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Coordination of Lead(II) in the Supramolecular Environment Provided by a “Two-Story” Calix[6]arene-based N_6 Ligand

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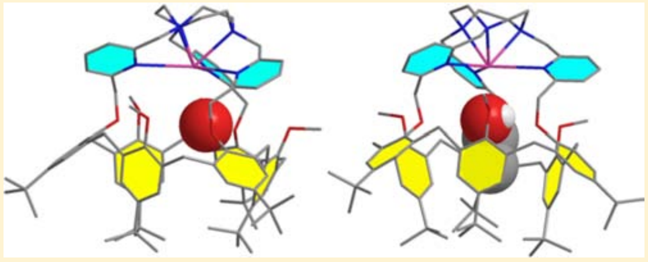
Supporting Information



ABSTRACT: First insights into the coordination properties and host−guest behavior of a “two story” calix[6]aza-cryptand (**1**) are described. The ligand is constituted of a triazacyclononane (TACN) cap and three pyridine (PY) spacers connected to the calix[6]arene small rim. The resulting N_6 donor site coordinates Pb^{II} ions to give complexes that are highly stable. X-ray diffraction structures reveal a hemidirected environment for Pb^{II} with strong coordination to the TACN cap and weaker bonds with the three PY residues. A guest molecule, either water or EtOH, sitting in the calixarene macrocycle and hydrogen-bonded to the phenoxyl units at the level of the small rim further stabilizes the complexes through electrostatic interactions with the metal center and the calixarene core. In-depth ^1H NMR studies confirm the host−guest behavior of the complexes in solution, with evidence of embedment of neutral guest molecules such as EtOH, BuOH, and *N*-Me-formamide. Hence, in spite of the presence of a N_6 donor, the calixarene macrocycle can be open to guest interaction, giving rise to seven-coordinate dicationic complexes. Noteworthy also is the flexibility of the macrocycle that allows Pb^{II} to adopt its preferred hemidirected environment in spite of the three covalent links connecting the calixarene core to the three PY groups. The flexibility of the system is further illustrated by the possible coordination of an exogenous anionic ligand in the exo position. Hence, compared to the previously described “one story” calix[6]aza-cryptands, ligand **1** displays several similar but also new features that are discussed.

INTRODUCTION

Elevated levels of lead(II) in the environment have disastrous impact on human health, and a large interest in the study of selective sequestering ligands for Pb^{II} has been generated.[1−6] Hence, much attention has been given to the stability of these complexes and the geometry around the Pb^{II} center.[7−11]

Because of the presence of the $6s^2$ electron pair, Pb^{II} complexes display either hemi- or holodirected geometries.[12] Hemidirected coordination is generally formed with O-donor ligands and coordination numbers smaller than six. Holodirected geometries are commonly observed for sterically demanding ligands[13−16] and coordination numbers higher than six, although complexes displaying a stereochemically active lone pair with high coordination numbers have been characterized.[17,18] Preorganization of a ligand is another key feature for stability and selectivity in metal ion binding. High levels of preorganization have been achieved in ligands by using rigid bridges between two N-donor sites.[19,20] Macrocyclic ligands, such as cryptands, have also been used to enforce metal complexation. We have studied for many years[21] the coordination chemistry of calix[6]aza-ligands (Scheme 1) in which the coordination core was constituted by either three imidazole arms (calix[6]Im_3)[22,23] or a tripodal cap (so-called calix[6]azacryptands) providing a N_4, (e.g., calix[6]-TREN)[24−27] or a PN_3 donor set.[28,29] In these systems, three or four N-donors bind the metal ion next to the calixarene macrocycle at a distance that is defined by a two-atom spacer separating the first nitrogen donor and an oxygen atom of the calixarene small rim. This creates a strong coordination site for metal ions such as $Cu^{I/II}$ or Zn^{II}, as well as Ni^{II} and Co^{II},[30] and a binding site for one guest ligand inside the cavity. The latter can be exchanged through a dissociative mechanism,[31,32] and the corresponding complexes have been coined “funnel complexes”. In these “one-story” systems, the guest ligand is in strong interaction with the oxygen atoms of the calixarene small rim that constitutes a well-defined second coordination sphere prone to hydrogen bonding and resistant to anion binding. The embedded guest alkyl chain undergoes further stabilizing CH-π interactions with the aromatic walls of the cavity.

Recently, we have described the synthesis of novel “two-story” calix[6]aza-cryptands in which is inserted an additional

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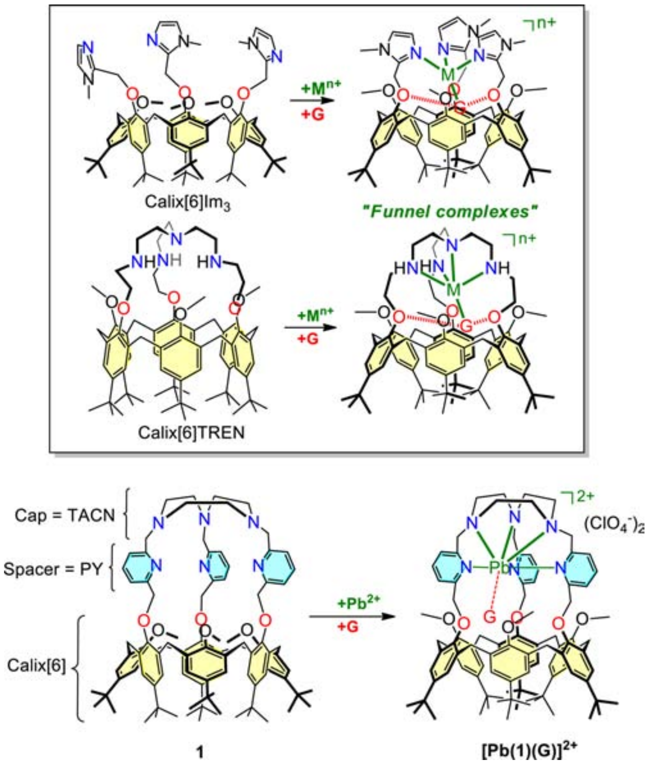
Scheme 1. (Top) Funnel Complexes Obtained with Calix[6]Arene-Based Tris(imidazole) and TREN "One Story" Ligands and (Bottom) Complexation of Pb^{II} by Ligand 1, a "Two Story" Ligand[a]



[a] G stands for a guest molecule.

spacer between a tripodal aza-cap and the macrocycle in order to vary the first and second coordination spheres of the metal ion.[33] Among these cryptands, one seemed to be particularly apt for selective lead binding. This ligand, calix[6]PY-TACN (**1**), is constituted of three 2,6-dimethyl-pyridine units (PY) grafted onto the calixarene moiety and the aza-cap 1,3,5-triazacyclononane (TACN) (Scheme 1), which provides a N_6 coordination site. It is important to note that, in this system, the pyridine units are not free to rotate, and their nitrogen donor atoms are at a distance that is constrained by the calixarene macrocyclic scaffold to which they are covalently attached.

Here we report the detailed investigation of the coordination chemistry of ligand **1** with Pb^{II} ions and the host−guest behavior of the corresponding $[Pb(\mathbf{1})]^{2+}$ complexes.

■ RESULTS AND DISCUSSION

The Pb^{II} complex was obtained by reaction of ligand **1** with 1 equiv of Pb^{II} perchlorate salt in a THF/CH_2Cl_2 solvent mixture (Scheme 1). It was isolated by precipitation in 92% yield and characterized as a dicationic complex by NMR, ESI-MS, IR and elemental analyses. Two XRD structures were determined: one with H_2O as a guest (G) in the cavity and the other with EtOH in the cavity.

Solid-State Structures of $[Pb(\mathbf{1})(G)]^{2+}$ (G = H_2O, EtOH). Single crystals were obtained by slow evaporation of a CH_2Cl_2 solution of complex $[Pb(\mathbf{1})]^{2+}$ with either ethanol or butanol[34] as a cosolvent, and two different structures were obtained (see Figure 1 and Table 1). In each case, the metal center is tightly bound to the aza cap with three short bonds (average: 2.53 Å) to the TACN moiety, and longer ones with the pyridine residues (average: 2.89 Å). The three pyridine N-donors and the Pb^{II} ion lie in one plane, and the angles between them are close to 120°, leaving a gap in the coordination sphere opposite to the TACN moiety where either a water or an ethanol guest is placed. The long distance from the metal center [d(Pb,O): 2.92 and 2.83 Å, respectively] denotes mainly electrostatic character for the Pb···O interaction. These structural features are characteristic of a hemidirected geometry and the presence of a stereochemically active lone pair, which is generally described by the shortening of the metal−ligand bond opposite to the lone pair, by a gap in the coordination sphere at the site of the lone pair and by important lengthening of metal−ligand bonds at the same site of the lone pair.[35]

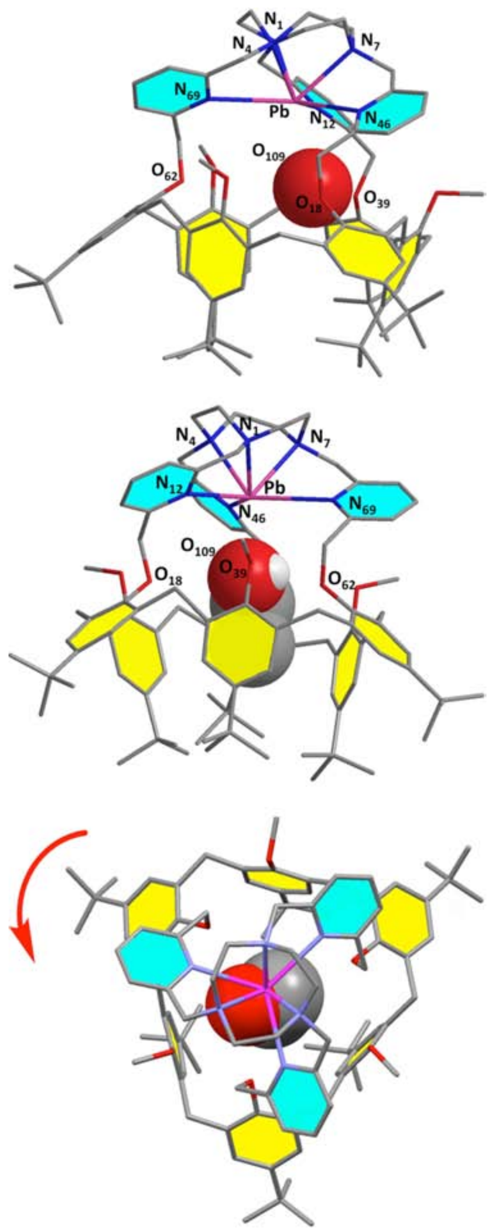


Figure 1. From top to bottom: XRD structures of $[Pb(\mathbf{1})(H_2O)]^{2+}$ and $[Pb(\mathbf{1})(EtOH)]^{2+}$ (side and top views).[36] The EtOH guest is disordered over two positions; only one of them is displayed here (see the Supporting Information for the other one). The hydrogen atom of the EtOH guest was calculated. Other hydrogen atoms, perchlorate counterions, and solvents of crystallization are omitted for clarity.

Table 1. Selected Bond Lengths, Angles, and O···O Distances between Guest and the Calixarene Small Rim of Complexes $[Pb(\mathbf{1})(H_2O)]^{2+}$ and $[Pb(\mathbf{1})(EtOH)]^{2+}$[35]

$[Pb(\mathbf{1})(H_2O)]^{2+}$		$[Pb(\mathbf{1})(EtOH)]^{2+}$	
	Bond Lengths [Å]		
$Pb-O_{109}$	2.923(5)	$Pb-O_{109}$	2.948(11)
$Pb-N_1$	2.565(6)	$Pb-N_1$	2.543(6)
$Pb-N_4$	2.538(6)	$Pb-N_4$	2.539(6)
$Pb-N_7$	2.528(5)	$Pb-N_7$	2.481(8)
$Pb-N_{12}$	2.852(5)	$Pb-N_{12}$	2.883(5)
$Pb-N_{46}$	2.859(5)	$Pb-N_{46}$	2.868(5)
$Pb-N_{69}$	2.980(3)	$Pb-N_{69}$	2.883(3)
	Angles [deg]		
$N_{12}-Pb-N_{46}$	116.70(13)	$N_{12}-Pb-N_{46}$	118.65(14)
$N_{46}-Pb-N_{69}$	120.38(13)	$N_{46}-Pb-N_{69}$	120.63(12)
$N_{69}-Pb-N_{12}$	122.22(14)	$N_{69}-Pb-N_{12}$	120.39(12)
$N_{12}-Pb-O_{109}$	74.61(15)	$N_{12}-Pb-O_{109}$	107.03(21)
$N_{46}-Pb-O_{109}$	84.21(13)	$N_{46}-Pb-O_{109}$	74.24(19)
$N_{69}-Pb-O_{109}$	102.47(14)	$N_{69}-Pb-O_{109}$	83.50(26)
	O···O Distances Guest-Calixarene [Å]		
$d(O_{109}\cdots O_{18})$	2.879(6)	$d(O_{109}\cdots O_{18})$	4.263(12)
$d(O_{109}\cdots O_{39})$	2.868(6)	$d(O_{109}\cdots O_{39})$	3.242(14)
$d(O_{109}\cdots O_{62})$	4.391(7)	$d(O_{109}\cdots O_{62})$	2.826(14)

A few crystal structures of Pb^{II} complexes presenting a hemidirected environment provided by a N_6 ligand have been reported in the literature. Among these, two of them were obtained with a TACN unit N-substituted by three benzopyridine or pyrazole groups. The structures are very similar to those described above, with short bonds between Pb^{II} and TACN (ca. 2.51 and 2.55 Å, respectively) and longer ones with the donor arms (ca. 2.78 and 2.64 Å, respectively).[37,38] Such similarities suggest that the calixarene macrocycle present in ligand **1** leaves enough freedom to the aza core to adapt to the stereochemical demand of the metal ion, undergoing twisting around it to allow such an "open geometry".

A more detailed look at the structures of $[Pb(\mathbf{1})(H_2O)]^{2+}$ and $[Pb(\mathbf{1})(EtOH)]^{2+}$ shows that in each case, the calixarene macrocycle adopts a flattened cone conformation with aromatic units in alternate *in* and *out* position relative to the cavity. The methoxy groups are projected away from the calix-cone, while the oxygen atoms linking the spacer arms point toward the C_3 axis of the structures. As shown by the top view displayed in Figure 1, the poly aza core wraps around the metal center to form a helix that is particularly pronounced at the level of the PY residues. Interestingly, such a helical wrapping of the pyridine spacers approaches the calixarene structure to the metal center, allowing thereby an interaction with a guest molecule. As a matter of fact, the guest molecule presents its oxygen atom at the level of the oxygen-rich small rim. Short O···O distances between the guest and the phenoxyl units indicate the presence of two strong H-bonds with G = H_2O and one with EtOH (see Table 1). Such H-bonding connections between the host and the guest have often been observed with calix[6]-based Zn^{II} funnel complexes.[22−24,39−41] Remarkably however, there is a difference with the Zn^{II}-aqua complexes obtained with calix[6]Im_3: in this "one-story" system, the water

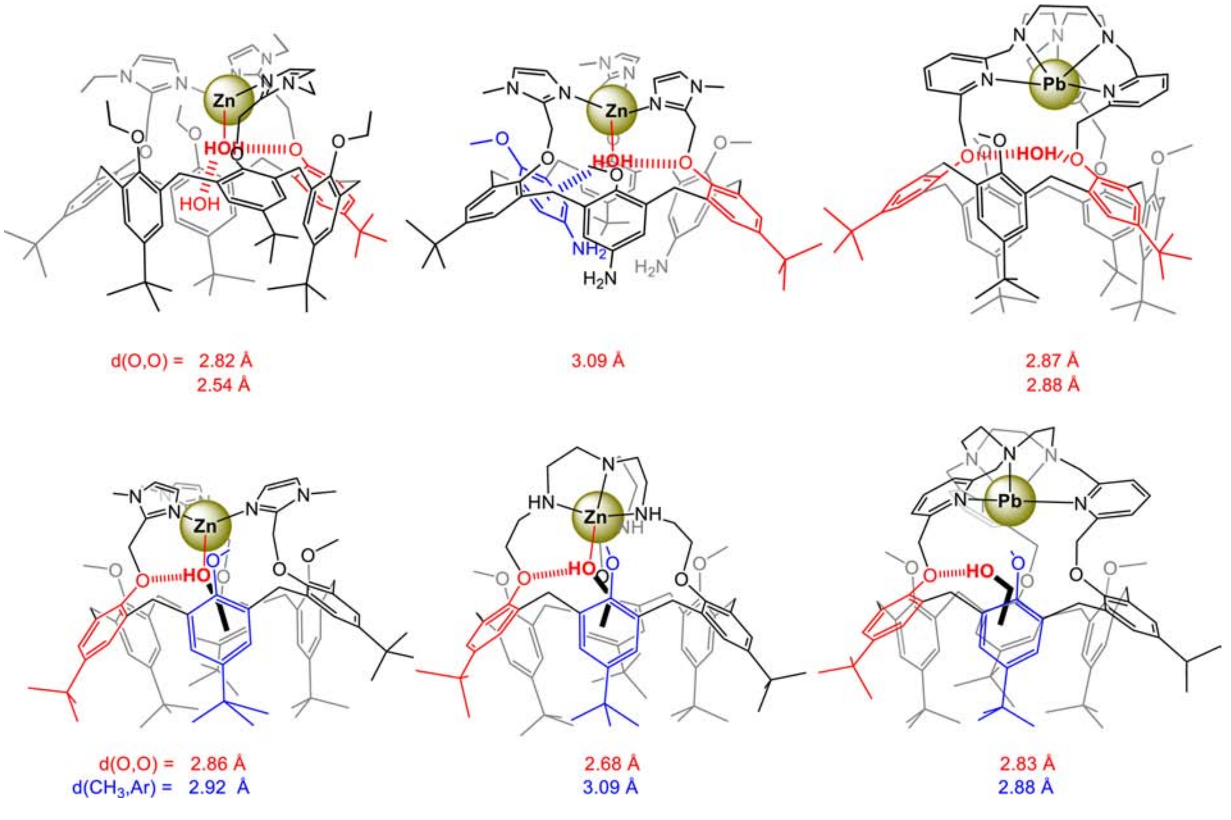


Figure 2. Schematic comparison of XRD structures of $M^{II}-OH_2$ and EtOH complexes obtained with calixarene ligands bearing different coordination cores at the small rim. Top, from left to right: aqua complexes obtained with calix[6]Im_3-Zn^{II},[38] ^{NH_2}calix[6]Im_3-Zn^{II},[39] calix[6]PY-TACN-Pb^{II}. Bottom, from left to right: EtOH complexes obtained with calix[6]Im_3-Zn^{II},[41] calix[6]TREN-Zn^{II},[24] calix[6]PY-TACN-Pb^{II}. The colored phenoxyl units are those which are involved in H- (red) and CH-π (blue) bonding with the guest. The O···O and Ar···Me distances between the calixarene and the guests are given in red and blue, respectively.

ligand undergoes only one H-bonding with the calixarene small rim, the other OH bond being either connected to a second water guest molecule[38] or involved in an OH−π interaction,[39] depending on the substitution pattern of the calix large rim (hexa-*t*Bu or tri*t*Bu-*tri*-NH_2, see Figure 2, top). In the "two-story" system, in spite of the helical flattening of the N_6 core, the guest water sits slightly higher with the O-atom further away from the calix aromatic rings, thus favoring double H-bonding over OH-π interaction. In contrast, a comparison of the host−guest relationship of the EtOH-Pb^{II} complex described above with EtOH-Zn^{II} complexes obtained with calix[6]Im$_3$[41] and calix[6]TREN[24] evidences impressive similarities (Figure 2, bottom). In all three solid-state structures, the EtOH guest adopts the same position relative to the calixarene macrocycle, with one H-bond on one side and CH/π interaction with its methyl group on the other side, both stabilizing interactions occurring with the same relative adjacent phenoxyl units.

Structural Characterization of [Pb(1)]$^{2+}$ in Solution. As characterized by ^{1}H NMR spectroscopy, ligand **1** adopts a C_{3v} symmetrical flattened cone conformation in solution.[33] The aromatic units of the calixarene moiety present alternate *in* and *out* positions relative to the center of the cavity as illustrated in Scheme 1. Such a flattened cone conformation is characterized by large differences in δ shifts for the *in* and *out* phenoxyl units ($\Delta\delta_{tBu}$ = 0.56 ppm and $\Delta\delta_{HAr}$ = 0.57 ppm). The pyridine spacer arms leave enough space above the small rim and flexibility for the methoxy groups to be oriented toward the center of the calix-cone, which is attested to by their high-field shifted resonance (δ = 2.40 ppm, Figure 3, bottom).

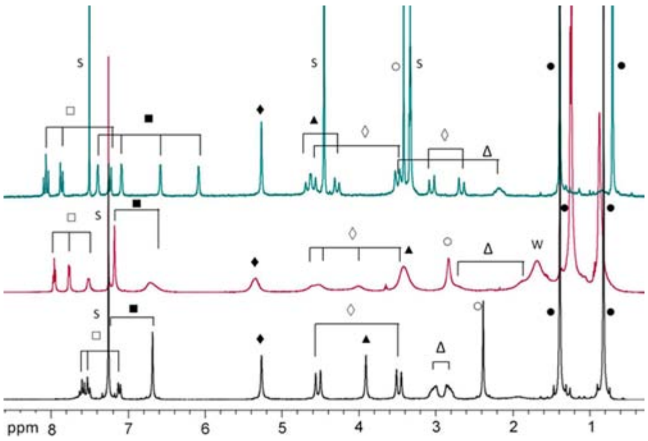


Figure 3. ^{1}H NMR (250 MHz, 300 K) Top: spectrum of [Pb(**1**)](ClO$_4$)$_2$, in a $CDCl_3/CD_3OD$ mixture (350/250 μL). Middle: spectrum of [Pb(**1**)](ClO$_4$)$_2$ in $CDCl_3$. Bottom: spectrum of free ligand **1** in $CDCl_3$. □: Pyr-H, ■: HAr, ♦: OCH_2, ▲: NCH_2, ◊: −CH_2−, ○: OCH_3, Δ: TACN, ●: *t*Bu; s = solvent.

The ^{1}H NMR spectra of [Pb(**1**)]$^{2+}$ recorded in a noncoordinating solvent such as chloroform present resonances that are quite broad (Figure 3, middle) but consistent with an average C_{3v} symmetry. The resonances of the pyridine hydrogen atoms are sharper compared to the rest of the spectrum and the corresponding chemical shifts (compared to the free ligand) together with those of the TACN unit attest to the coordination of the metal ion in the N_6 environment provided by the aza cap. In contrast, the broadness of the resonances associated to the calix structure is indicative of conformational mobility, stemming either from guest exchange at a rate that is similar to the time scale of the NMR analysis or from a lack of structuration of the cone due the absence of guest.[26] Whereas the X-ray structure of the Pb^{II} complex containing one water molecule in the cavity shows clearly that the methoxy groups are in an *out* position, the chemical shift of these OMe groups (δ = 2.83 ppm) in a chloroform solution indicates partial inclusion. This is rather suggestive of an "empty-cavity state" with no water hydrogen-bonded to the small rim, or if any, of a very weakly bound and "floating" guest in the cavity. This is corroborated by the relatively small chemical shift difference between the two *t*Bu groups ($\Delta\delta$ = 0.38 ppm) that reflects a cone conformation not as flattened as those usually obtained with bound guest ligands.[26]

Upon addition of methanol as a cosolvent, the spectrum of the [Pb(**1**)]$^{2+}$ complex became very well-defined, with sharp peaks for all protons (Figure 3, top). Complete assignment of the resonances of the spectra for both complexes was obtained by 2D NMR experiments (see the Supporting Information).

The new spectrum now reveals C_3 symmetry for the metal complexes, as evidenced by the splitting of a series of resonances into two sets of signals compared to the free ligand.[42,43,23] For the calixarene core in particular, the aromatic (■) and methylene (◊) protons give rise to four singlets and four doublets, respectively, each of them integrating for three protons. Such a diastereotopic differentiation is characteristic of a helical structure.[42,43,23] The right and left helices are in slow exchange at the NMR analysis time scale (confirmed by EXSY experiments). Hence, the overall structure of this complex in solution is a twisted flattened cone with alternate *in* and *out* positions for the *t*Bu groups, as can be seen by the corresponding large chemical shift separation ($\Delta\delta_{tBu}$ = 0. 68 ppm). The methoxy groups clearly point away from the cavity with an associated low-field shifted δ_{OMe} value of 3.59 ppm compared to the free ligand (2.40 ppm). Hence, the presence of MeOH as a cosolvent led to the rigidification of the complex (sharp resonances associated to slow helical motion) into a flattened cone conformation with the methoxy groups expulsed from the cavity. This is indicative of guest inclusion, likely a solvent molecule, MeOH, bound in the cavity. Such an architectural arrangement, commonly observed with funnel complexes, fits very well the above-described solid state structures.

In order to test the stability of this complex in solution [Pb(**1**)](ClO$_4$)$_2$ was heated for several days to 50 °C in a $CDCl_3/CD_3OD$ mixture: no change in the ^{1}H NMR spectrum was observed even after addition of 1 equiv of a strong acid such as trifluoroacetic acid (in order to labilize the ligand). This accounts for good thermodynamic and kinetic stability of this complex.

Host−Guest Studies of Complexes [Pb(1)(G)]$^{2+}$ (G = EtOH, NMF). In general, any guest ligand in the cavity of a calix[6]arene ligand experiences the anisotropy of the aromatic walls. Because of this effect, the resonances of a guest ligand are shifted upfield in the ^{1}H NMR spectra, and, depending on their relative position in the cavity, the NMR shift is more or less important.[22,44] All experiments were performed in chloroform as it is a noncoordinating solvent.

Guest Ligand Ethanol. As has been shown by the XRD structure of [Pb(**1**)(EtOH)]$^{2+}$, EtOH is a guest ligand for this type of complex. When 20 equiv of ethanol were added to a $CDCl_3$ solution of [Pb(**1**)](ClO$_4$)$_2$ the NMR spectrum, which displays broad resonances at RT in this solvent (Figure 3, middle), changed, the resonances sharpened and new peaks appeared (Figure S6, Supporting Information). Lowering the temperature down to 266 K led to even sharper resonances without changing the overall profile of the spectrum, thus indicating that the same species was present in solution (Figure 4, top). A detailed NMR study with 2D experiments allowed us to assign all resonances in the spectrum (see the Supporting Information). As in the case of the complex dissolved in a solution containing methanol, the NMR signature of the complex corresponds to C_3 symmetry and attests to the coordination of the metal center to the TACN moiety and all three PY. Importantly, a new resonance accounting for three protons relative to the calixarene core appeared in the high-field region at ca. −2 ppm. This attests to the encapsulation of 1 equiv of EtOH in the cavity, which is in slow exchange (vs the NMR analysis time scale) with free EtOH. All peaks corresponding to the protons of the EtOH guest have been identified, and the corresponding δ shifts are reported Table 2. First, the methylene groups display two resonances due to their diastereotopic relationship. This indicates that they feel the helical chirality of the host, as has been observed for other calixarene-based complexes.[22,45] Second, the complexation induced shift values (CIS, see Table 2) give information relative to their spatial position.[22] The positive CIS value of the OH group is consistent with its interaction with the Lewis acidic metal center and hydrogen bonding to the calix small rim, as evidenced in the XRD structure of the Pb^{II} complex. Those corresponding to the protons in α and β positions relative to the O atom indicate, being negative, that the corresponding methylene and methyl groups sit near the center of the cavity. For comparison purposes, the CIS values measured for the parent Zn^{II}-EtOH calix-complexes are also reported in Table 2. The high similarity of the values for all three complexes confirms that in solution as in the solid state (Figure 2), the EtOH guest stands in a similar position relative to the cavity, independently of the cap and the divalent metal ion. This further highlights the strength of the stabilizing supramolecular host−guest interactions in these systems.

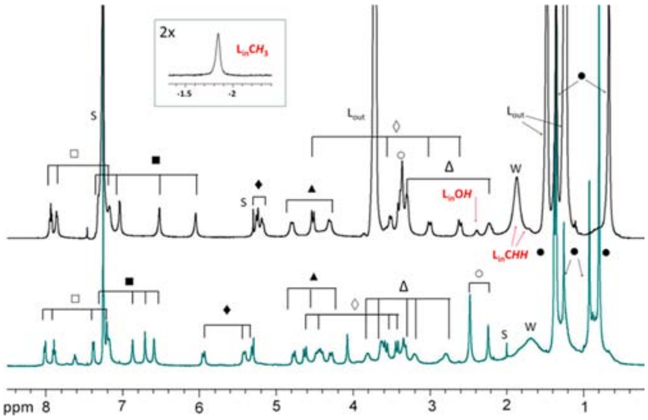


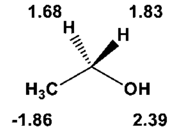
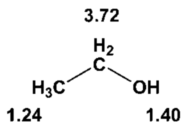
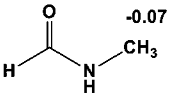
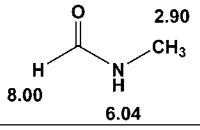
Figure 4. ^{1}H NMR spectra ($CDCl_3$, 266 K) of complexes $[Pb(\mathbf{1})(EtOH)]^{2+}$ (top, 250 MHz) and $[Pb(\mathbf{1})C_5H_{11}CO_2]^+$ (bottom, 500 MHz) obtained upon addition of 10 equiv of EtOH and 3 equiv of sodium hexanoate (as a solid), respectively, to a solution of $[Pb(\mathbf{1})](ClO_4)_2$. The inset shows the CH_3 resonance of the encapsulated EtOH. Residual water and solvent peaks are noted w and s, respectively. □: Pyr-H, ■: HAr, ◆: OCH_2, ▲: NCH_2, ◊: $-CH_2-$, ○: OCH_3, Δ: TACN, ●: *t*Bu.

Other Neutral Guest Ligands. *n*BuOH displayed a lower affinity for the Pb^{II} complex as the resonance attesting to its embedment could only be observed at low *T* (266 K with 10 equiv: δ_{Me} = −1.85 ppm, Figure S9, Supporting Information). Such a decrease in affinity as the alkyl chain becomes longer[34] than a propyl group is typical of funnel complexes presenting an hexa-substitution pattern with bulky *t*Bu groups at the entrance of the cavity, that is, the calixarene large rim.[22] Interestingly however, the CIS value of its methyl group, −2.8 ppm, is more negative than expected for such a position relative to the OH group [ca. −1.6 to −1.8 with the calix[6]Im_3 Zn^{II} system].[22] This indicates that the methyl group of the BuOH guest faces the center of the aromatic units of the cone, which places it higher in the cavity (e.g., in the direction of the metal ion) than in the first story systems.

The affinity of the complex $[Pb(\mathbf{1})]^{2+}$ for *N*-methylformamide (NMF, a linear amido-guest) was studied as well by NMR in $CDCl_3$ (Figure S10, Supporting Information). As for BuOH, the inclusion of the guest was detected only at low T (266 K with 10 equiv: δ_{Me} = −0.07 ppm). The corresponding CIS value (Table 2) shows again that the methyl group sits in the heart of the cavity.

Guest Ligand $C_5H_{11}COO^-$: Exocoordination. Up to now, the guest ligands studied did interact with the metal center through the cavity, hence in an endo fashion. As a result, these compounds displayed a pseudo 3-fold symmetry axis (the guest is rotating fast in the cavity). When, however, the anionic $C_5H_{11}CO_2^-$ was added to the complex (as a sodium or tetrabutylammonium salt), the spectrum changed dramatically, evidencing a symmetry change to C_2 for the Pb^{II} adduct (Figure

Table 2. The Complexation Induced Shifts (CIS) of Organic Guests (G) Observed by ^{1}H NMR Spectroscopy in $CDCl_3$[a]

G_{in} δ_{in}	G_{out} δ_{out}	$[Pb(\mathbf{1})(G)]^{2+}$ CIS	$[Zn(calix[6]Im_3)(G)]^{2+}$ CIS[22]	$[Zn(calix[6]TREN)(G)]^{2+}$ CIS[26]
		CH_3: -3.10 C*H*H: -2.04 CH*H*: -1.89 OH: 0.99	CH_3: -2.78 CH_2: -2.00 OH: 1.30	CH_3: -2.87
		CH_3: -2.97	(G = DMF) CH_3: -2.89, -2.76	

[a] CIS = $\delta_{in} - \delta_{out}$ (ppm). The chemical shifts for $EtOH_{in}$ and NMF_{in} were measured at 266 K (250 MHz). CIS values for $[Zn(calix[6]Im_3)(G)]^{2+}$ and $[Zn(calix[6]TREN)(G)]^{2+}$ are given for comparison.

4, bottom). Again, 2D NMR experiments allowed the complete assignment of the resonances (see the Supporting Information). The OMe groups display two resonances with an averaged chemical shift of 2.36 ppm, indicating that these groups are now partially included in the cavity. No species with C_3 symmetry has ever been detected, even after prolonged heating of the solutions (48 h at 70 °C), nor resonances below 0 ppm, which would have been indicative of endo coordination of the hexanoate. Hence, the anion must be bound in exoposition, which may be due to repulsive interaction between the carboxylate and the oxygen-rich small rim, a second coordination sphere effect evidenced for the calix[6]Im$_3$[46] and TREN Zn^{II} complexes.[47]

DISCUSSION AND CONCLUSION

This study provides first insights into the coordination properties and host−guest properties of the resulting metal complexes of a so-called "two-story" calix[6]azacryptand. This ligand (**1**) exhibits a N_6 coordination site that is constrained by the calix macrocycle. The TACN cap provides a strong trigonal coordination core and the PY spacers three additional N-donors. Their covalent linkage to the calix small rim preorganizes them in an orientation that is well suited for further binding to the metal center coordinated to the TACN cap. Indeed, Pb^{II} is strongly bound to the N_6 core, being resistant to heating in acidic and coordinating media. In this "two-story" system, the covalent linkages of the PY residues to the calixarene small rim have two other important consequences: they assemble a cavity receptor next to the metal binding site, thus favoring the encapsulation of exogenous guests in interaction with the metal center; they impose a structural constraint on the three PY donors that are not free to rotate relative to the TACN unit. Remarkably however, the Pb^{II} complexes herein characterized with **1** as a ligand display hemidirected environment. This indicates that in spite of the covalent links to the macrocycle, the N_6 core keeps enough freedom to wrap the metal center in this "open" geometry. This maintains a seventh site open for an interaction with an exogenous molecule bound in endoposition as observed with small neutral guests such as water, EtOH, and NMF. Interestingly, solution studies confirm the host−guest behavior of the complexes in solution, with evidence of embedment of neutral guest molecules such as EtOH, BuOH, and *N*-Me-formamide. They also suggest that the guest molecule is able to adapt its position in the cavity in order to optimize stabilizing interactions with the aromatic walls (CH-π with the Me group): EtOH goes down, BuOH goes up in order to position their methyl group in front of an aromatic nucleus. The overall flexibility of the system is further illustrated by the fact that an anionic ligand can bind in exoposition (illustrated by hexanoate). Hence, although ligand **1** can be considered as a N_6 cryptand, a seventh site remains open to interaction with exogenous ligands and allows either endo or exo binding. This stems from the introduction of the PY spacers that leave some flexibility to the calix cone: the endo complexation is associated with OMe expulsion, and exo binding is associated with OMe inclusion.

Compared to "one-story" systems (depicted in Scheme 1) for which the capping tripod is connected via a two-atom spacer to the calixarene core, ligand **1** presents a longer linker (formally, an aromatic nucleus has been inserted into the two-atom spacer) and a second level of donors (the three PY groups). As a result, this new ligand displays several common and several different features that have been highlighted through the study of its Pb^{II} complexes.

The main common features are (i) the presence of the triaza cap insures strong metal ion binding; (ii) three covalent links to the triaza cap constrains the calix[6]arene macrocycle into a cone conformation; (iii) this preorganizes the cavity for guest inclusion; (iv) the guest interacts with the metal center.

The most striking differences are (i) the metal coordination site is further away from the cavity; (ii) this favors electrostatic vs covalent metal-guest interaction; (iii) the calix-azacryptand structure is much more flexible; (iv) there is more space at the level of the small rim for the MeO groups that can now be included into the top of the truncated cone; (v) an exo coordination site becomes accessible, which is not the case with the "one-story" calix[6]azacryptands.

We are currently exploring the coordination and host−guest properties of this new calix-ligand with other metal ions, as well as orienting our efforts toward the synthesis of a water-soluble version of ligand **1**.

EXPERIMENTAL SECTION

Material and Methods. ^{1}H NMR spectra were recorded on a Bruker Avance 500 or a Bruker AC 250 spectrometer. IR spectra were recorded with a Perkin-Elmer Spectrum One spectrometer. Elemental analyses were performed at the Institut des Substances Naturelles, Gif sur Yvette, France.

Safety note: *Caution!* Although we have not encountered any problems, it is noted that perchlorate salts of metal complexes with organic ligands are potentially explosive and should be handled only in small quantities with appropriate precautions. For this reason, the isolated metal complexes were not strongly dried under a vacuum.

Synthetic Procedures for the Preparation of [Pb(1)](ClO$_4$)$_2$. To a suspension of ligand **1** (72.6 mg, 0.05 mmol) in 1.5 mL of THF was added 1 equiv of $Pb(H_2O)_3(ClO_4)_2$ salt. To this suspension CH_2Cl_2 (1 mL) was added in order to dissolve all reactants. The solution was stirred for 1 h at room temperature and then concentrated to about 150 μL. The product was precipitated by addition of pentane (5 mL) and collected by centrifugation. The resulting solid was washed twice with diethylether and pentane (5 mL × 2), then redissolved in CH_2Cl_2, filtered over Celite in order to remove any trace of inorganic salt, and finally evaporated to give a pure complex as a yellow solid (77,2 mg, yield: 92%).

[Pb(**1**)](ClO$_4$)$_2$. ^{1}H NMR (250 MHz, $CDCl_3/CD_3OD$ (1:1 v/v), 300 K): δ = 8.05 (t, 3H, J = 7.7 Hz, *p*-Py), 7.85 (d, 3H, J = 7.5 Hz, *m*-Py), 7.37 (s, 3H, Ar−H$_{out}$), 7.21 (d, 3H, J = 7.5 Hz, *m*-Py), 7.07 (s, 3H, Ar−H$_{out}$), 6.56 (s, 3H, Ar−H$_{in}$), 6.07 (s, 3H, Ar−H$_{in}$), 5.25 (s, 6H, OCH$_2$), 4.66 (d, 3H, J = 15.1 Hz, NCH$_2$), 4.56 (d, 3H, J = 15.5 Hz, ArCH$_2$(ax)), 4.27 (d, 3H, J = 13.7 Hz, NCH$_2$), 3.54−3.20 (m, 6H, TACN), 3.48 (d, 3H, J = 14.4 Hz, ArCH$_2$(eq)), 3.40 (s, 9H, OCH$_3$), 3.03 (d, 3H, J = 16.8 Hz, ArCH$_2$(ax)), 2.65 (d, 3H, J = 16.3 Hz, ArCH$_2$(eq)), 2.16 (bs, 6H, TACN), 1.37 (s, 27H, *t*Bu), 0.68 (s, 27H, *t*Bu). ^{13}C NMR (2D-HSQC only, no 1D ^{13}C spectrum due to solubility problems could be obtained), (125 MHz, $CDCl_3/CD_3OD$ (1:1 v/v)): δ = 141.3, 128.8, 128.8, 127.4, 125.9, 12.5, 122.5, 76.5, 65.9, 65.7, 61.7, 60.3, 60.3, 30.9, 30.8, 30.8, 30.7, 28.6, 28.1 ppm. IR (CH_2Cl_2) ν (cm^{-1}): 2960, 2923, 2859, 1598, 1575, 1481, 1461, 1362, 1260, 1194, 1182, 1104, 1011. ESI-MS (MeOH): m/z = 830.5 (1660.9/2) for [M^{2+}] (100) and 1759.8 for [M, ClO$_4^+$] (20) (Figure S2, Supporting Information). HRMS (ESI, MeOH): m/z = 1759.8582, calcd. for [M,ClO$_4^+$]: 1759.8530. Anal. Calcd for $C_{96}H_{120}Cl_2N_6O_{14}Pb$, 4 CH_2Cl_2: C, 54.60; H, 5.86, N, 3.82. Found: C, 54.95; H, 5.99,N, 3.74. Melting point: 250 °C (decomp.).

ASSOCIATED CONTENT

Ⓢ Supporting Information

Full characterization of the metal complexes and host−guest adducts. Crystallographic data (CIF file), 1D, 2D NMR, and mass spectra of the complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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