



Synthesis and Properties of New Thiacalixarene Derivatives with Palladium Ion

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Abstract

Three new thiacalix[4]arene derivatives, 5,11,17,23-tetra-*tert*-butyl-25,27-di(2-hydroxyethoxy)-26,28-dihydroxythiacalix[4]arene (**2**), 5,11,17,23-tetra-*tert*-25, 26,27,28-tetrakis[(methylcarboxyl)methoxy]thiacalix[4]arene (**3**), 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(2-hydroxy-1-propanoxy)thiacalix[4]arene (**4**), were synthesized for the first time. The coordination properties of thiacalix[4]arene(**1**) and its derivatives (**2** and **4**) were investigated by detecting the interactions between these compounds and two palladium complexes, *cis*-[Pd(en)(H₂O)₂]²⁺ and *cis*-[Pd(dtco-3-OH)(H₂O)₂]²⁺, by means of electrospray ionization mass spectrometry (ESI-MS) technique.

Introduction

Calix[n]arenes, assembled by the base-catalyzed condensation of *p*-alkylphenols with formaldehyde [1, 2], continue to be of active research interest recently. Hetero atoms such as O, S, and N are introduced into the molecules through modifications either at the phenolic hydroxyl groups on the lower rim or at the *p*-positions on the upper rim [3–5]. In the early 1990's, Sone and his co-workers reported the synthesis of the analogues of *p-tert*-butylcalix[4]arene in which one to four of the methylene linkages were replaced by sulfide bridges [6, 7]. This is the precedent of introducing hetero atoms into calixarenes at the ring structure in the middle of the molecules rather than on the lower or upper rims. That means that we can expect the emergence of a new family of macrocycles named thiacalixarenes. But no further research on those compounds was reported until 1997 when Miyano et al. reported a convenient and easy synthesis of *p-tert*-butylthiacalix[4]arene **1** in a satisfactory yield by simply heating *p-tert*-butylphenol with elemental sulfur in the presence of a base [8]. A few groups now focus their research on this new type of calixarene, because these thioethers offer promising alternatives to the original design of this class of molecules leading to dramatic changes of their dynamic and coordination properties. Besides their similar chemistry to that of calix[4]arene, the presence of the four sulfur atoms in the ring should bring some new features into the chemistry of 'classical' calixarenes. As one of the remarkable results of the replacement of CH₂ by S, it was shown that the thiacalixarenes can quantitatively extract transition metal ions such as Co²⁺, Cu²⁺ and Zn²⁺ from an aqueous phase into chloroform [9]. Their abilities to complex with toxic

and rare heavy metal ions may have potential applications in separations and environment protection.

The coordination of macrocycles including thiacalixarenes to metal ions or small molecules often form a supramolecular system or host–guest system in which the host and guest species generally connect to each other by weak non-covalent bond forces. Therefore, new techniques are needed to investigate these kinds of systems. With the development of soft ionization techniques, such as electrospray ionization (ESI) [10–11] and matrix-assisted laser desorption/ionization (MALDI) [12–13], mass spectrometry (MS) has become an indispensable tool for obtaining structural information about transition metal complexes [14–15].

Herein we report the synthesis of three new thiacalix[4]arene derivatives. The coordination properties of thiacalix[4]arene and its new derivatives with Pd(II) were studied by detecting the interactions between those macrocycles and palladium (II) complexes, *cis*-[Pd(en)(H₂O)₂]²⁺ and *cis*-[Pd(dtco-3-OH)(H₂O)₂]²⁺, using the ESI-MS technique as a major tool. A variety of structural information has been obtained by precise determination of molecular masses. It also proved that the ESI-MS technique is a powerful tool for this kind of study.

Experimental

Materials

PdCl₂ and dithiacyclooctan-3-ol were purchased from Aldrich Chem. Co. The ligand *p-tert*-butylthiacalix[4]arene (**1**) was synthesized according to the literature [8]. The two dichloro complexes, *cis*-[Pd(en)Cl₂] (en = ethylenediamine)[16], *cis*-[Pd(dtco-3-OH)Cl₂] (dtco = 3-OH-dithiacyclooctan-3-ol), were prepared according to pub-

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lished procedures [17–18]. The corresponding diaqua complexes were obtained by treating each of these complexes with 2.0 equivalents of anhydrous AgBF_4 in H_2O , and stirring for 4 h at 35 °C. Then solid AgCl was removed by centrifugation in the dark. Only freshly prepared diaqua complexes were used. All other chemicals were of reagent grade.

Instrumentation

^1H NMR spectra were collected on an AM 500 spectrometer at 500 MHz with CDCl_3 as solvent and TMS as the initial standard. IR spectra were recorded on a Nicolet 170SX FT-IR spectrometer and the most relevant absorption peaks were reported. UV-Visible spectra were collected using a Shimadzu UV-3100 spectrometer. Elemental analysis was performed on a Perkin-Elmer 240 instrument. A LCQ electrospray ionization mass spectrometer (ESI-MS, Finnigan) was employed for molecular mass determination of the samples.

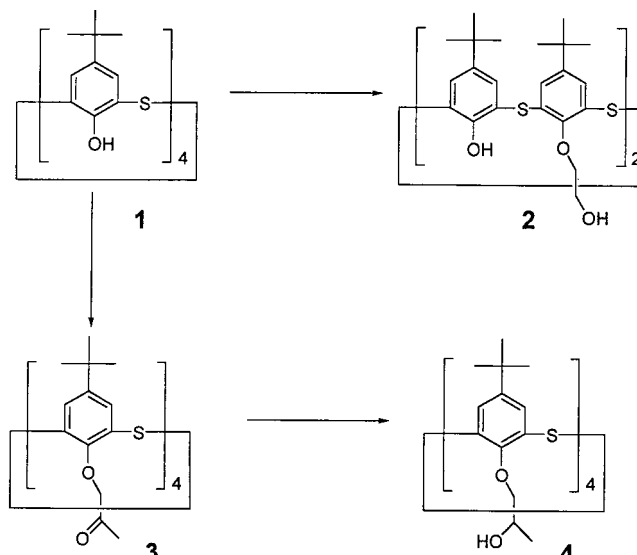
Synthesis

Synthesis of 5,11,17,23-tetra-tert-butyl-25,27-di(2-hydroxyethoxy)-26,28-dihydroxythiacalix[4]arene (2)

After stirring the mixture of sodium iodide (1.44 g, 0.025 mol) and 2-chloroalcohol (2.5 mL, 0.025 mol) in dry acetone (5 mL) for 20 minutes, potassium carbonate (0.8 g, 0.025 mol), compound **1** (0.72 g, 0.001 mol) and acetone (50 mL) were added. The reaction mixture was heated and stirred (in N_2 atmosphere) under reflux for five days, and then cooled and filtered. Evaporation of the solvent furnished a light-red solid, which was then extracted by dichloromethane and washed with 0.1 mol·L $^{-1}$ solution of sodium thiosulfate. Chromatography of the light-red solid on silica gel afforded the primary product. Recrystallization from chloroform-methanol gave the pure product **2** (white prism). Yield: 58%. m.p. 330 °C (decomposition); MS (m/z) 831 ($\text{M}+\text{Na}^+$); IR (KBr, in cm^{-1}) 2959($-\text{C}(\text{CH}_3)_3$); 3492, 3397, 3362, 3285($-\text{OH}$); ^1H NMR (CDCl_3 , in ppm) 7.58 (4H, s, ArH), 7.47 (4H, s, ArH), 4.49 (4H, t, $-\text{O}-\text{CH}_2-$), 4.24 (4H, t, $-\text{O}-\text{CH}_2-$), 1.19 (18H, s, $\text{C}(\text{CH}_3)_3$), 1.06 (18H, s, $-\text{C}(\text{CH}_3)_3$). Elemental analysis for $\text{C}_{44}\text{H}_{56}\text{O}_6\text{S}_4$ (%): Calc.: C, 65.31; H, 6.98; S, 15.85. Found: C, 65.28; H, 7.09; N, 15.72.

Synthesis of 5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis(methylcarboxyl) methoxythiacalix[4]arene (3)

Compound **1** and potassium carbonate and dry acetone were added to the mixture of chloroacetone and sodium iodine in acetone. The reaction mixture was heated and stirred under reflux (N_2 atmosphere) for 6 h. After cooling the mixture was filtered through a bed of celite which was washed thoroughly with fresh acetone. Evaporation of the solvent furnished an orange-red solid which was then suspended in water at 60 °C and stirred. The product was extracted into dichloromethane and washed with 0.1 mol·L $^{-1}$ solution of sodium thiosulfate. Removal of the solvent left a



Scheme 1. The synthesis route of thiacalixarene derivatives.

yellow solid. Chromatography of the solid on silica gel (acetone/petroleum ether 1:5) afforded the product **3** (white prism). Yield: 63%. m.p. 270–272 °C. MS (m/z) 944 (M^+). IR (KBr, in cm^{-1}) 2964($-\text{C}(\text{CH}_3)_3$), 1763($-\text{CO}-$); ^1H NMR (CDCl_3 , in ppm) 7.34 (8H, s, ArH), 4.47 (8H, s, $-\text{O}-\text{CH}_2$), 1.50 (12H, s, CH_3), 1.23 (36H, s, $-\text{C}(\text{CH}_3)_3$). Elemental analysis for $\text{C}_{52}\text{H}_{64}\text{O}_8\text{S}_4$ (%): Calc.: C, 66.07; H, 6.82, S, 13.54. Found: C, 66.15; H, 6.77; N, 13.42.

Synthesis of 5,11,17,23-tert-butyl-25,26,27,28-tetrakis(2-hydroxypropanoxy) thiacalix[4]arene (4)

A solution of compound **3** (1 mmol) in 40 mL of dry THF was added dropwise to a stirred suspension of 95% LiAlH_4 (1.3 molar excess in respect to the corresponding stoichiometric ratio) in 40 mL of dry THF. The reaction mixture was stirred for 30 minutes in an inert atmosphere. The excess of LiAlH_4 was then destroyed by careful addition of water and the solvent was evaporated under reduced pressure. The residue was taken up in chloroform and washed successively with diluted sulfuric acid and water. The organic phase was dried over MgSO_4 . The solvent was removed *in vacuo*, and the crude product was recrystallized from dichloromethane-methanol to give pure product **4**. Yield: 78%. m.p. 358 °C (decomposition); MS (m/z) 975 ($\text{M}+\text{Na}^+$); IR (KBr, in cm^{-1}) 3535, 3458($-\text{OH}$), 2964($-\text{C}(\text{CH}_3)_3$). ^1H NMR (CDCl_3 , in ppm) 7.32 (8H, s, ArH), 3.64–3.89 (8H, m, $-\text{O}-\text{CH}_2$), 3.41–3.50 (4H, m, $-\text{CH}^*=\text{}$), 2.95 (4H, s, $-\text{OH}$), 1.28 (36H, s, $-\text{C}(\text{CH}_3)_3$), 0.90–0.95 (12H, d, $-\text{CH}_3$). Elemental analysis for $\text{C}_{52}\text{H}_{72}\text{O}_8\text{S}_4$ (%): Calc.: C, 65.55; H, 7.56, S, 13.45. Found: C, 65.62; H, 7.62; N, 13.34.

ESMS measurement

A LCQ electrospray ionization mass spectrometer (ESI-MS, Finnigan) was employed for molecular mass determination of the samples. A sample was dissolved in methyl cyanide and diluted to 100 $\mu\text{mol}\cdot\text{L}^{-1}$ with methanol. 1.0 μL of this solution was loaded into the injection valve of the LCQ unit

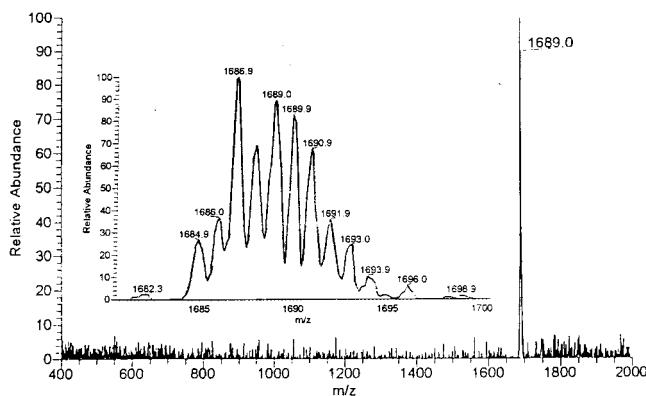


Figure 1. ESI-MS spectra for the tetranuclear ligand **1** with Cu(II).

and then injected into the mobile phase solution and carried through the electrospray interface into the mass analyzer at a rate of $200 \mu\text{L}\cdot\text{min}^{-1}$. The employed voltage at the electrospray needles was 5 kV and the capillary was heated to 200°C . A maximum ion injection time of 200 ms along with 10 scans was set. Positive ion electrospray mass spectra were obtained. Zoom scan was used in these experiments. The results were compared with the predicted isotope distribution patterns for each of complexes which were calculated using the IsoPro 3.0 program.

Results and discussion

Interaction of ligand **1** (L^1H_4) with $\text{Cu}(\text{ClO}_4)_2$

After mixing of copper ion with ligand **1**, in a two-to-one molar ratio of Cu(II) to **1**, the ESI-MS was measured ten min after mixing. As seen from Figure 1, peaks separated by 1.0 m/z unit are attributed to the single charged cationic complex. The molecular masses calculated for $[\text{Cu}_4(\text{L}^1_2\text{H})]^+$ with different isotopic masses of Cu(II) are exactly equal to the values observed by ESI-MS. This result is in accordance with the reported structure of the complex [13] in which four Cu(II) ions, which were sandwiched between two fully deprotonated *p-tert*-butylthiacalix[4]arene, are coordinated in a square configuration by a μ_2 -pheoxo anion and a μ_2 -sulfur atom. That proved that ESI-MS is a powerful tool for investigating the formation of the complex between ligand (L^1H_4) and Cu(II) or other metals.

Interaction of ligand **1** (L^1H_4) **2** (L^2H_4) or **4** (L^4H_4) with $\text{cis}[\text{Pd}(\text{dtco}-3\text{-OH})(\text{H}_2\text{O})_2]^{2+}$ or $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$

The ESI-MS spectra were measured ten minutes after mixing ligand **1** with $\text{cis}[\text{Pd}(\text{dtco}-3\text{-OH})(\text{H}_2\text{O})_2]^{2+}$ (or $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$) in a 2:1 molar ratio of Pd(II) to **1**. As shown in Figure 2, the isotopic peaks of Pd(II) separated by 0.5 m/z unit are attributed to the double charged cationic complex. The molecular mass observed is exactly the same as that calculated for $[(\text{Pd}(\text{dtco}-3\text{-OH}))_2(\text{L}^1\text{H}_2)]^{2+}$, which is a binuclear complex. When **1** reacted with $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ in the same condition, $[(\text{Pd}(\text{en}))_2(\text{L}^1\text{H}_2)]^{2+}$ was detected with the aid of ESI-MS (see Table I).

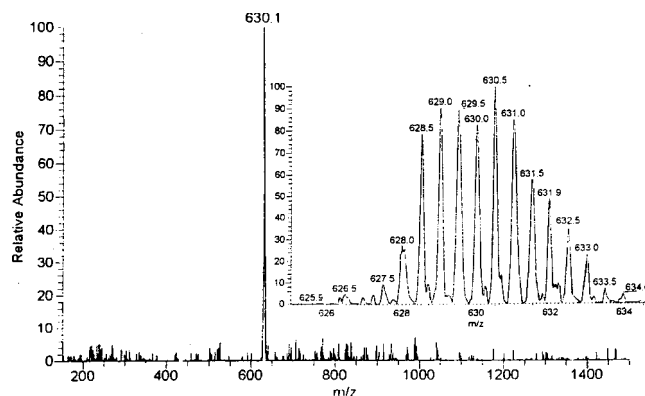


Figure 2. ESI-MS spectra for the binuclear ligand **1** with $\text{cis}[\text{Pd}(\text{dtco}-3\text{-OH})(\text{H}_2\text{O})_2]^{2+}$ with different isotopic masses of Pd(II).

Besides the formation of the binuclear complex as a dominant species, a small amount of mononuclear complex was also detected for both $\text{cis}[\text{Pd}(\text{dtco}-3\text{-OH})(\text{H}_2\text{O})_2]^{2+}$ and $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$, even in a mole ratio of 1:1 (ligand **1**/Pd complex). The molecular masses observed are precisely equal to those calculated for $\text{cis}[\text{Pd}(\text{dtco}-3\text{-OH})(\text{L}^1\text{H}_3)]^+$ or $\text{cis}[\text{Pd}(\text{en})(\text{L}^1\text{H}_3)]^+$. For $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$, a tiny amount of trinuclear complex was also detected with its isotopic peaks separated by 0.3 m/z. The molecular masses measured are the same as that calculated for $\text{cis}[(\text{Pd}(\text{en}))_3(\text{L}^1\text{H})]^{3+}$. The results are summarized in Table 1.

ESI-MS spectra were recorded ten minutes after ligand **2** (or **4**) was mixed with $\text{cis}[\text{Pd}(\text{dtco}-3\text{-OH})(\text{H}_2\text{O})_2]^{2+}$ or $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ at the same reacting conditions. It is found that only ligand **2** can react with $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ to form mono- and binuclear complexes (see Table 1). The molecular mass observed is the same as that calculated for $[(\text{Pd}(\text{en}))_2(\text{L}^2\text{H}_2)]^{2+}$, which is also a binuclear complex. But no evidence was found for the reactions between ligand **4** and the two kinds of Pd(II) complexes.

The above experimental results also provide some information about how the palladium is coordinated by hetero atoms. Each of compounds **1**, **2** and **4** has four sulfur atoms which are easy to coordinate to 'soft' metal atoms such as palladium. They also have some oxygen atoms but of different situations: compound **1** only having phenol hydroxyl groups, compound **4** having alcohol groups but no phenol hydroxyl group, and compound **2** having both alcohol groups and phenol hydroxyl groups. It is rational to imagine that if there are enough suitable coordination atoms and the space allows, a new complex would form from the interaction between those macrocycles and palladium complexes. It is known that phenol hydroxyl groups are active and easily deprotonated, therefore, when the Pd(II) complexes react with ligand **1**, similar to the case with Cu(II), the ligand **1** coordinates to the palladium ion through thioether-S and deprotonated hydroxyl-O, to form stable binuclear complexes with a five-membered chelate ring. There even was a tiny amount of the trinuclear complex of ligand **1** with $\text{cis}[\text{Pd}(\text{en})(\text{H}_2\text{O})_2]^{2+}$ formed here, but no trinuclear complex of ligand **1** with cis -

Table 1. The observed m/z (z) values and calculated molecular masses for mono-, di- and tri-nuclear complexes of ligand **1** and **2** with cis -[Pd(dtco-3-OH)(H₂O)₂]²⁺ or cis -[Pd(en)(H₂O)₂]²⁺

Ligand	Species	Observed m/z (z)	Calculated m/z*
1	cis -[Pd(dtco-3-OH)(L ¹ H ₃)] ⁺	988.2, 989.2, 990.3, 992.2, 994.2 (1)	988.3(¹⁰⁴ Pd)
	cis -[Pd(en)(L ¹ H ₃)] ⁺ ·3CH ₂ Cl ₂	1135.1, 1136.1, 1137.0, 1138.9, 1140.9 (1)	1135.2(¹⁰⁴ Pd)
	cis -[(Pd(dtco-3-OH)) ₂ (L ¹ H ₂)] ²⁺	627.5, 628.0, 628.5, 629.0, 629.5, 630.0, 630.5, 631.0, 631.5, 632.0, 632.4, 633.0, 633.5(2)	627.5, 628.0, 628.5, 629.0, 629.5, 630.0, 630.5, 631.0, 631.5, 632.0, 632.5, 633.0, 633.5
	cis -[(Pd(en)) ₂ (L ¹ H ₂)] ²⁺	523.0, 523.6, 524.1, 524.6, 525.1, 525.6, 526.1, 526.6, 527.1, 527.5, 528.0, 528.6, 529.1, 529.5(2)	523.1, 523.6, 524.1, 524.6, 525.1, 525.6, 526.1, 526.6, 527.1, 527.6, 528.1, 528.6, 529.1, 529.6
	cis -[(Pd(en)) ₃ (L ¹ H)] ³⁺	403.1, 403.4, 403.7, 404.1, 404.5, 404.8, 405.1, 405.5, 405.8, 406.1, 406.4, 406.7, 407.1, 407.5, 407.8, 408.0, 408.4, 408.7, 409.1 (3)	403.1, 403.4, 403.7, 404.0, 404.4, 404.7, 405.1, 405.4, 405.7, 406.0, 406.4, 406.7, 407.0, 407.4, 407.7, 408.0, 408.4, 408.7, 409.0
	2	cis -[Pd(en)(L ² H ₃)] ⁺	1135.1, 1136.1, 1137.0, 1138.9, 1140.9 (1)
cis -[(Pd(en)) ₂ (L ² H ₂)] ²⁺		566.8, 567.2, 567.7, 568.2, 568.7, 569.2, 569.7, 570.2, 570.7, 571.2, 571.6, 572.1, 572.6, 573.2(2)	566.6, 567.1, 567.6, 568.1, 568.6, 569.1, 569.6, 570.1, 570.6, 571.1, 571.6, 572.1, 572.6, 573.1

*The remaining m/z values can be deduced based on the isotopic abundance of Pd.

[Pd(dtco-3-OH)(H₂O)₂]²⁺ was observed – this fact is due to the fact that the dtco in cis -[Pd(dtco-3-OH)(H₂O)₂]²⁺ is larger than en in cis -[Pd(en)(H₂O)₂]²⁺, hence has a bigger steric hindrance which inhibits the formation of the accordant trinuclear complex. The steric hindrance also affects the formation of the complex of ligand **2**. The ESI-MS results indicate the formation of a stable binuclear complex of ligand **2** with cis -[Pd(en)(H₂O)₂]²⁺, but no binuclear complex of ligand **2** with cis -[Pd(dtco-3-OH)(H₂O)₂]²⁺ was found. The reason could be that the lower rim cavity of ligand **2** has two chains which cause a larger steric hindrance than the case of ligand **1** and inhibit stable complexing of ligand **2** with cis -[Pd(dtco-3-OH)(H₂O)₂]²⁺, which is larger than cis -[Pd(en)(H₂O)₂]²⁺. Therefore, even if some weak connections exist between ligand **2** and cis -[Pd(en)(H₂O)₂]²⁺ they are too weak to be kept during the ESI process and cannot be detected. Comparing the situations of ligand **1** and **2** with compound **4**, the experimental results shows that the former two compounds can form stable complexes with palladium but the latter one cannot. That should due to the difference between them: the former two compounds all have some phenol groups, while the latter one has no phenol groups. This fact indicates the ligand **2** coordinates to Pd(II) through thioether-S and phenol hydroxyl-O forming two five-membered chelate rings, and its ethanol hydroxyl-O does not participate in the coordination.

Conclusion

The experimental results shows that *p*-*tert*-butylthiacalix[4]-arene and its derivatives are new ligands for palladium cation. Both precise molecular masses and the structural information can be obtained by means of the ESI-MS technique. The thioether sulfur in thiacalix[4]arene together with the deprotonated hydroxyl oxygen can chelate to Pd(II) to

form stable binuclear complexes as the main products when the space permits.

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