 1. The results for others are illustrated in Figure 4.

As shown in Figure 4, the nitrogen-containing derivatives **5**, **6** and **7** have much higher extractabilities than the oxygen-containing calix[8]arene derivative **2** in a wide pH range. Although it was reported that tetracarboxylic acid derivatives could extract Pb^{2+} efficiently from acidic aqueous solution [33], no similar report for neutral derivatives containing donor atoms has been published to date. Sulfur-containing derivatives were found to be efficient extractants for Hg (II), Pd (II), Ag (I), but not for Pb^{2+} [8, 34]. So we can see that the introduction of a nitrogen atom to the lower rim of the calixarene increases the extractability of the calixarene appreciably. However, the calixarene derivative **8**, which also contains nitrogen in the lower substituted group, has no obvious extraction under our experiment conditions and also the acetonepyrrole **9**, which has a similar structure with the calixarenes. Comparison of the piperidine-containing derivatives **5**, **6**, and diethane-containing derivative **7** gives some

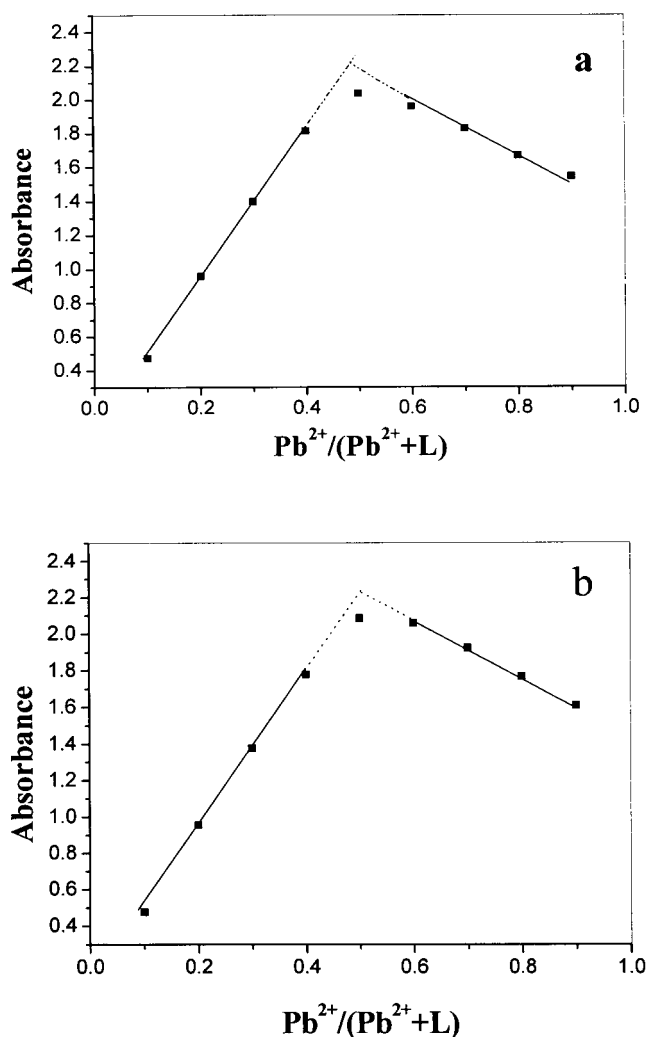


Figure 3. Continuous variation plots for the formation of lead-ligand (**6** or **7**) complex; L stands for **6** (a) and **7** (b).

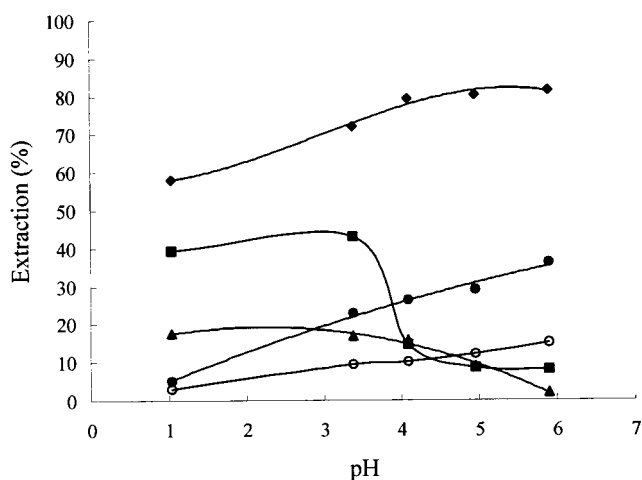


Figure 4. Extraction of Pb^{2+} with derivatives **2**, **5**, **6** and **7** as extractants under different pH: (\blacktriangle) **2**, (\blacksquare) **5**, (\blacklozenge) **6**, (\bullet) **7**, (\circ) for lead acetate.

indications that the extractability of the piperidine group is much bigger than that of the diethylamine functional group although the stability constant of **7** is a little bigger than that of **6** in THF. The higher extractability for **6** (compared to **5**) may be ascribed to the bigger cavity size of derivative **6**. Among all the derivatives tested, derivative **6** shows the highest extractability for Pb^{2+} . And higher extraction percentages for calix[8]arene derivatives **2**, **6** and **7** were observed when the pH value of the aqueous phase increased.

To give some views on the practical application, further studies on the extraction were investigated through the successive extraction and the stripping of the loaded Pb^{2+} . After the successive extraction with derivative **6**, the Pb^{2+} in the aqueous phase can be extracted into the organic phase completely (ca. 100%). Although the extraction efficiencies of the other two nitrogen-containing derivatives **5** and **7** are not so excellent as that of derivative **6**, they also can reach 50–80%. The stripping studies suggested that metal removal from these derivatives could be accomplished with nitric acid and complete stripping achieved by nitric acid at a concentration greater than 1 mol/L. All these studies indicate that these derivatives have potential application to separate and recover the Pb^{2+} by extraction.

Discussion on the mechanism of the extraction

The pH value of the aqueous phase was measured before and after the extraction experiment. No obvious change was found. The experiment results demonstrated that the ratio of picrate anions and Pb^{2+} extracted into the organic phase was about 2:1, which means one Pb^{2+} was extracted into the organic phase together with two picrate anions. These facts imply an association mechanism instead of a substitution mechanism for the extraction of Pb^{2+} . That is, Pb^{2+} was extracted from the aqueous phase into the organic phase in the form of an "ion-pair" with picrate ion by these nitrogen-containing extractants.

No obvious extraction of Pb^{2+} was observed if the picrate anion was replaced by the sulfosalicylic anion, which has a high polarity and so is insoluble in organic solvent. With the acetate anion instead of picrate anion as counter-ion, the extraction percentage was found to decrease obviously for **7** (see Figure 4). These experiments revealed that the nature of the counter-ion could strongly influence the result of extraction. This further confirmed the assumption of the association mechanism.

So a conclusion may be drawn that Pb^{2+} coordinates with the extractant to form a coordinating cation with two charges, which was extracted into the organic phase from the aqueous phase accompanied by two picrate anions.

Conclusion

Several new nitrogen-containing calixarene derivatives (**5**, **6** and **7**) were synthesized. The UV spectroscopy and extraction studies showed they could bind Pb^{2+} and efficiently extract Pb^{2+} from the aqueous phase into chloroform in the form of an ion-pair with picrate anion. The introduction of

nitrogen donor atoms to the lower rim of calixarenes increases the complexation ability for lead ion appreciably. These results imply the nitrogen-containing calixarene derivatives are a kind of new good receptors and they have potential uses in extraction separation, phase transform, recovery of metal and exclusion of the toxic metal ions.

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