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Supramolecular Control of Hetero-multinuclear Polytopic Binding of Metal Ions (Zn^{II}, Cu^{I}) at a Single Calix[6]arene-Based Scaffold

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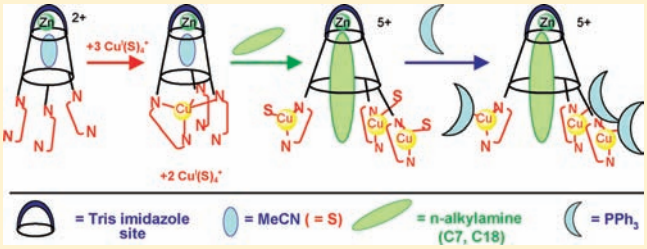
Supporting Information

ABSTRACT: A Calix[6]arene scaffold was functionalized to provide a tridentate binding site at the small rim and three bidentate chelate sites at the large rim of the cone to generate a heteropolytopic ligand. Its complexation to one equivalent of Zn^{II} at the small rim yields a *funnel* complex displaying both host−guest properties and preorganization of the three chelate groups at the large rim. These two aspects allowed the full control of the binding events to regioselectively form dinuclear Zn^{II} and heteropolynuclear Zn^{II}/Cu^{I} complexes. The heteropolynuclear systems all rely on the host−guest relationship thanks to the induced-fit behavior of the calix cavity. With the short guest MeCN, the large rim is preorganized into a trigonal tris-triazole core and accommodates a single Cu^{I} ion. A long guest breaks this spatial arrangement, and three Cu^{I} ions can then be bound at the tris-bidentate triazole-dimethylamine site at the large rim. In a noncoordinating solvent however, the tetranuclear complex is submitted to scrambling and the addition of exogenous π-acceptor ligands is required to control the binding of Cu^{I} in a well-defined environment. Hindrance selectivity was then induced by the accessibility at the small rim site. Indeed, while CO can stabilize Cu^{I} at both coordination sites, PPh_3 cannot fit into the cavity and forces Cu^{I} to relocate at the large rim. The resulting well-defined symmetrical tetranuclear complex thus arises from the quite remarkable selective supramolecular assembly of nine partners (1 Zn^{II}, 3 Cu^{I}, 1 calixarene, 1 guest alkylamine, 3 PPh_3).



INTRODUCTION

The function of complex systems is often based on multicomponent interactions. Such supramolecular assemblies are encountered in enzymes, where various subunits (for instance, oxidase, reductase, regulatory subunits in redox enzymes[1]) must interact synergistically for optimal activity. These self-assembly processes are based on exquisitely encoded interactions between the different components.

The building of discrete well-defined chemical architectures involving more than three components is tricky, as it often competes with the formation of polymeric species and/or assemblies based on fewer building blocks.[2−7] Coordination is one of the driving forces that can be used to assemble components. Nevertheless, incorporation of different metal ions into a polytopic scaffold faces a selectivity problem due to the difficult assignment of a specific role to each part. Heteroditopic ligands must be designed to build well-defined heterobimetallic systems. The existing strategies include the sequential formation of an inert complex at one site and a labile one at the other,[8−13] the use of a ligand bearing a "soft" site and a "hard" site to generate mixed hard/soft bimetallic complexes,[14−18] or imposing a geometrical constraint at one site to discriminate between two metal ions.[19] Most often, the coordination sphere in these systems is saturated,[20−23] and the lack of a labile site on the metal ions prevents their use as a coordination-based receptor or catalyst.

Synthesis of a heteropolymetallic coordination-based molecular receptor is thus a challenge, as it involves the regioselective assembly of at least four components: the host (a polytopic ligand), two different metal ions with a labile site, and a guest.[24−27] The first bimetallic complex based on a calix[6]-arene scaffold we have reported was a homodinuclear Zn^{II} complex with ligand L^{NH2} (Scheme 1).

Like all related tris-imidazole-based calix[6]-ligands, L^{NH2} was shown to strongly bind the first Zn^{II} ion at the small rim. The coordination of the second Zn^{II} at the tris-anilino site, however, required the presence of a $(H_3O_2)^-$ bridging unit inside the cone. This dinuclear species actually was found to be very sensitive to the environment due to the too weak donor tris-anilino site. Indeed, it readily lost its large rim metal ion upon competition with a coordinating solvent.[30] Replacing the tris-anilino core by a tris-triazolo one yielded a stronger ligand (L^{TOAr}, Scheme 1), which allowed the stabilization of homo- and heterodinuclear complexes with Zn^{II}, Cu^{I}, and Cu^{II} in acetonitrile.[28,31] Quite remarkably, the difference in donor properties and geometrical constraints between the small and large rim tris-aza sites allowed a very unique process of electrochemically triggered double translocation of the metal ions ($Cu^{I/II}$ and Zn^{II}). The next step of sophistication we thought to implement in our system was to increase the

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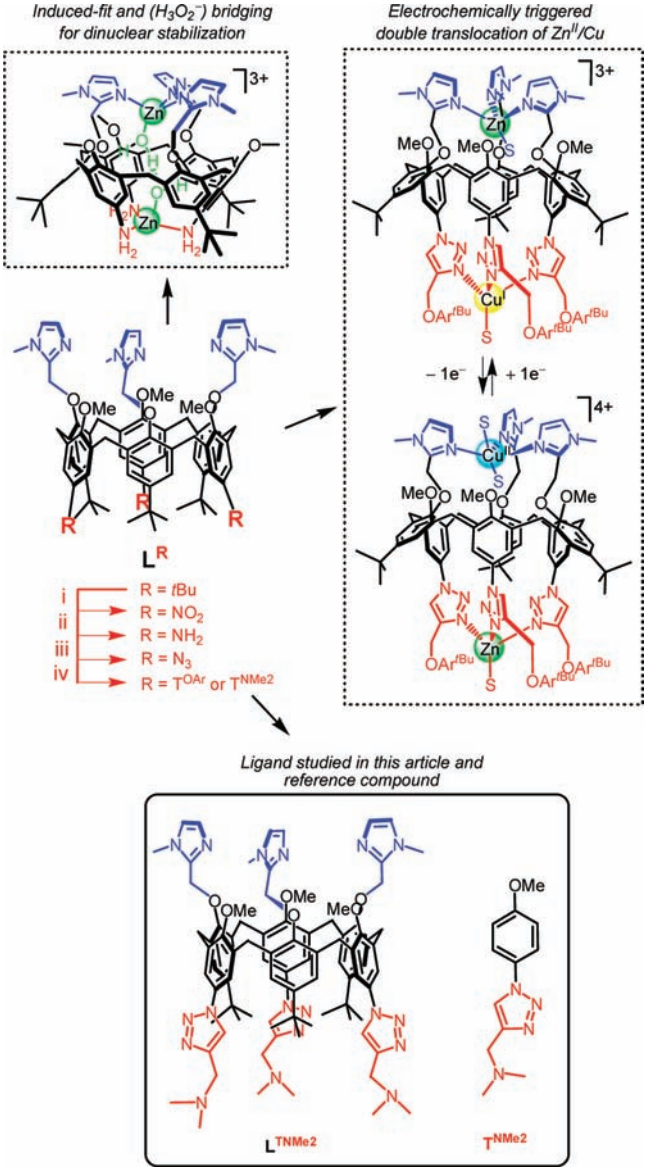
Scheme 1. (Bottom) Synthesis of L^{TNMe2};[a] (Top) Previously Described Dinuclear Complexes Based on L^{NH2} (left) and L^{TOAr} (right)



[a]Bottom: (i)−(iii) overall yield = 69%;[28] (iv) dimethylpropargylamine, $CuSO_4 \cdot 5H_2O$, sodium ascorbate, THF/water, yield = 80%.[29] The small rim site is highlighted in blue, the large rim site in red. Reference compound, T^{NMe2}, is a fragment of L^{TNMe2} without a cavity.

denticity of the ligands present at the large rim in order to coordinate more than two metal ions to the calix scaffold.

In the system reported herein, chelate bidentate ligands were grafted onto the calixarene large rim (see L^{TNMe2}, Scheme 1). The coordination of this new scaffold toward Zn^{II} and Cu^{I} and the host−guest behavior of the corresponding complexes were studied. Metal coordination to this heteropolytopic ligand remarkably occurs in a sequential and regioselective manner, giving access to regio-controlled mono- and polymetallic complexes. In particular, we report the selective formation of highly unusual heteropolynuclear assemblies {calixarene··Zn^{II}·Amine·$(Cu^{I})_3$·L_3}, where up to five distinct components selectively interact with each other. In these complexes, each metal ion is assigned to a specific site of the polytopic calix[6]arene scaffold through a guest-triggered switch of the Cu^{I} binding mode.

RESULTS AND DISCUSSION

Complexation Studies of Ligand L^{TNMe2} with Zn^{II} and Host−Guest Properties. Similarities with L^{TOAr}. *Sequential Coordination at the Small and Large Rim.* Ligand L^{TNMe2} was synthesized according to a reported procedure[29] and further characterized by HR-MS and ^{1}H NMR spectroscopy (Figures S1−S4). In CD_3CN, the ligand spectrum displayed broad resonances at 300 K; however, in the presence of one equivalent of Zn^{II}, a new set of well-defined and sharp resonances attested to the formation of a mononuclear complex as a single species (Figures 1 and S5), as previously observed

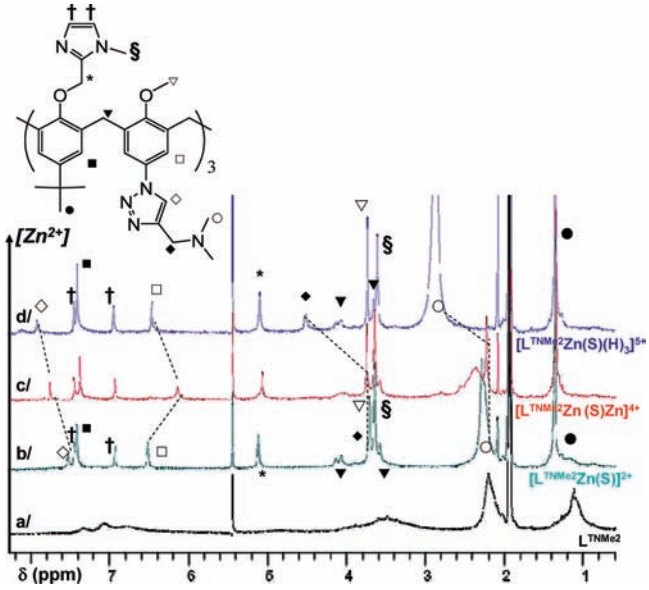


Figure 1. ^{1}H NMR spectra (250 MHz, 300 K, CD_3CN) of the different Zn^{II} complexes obtained with calix[6]arene L^{TNMe2} and isolated as single species (see the SI and Figure S10): (a) L^{TNMe2}; (b) $[L^{TNMe2}Zn(S)]^{2+}$; (c) $[L^{TNMe2}Zn(S)Zn]^{4+}$; (d) $[L^{TNMe2}Zn(S)(H)_3]^{5+}$. § = H_{NMe}; ▽ = H_{OMe}; ● = H_{tBu}; ∗ = H_{CH2Im}; † = H_{Im}; ▼ = H_{CH2Ar}; ○ = H_{NMe2}; □ = H_{ArTria}; ■ = H_{ArtBu}; ◇ = H_{Tria}; ♦ = $H_{CH2Tria}$. S = MeCN.

with ligand L^{TOAr}. This complex, namely, $[L^{TNMe2}Zn(S)]^{2+}$, displays the C_{3v} symmetry associated with the classical coordination observed for calix[6]arene complexes: Zn^{II} is tetrahedrally bound to the three imidazolyl arms and one guest solvent molecule inside the cavity with a calixarene scaffold constrained in a flattened cone conformation,[28,32] as shown in Scheme 2. The corresponding diperchlorato salt can be conveniently prepared in a mixture of MeCN and THF and isolated as a pure solid. Changing the perchlorate to triflate counterions did not affect the dicationic monozinc complex, as its NMR signature remained identical.

The addition of a second equivalent of Zn^{II} to $[L^{TNMe2}Zn(S)]^{2+}$ (Figure 1c) yielded the tetracationic dinuclear complex $[L^{TNMe2}Zn(S)Zn]^{4+}$ depicted in Scheme 2. The charge of the complex was confirmed by elemental analysis through the presence of four counterions. Its structure was identified by NMR spectroscopy (Figures 1 and S7), which showed a C_{3v} symmetrical complex as a single species that is very similar to that previously described with ligand L^{TOAr} (Scheme 1, Table S1).[28,33]

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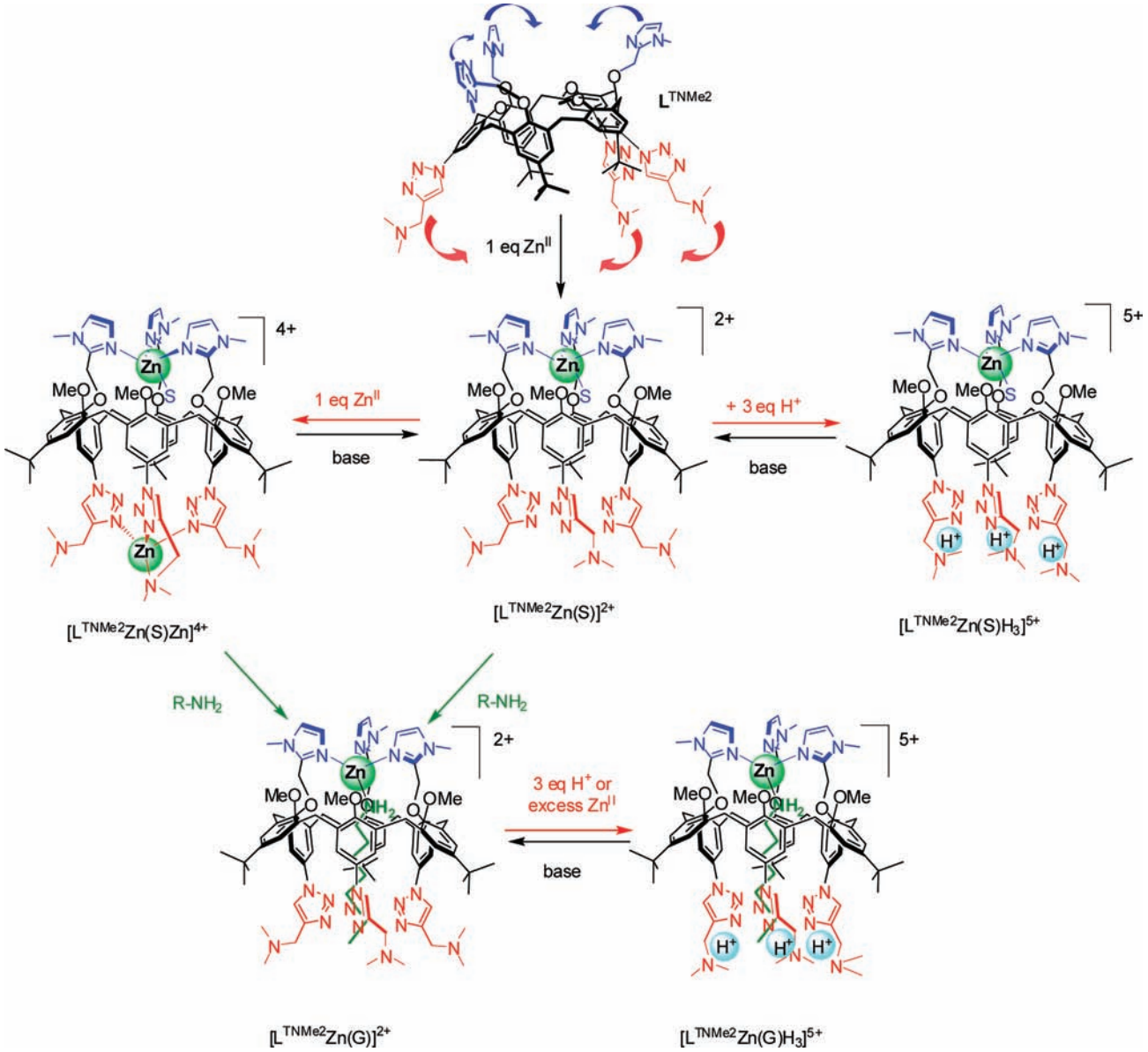
Scheme 2. Equilibria between $[L^{TNMe2}Zn(S)]^{2+}$, $[L^{TNMe2}Zn(S)Zn]^{4+}$, and $[L^{TNMe2}Zn(S)H_3]^{5+}$ and Host–Guest Properties of $[L^{TNMe2}Zn(S)]^{2+}$, $[L^{TNMe2}Zn(S)Zn]^{4+}$, and $[L^{TNMe2}ZnH_3]^{5+}$[a]



[a]G (guest) = *n*-heptylamine, S (solvent) = CD_3CN, and base = Et_3N.

Host–Guest Chemistry of the Zn^{II} Complexes. Like all previously described calix[6]trisimidazole-based mononuclear complexes, $[L^{TNMe2}Zn(S)]^{2+}$ displayed good host–guest properties with induced fit behavior. Indeed, the addition of one equivalent of *n*-alkylamines (G) to $[L^{TNMe2}Zn(S)]^{2+}$ led to the clean formation of the endo-bound complexes $[L^{TNMe2}Zn(G)]^{2+}$ (Figures 2 and S12). The corresponding NMR C_{3v} symmetrical signatures displayed the characteristic set of high-field resonances between 0 and −2 ppm, attesting to the endo coordination of the amines.[32] Interestingly, the degree of cavity opening as a function of the guest alkyl chain length could be conveniently monitored by the δ-shift of the H_{ArTria} protons, thus playing the role of reporters (Figure S12). Whereas δ = 6.50 ppm with the small MeCN guest, it shifted up to 6.93 ppm for heptylamine and octadecylamine, with intermediate values for an amine of medium size (6.78 ppm for propylamine). Indeed, it is known that the terminal methyl group of heptylamine is located just at the entrance of the large rim, at the *t*Bu level (Scheme 2).[32] The cavities of the heptylamine and

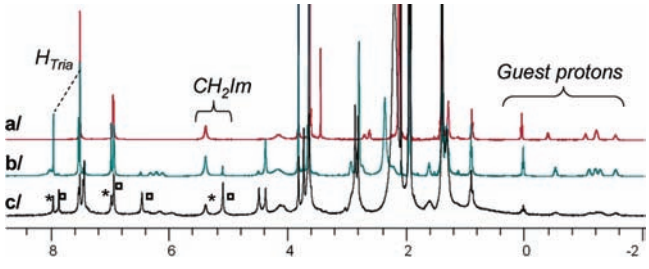


Figure 2. Implementation of Brønsted acid sites at the large rim (CD_3CN, 500 MHz, 300 K): (a) $[L^{TNMe2}Zn(G)]^{2+}$ (G = heptylamine); (b) $[L^{TNMe2}Zn(G)]^{2+}$ + 3 equiv of $Zn(OTf)_2$; (c) $[L^{TNMe2}Zn(G)]^{2+}$ + 3 equiv of $HClO_4$. * indicate peaks of $[L^{TNMe2}Zn(G)\ H_3]^{5+}$, and white squares peaks of $[L^{TNMe2}Zn(S)\ H_3]^{5+}$.

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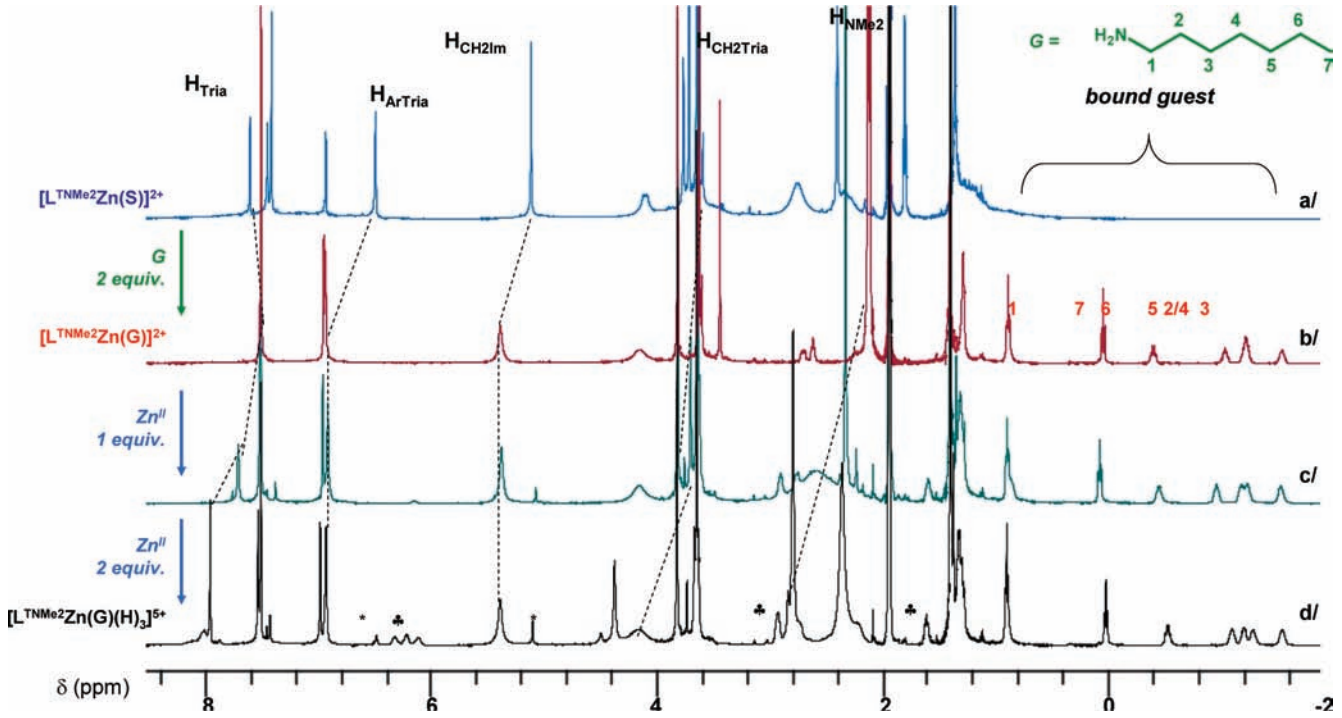

Figure 3. Evolution of the ^{1}H NMR spectrum (CD_3CN, 500 MHz, 300 K) of $[L^{TNMe2}Zn(S)]^{2+}$ (a) upon the successive addition of *n*-heptylamine (b, 2 equiv) and $Zn(OTf)_2$ (c, 1 equiv; d, 3 equiv). * correspond to the peaks of the minor species $[L^{TNMe2}Zn(S)\ H_3]^{5+}$. Clover symbol highlights the peaks of free heptylammonium.

octadecylamine adducts thus have similar openings, as the alkyl chain of the latter just extends further outside the cavity. This is shown by their quasi-superimposable spectra (Figure S12). With the shorter propylamino guest, however, the intracavity methylene protons are slightly shifted (with respect to heptylamine or octadecylamine). These observations indicate that the cavity shape is slightly different with a "gate closing" at the large rim that optimizes the host–guest interactions.[34] Finally, in a way also similar to what was observed with L^{TOAr}, addition of heptylamine to the dinuclear complex $[L^{TNMe2}Zn(S)Zn]^{4+}$ led to the decoordination of the large rim Zn^{II} ion and formation of the mononuclear host–guest adduct, $[L^{TNMe2}Zn(G)]^{2+}$.

Hence, this first study showed that, quite remarkably, the implementation of three dimethylamino donors at the large rim (compared to ligand L^{TOAr}) did not affect the Zn^{II} binding selectivity nor the host–guest properties of the system: the small rim tris-imidazole site remains the strongest site for the coordination of Zn^{II}, whereas the tris-triazole core still allows the binding of a second Zn^{II} in a trigonal environment. We then explored the potential binding properties of these "free" dimethylamino sites at the large rim and initiated the study with the exploration of their acid–base properties.

Implementation of Brønsted Acid Sites on the L^{TNMe2} Zn^{II} Host–Guest System. *Selective Protonation of the Large Rim.* Further addition of Zn^{II} to $[L^{TNMe2}Zn(S)Zn]^{4+}$ actually did not yield a complex of higher nuclearity. Instead, protonation of the large rim occurred, leading to the selective decoordination of one zinc ion. After the addition of three molar equivalents of Zn^{II}, a mononuclear tris-protonated complex, $[L^{TNMe2}Zn(S)H_3]^{5+}$, was obtained as a single species (Scheme 2, Figure S8). Hence, the additional Zn^{2+} dication has activated residual water present in solution, which behaved as a Brønsted acid $[ZnOH_2^{2+} \Rightarrow ZnOH^+ + H^+]$, rather than being coordinated to the poly aza core at the large rim. Indeed, the same species was generated by direct reaction of a strong acid with the mono-Zn complex: titration of $[L^{TNMe2}Zn(S)]^{2+}$ by $HClO_4$ (Figure S9) was characterized by a continuous downfield shift of the resonances of the H_{Tria}, $H_{CH2Tria}$, and H_{NMe2} protons, leading to the spectrum displayed in Figure 1d after three equivalents of acid. No shift was observed for the other resonances. Such a behavior indicates the selective protonation of the complex at the large rim sites, affecting simultaneously the triazole and the tertiary amino groups. The corresponding complex can be formulated as $[L^{TNMe2}Zn(S)(H)_3]^{5+}$ (Scheme 2). The proton stoichiometry was confirmed by elemental analysis and ESI-MS spectrometry of the isolated complex (SI). Further addition of $HClO_4$ led to full decomplexation and protonation of the ligand (Figure S9).

Displacement of Equilibria. As above-mentioned, a solution containing a 1:4 mixture of L^{TNMe2} and Zn^{II} led to the selective formation of the mono-Zn trisprotonated species $[L^{TNMe2}Zn(S)H_3]^{5+}$. Addition of base (triethylamine) to this solution led first to the clean formation of the dinuclear $[L^{TNMe2}Zn(S)Zn]^{4+}$ complex. Further addition of base led to the loss of the large rim Zn^{II} center, probably through Zn^{II}-hydroxide precipitation (Figure S11), yielding $[L^{TNMe2}Zn(S)]^{2+}$. This process was fully reversible, as subsequent addition of acid regenerated the starting species. Equilibria between $[L^{TNMe2}Zn(S)]^{2+}$, $[L^{TNMe2}Zn(S)Zn]^{4+}$, and $[L^{TNMe2}Zn(S)H_3]^{5+}$ can thus be easily displaced in one direction or the other by simple addition of Zn^{2+}, acid, or base (Scheme 2).

Formation of the Tris-protonated Pentacationic Host–Guest Complex. When a second equivalent of Zn^{II} was added to a solution containing $[L^{TNMe2}Zn(G)]^{2+}$ with G = *n*-heptylamine, a strong downfield shift of the H_{Tria}, H_{NMe2}, and $H_{CH2Tria}$ resonances was observed (Figure 3b and c), while

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other calixarene peaks remained little affected. This is indicative of the partial protonation of the host-adduct at the large rim.

The full Zn^{II} titration yielded the tris-protonated adduct $[L^{TNMe2}Zn(G)H_3]^{5+}$ as a single species for three equivalents added (Figure 3d). Indeed, the same species was produced by direct addition of $HClO_4$ to $[L^{TNMe2}Zn(G)]^{2+}$ (Figures 2 and S13). Interestingly, bound guest protons revealed to be sensitive to the change of the environment. This was indicated by the upfield shift of their resonances and the splitting of the peaks of methylene groups 2 and 4. Hence, the presence of a long guest such as heptylamine prevents the coordination of a second equivalent of Zn^{II} at the large rim, whereas selective protonation of the large rim remains possible, inducing a subtle conformation change with a guest alkyl chain packed deeper in the cavity.

Having evidenced a Brønsted acid−base chemistry induced by additional Zn^{II} (through O−H bond polarization of bound water), the coordination ability of the bidentate nitrogenous groups at the large rim was then explored with a weaker Lewis acidic and softer metal ion, Cu^{I}.

Heteropolymetallic Zn^{II}/Cu^{I} Complexes of L^{TNMe2} and Their Host−Guest Behavior. *Heterodinuclear Complex.* Addition of $Cu(MeCN)_4BArF$ (BArF = tetra-perfluorophenylborate) to $[L^{TNMe2}Zn(S)]^{2+}$ was characterized by a downfield shift of the H_{Tria} resonances ($\Delta\delta \approx 0.15$ ppm) and an upfield shift of the H_{ArTria} ones ($\Delta\delta \approx 0.16$ ppm, Figure 4, Table S1).

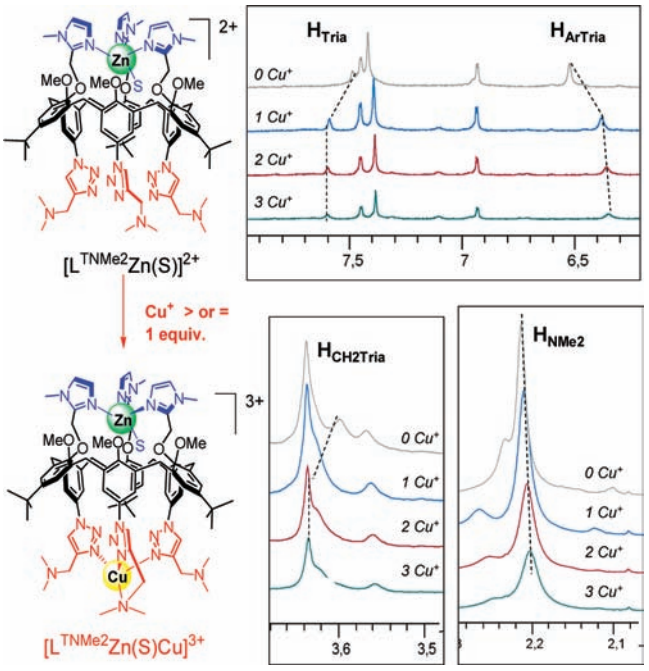

Figure 4. ^1H NMR titration of $[L^{TNMe2}Zn(S)]^{2+}$ by $Cu^{I}(MeCN)_4BArF$ (CD_3CN, 250 MHz, 300 K).

By analogy with Zn^{II} coordination, this was ascribed to the binding of one Cu^{I} center to the three triazole groups at the large rim, while maintaining Zn^{II} bound at the small rim. Full complexation was almost reached for one equivalent. Addition of up to three equivalents of Cu^{I} did not yield any new species but displaced the equilibrium (fast on the NMR time scale) toward Cu complexation, as indicated by the slight shift of the above-mentioned peaks. Such a ditopic complexation was already reported for L^{TOAr} (Scheme 1, Table S1) with similar values of $\Delta\delta$.[31,33] The structure depicted as $[L^{TNMe2}Zn(S)Cu]^{3+}$ in Figure 4 is thus proposed. Cu^{I} binding at the large rim in the trigonal environment provided by the triazole core was further confirmed by CO coordination. Indeed, when CO gas was bubbled into a dichloromethane solution of $[L^{TNMe2}Zn(S)Cu]^{3+}$, the IR spectrum (Figure S15b) displayed a single ν_{CO} stretch at 2099 cm^{-1}, in accordance with the formation of a N_3CuCO core, as expected given the structure proposed for the dinuclear complex.[31]

Heterotetranuclear Complex. Titration of $[L^{TNMe2}Zn(G)]^{2+}$ by Cu^{I} was carried out (Figure 5, G = heptylamine). As above-

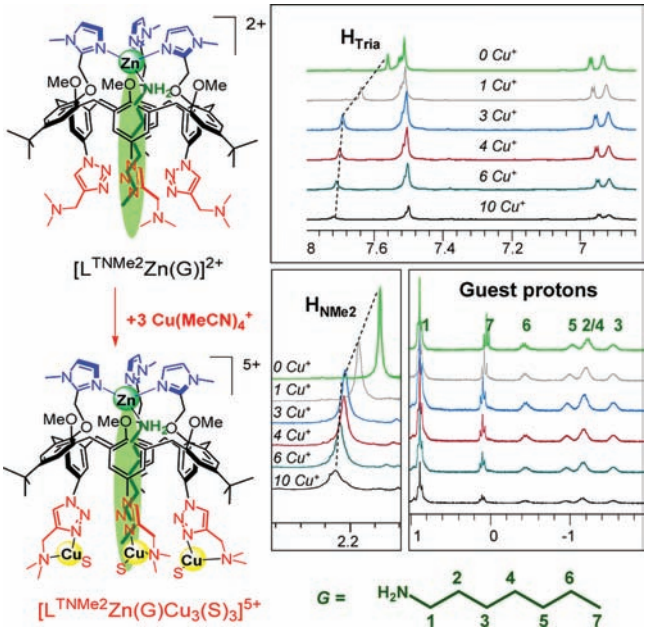

Figure 5. ^1H NMR titration of $[L^{TNMe2}Zn(G)]^{2+}$ (triflate salt, G = heptylamine) by $Cu^{I}(MeCN)_4PF_6$ (CD_3CN, 250 MHz, 300 K).

mentioned, the inclusion of heptylamine in the cavity can be monitored by its shielded resonances between 0 and −2 ppm. After the addition of increasing quantities of $Cu(MeCN)_4^+$ to $[L^{TNMe2}Zn(G)]^{2+}$, the ^1H NMR spectra were almost unchanged with the exception of the H_{Tria} and the H_{NMe2} peaks, which were shifted downfield (Figure 5, Table S1). The fact that the H_{ArTria} resonance was not shifted rules out a tris-triazole environment for Cu^{I}. Cu^{I} coordination thus occurred at the triazole and tertiary amine sites in a bidentate fashion with retention of the guest. A fast exchange at these large rim sites likely occurred, explaining the observed C_{3v} symmetrical pattern and the continuous shifts observed for the H_{Tria} and H_{NMe2} resonances. Full complexation was almost reached for three equivalents, in accordance with the formation of a tetranuclear complex, $[L^{TNMe2}Zn(G)(Cu)_3(S)_3]^{5+}$ (Figure 5, Scheme 3).[35]

Selective Ligand Exchange at the Cu(I) Centers of the Heterotetranuclear $ZnCu_3$ Complex. *Noncoordinating vs Coordinating Solvent: N-Donor Site Scrambling.* In a noncoordinating solvent such as CD_2Cl_2, a mixture of L^{TNMe2}, Zn^{II}, heptylamine, and Cu^{I} in a 1:1:2:3 ratio did not yield a clean C_{3v} symmetrical species like in MeCN, but rather a mixture of several species, as shown by a very complicated NMR signature ascribed to N-donor site scrambling (Figure S16). The origin of this scrambling is probably due to the absence of a stabilizing ligand for Cu^{I} to adopt a trigonal geometry (triazole/NMe_2/S in MeCN). Only in large excess (pure solvent) could MeCN stabilize Cu^{I} in a trigonal

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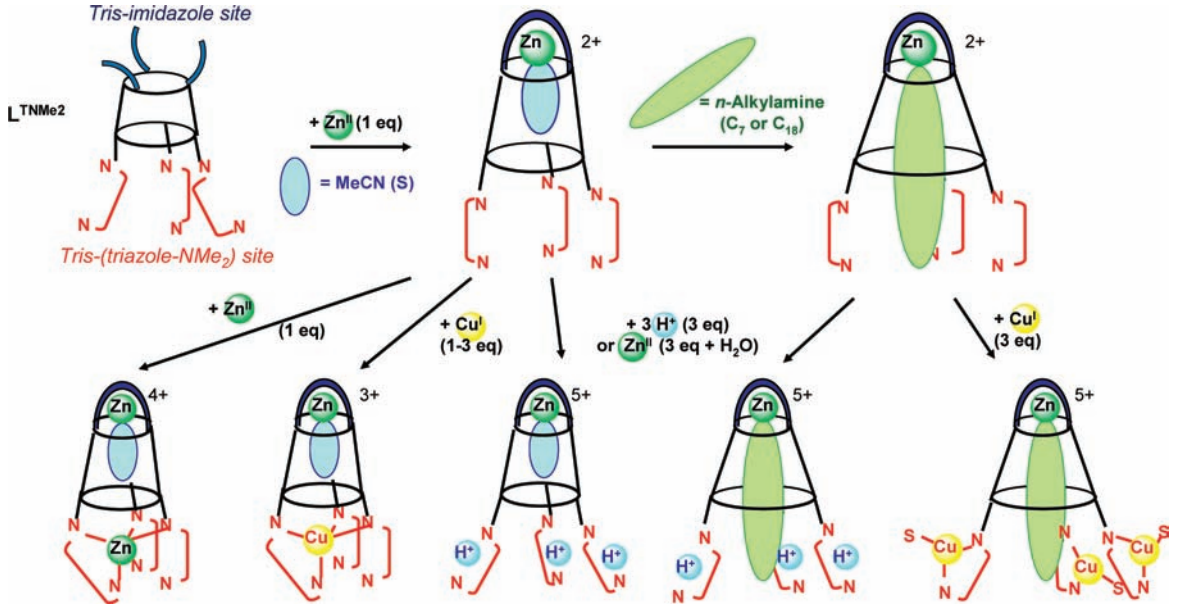
Scheme 3. Sequential and Regioselective Synthesis of Seven Homo- and Heteropolymetallic Complexes As Single Species in Solution



environment at the large rim. We thus tested the ability of other exogenous ligands to bind to the cuprous sites.

"On Site" Stabilization of Cu^{I} by CO Binding. CO was bubbled into a solution containing the above-described scrambled tetranuclear species in $CD_3CN/CDCl_3$ (1:4 v/v). Although several species remained in solution, the NMR spectra recorded before and after CO bubbling indicated a loss of endo-bound amino guest G (Figure S16). The corresponding IR spectrum exhibited two ν_{CO} absorptions at 2112 and 2099 cm^{-1}, assignable to N_2CuCO and N_3CuCO cores, respectively (Figure S15).[36−38] All this indicates that Cu^{I} adopts a well-defined coordination sphere upon CO binding and that either the Td (tetrahedral) Cu^{I}(CO) core at the tris-imidazole site efficiently competes with Zn^{II}(G) binding or a Td Cu^{I}(CO) tris-triazole core at the large rim site prevents guest binding at the small rim. However, the latter appears less probable, as this binding mode would limit the overall nuclearity to two (one metal at the large rim and one at the small rim). The two extra metal ions would have to remain free in solution, which is unlikely in a noncoordinating solvent.

Selective Binding of PPh_3: Relocation of Cu^{I} at the Large Rim. In contrast to CO, the addition of three equivalents of PPh_3 generated a ^{1}H NMR symmetrical C_{3v} pattern (Figure 6d) very similar to that of $[L^{TNMe2}Zn(G)Cu_3(S)_3]^{5+}$ in CD_3CN. The new set of aromatic protons ascribed to PPh_3 indicated that it was bound to Cu^{I}, as the resonances of its phenyl protons were well split with respect to the free phosphine (Figure S17). The ^{1}H and ^{31}P chemical shifts were different from those recorded for a simple equimolar mixture of $Cu(MeCN)_4BArF$ and PPh_3 without calixarene (Figure S17), which confirms that Cu^{I} is still bound to the bidentate groups at the large rim. Further addition of PPh_3 demonstrated that free and bound "Cu^{I}-PPh_3" are in fast exchange on the NMR time scale (Figure S17i,j,k). The complex formed with three equivalents of PPh_3 can thus be formulated as $[L^{TNMe2}Zn(G)Cu_3(PPh_3)_3]^{5+}$ (Figure 6).

These various results confirm that the three triazole-dimethylamino groups at the large rim are able to bind Cu^{I} in a bidentate fashion, provided an extra ligand (MeCN, CO, or

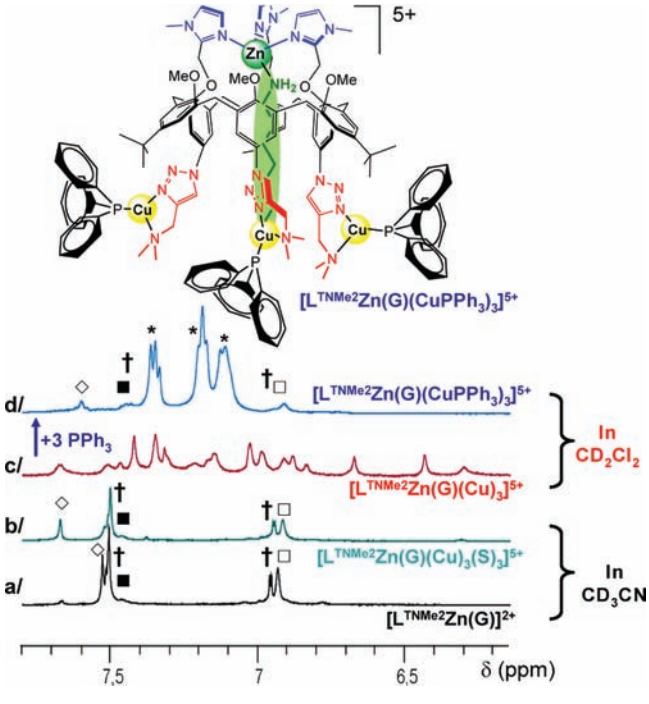


Figure 6. Formation of the triphenylphosphine adduct $[L^{TNMe2}Zn(G)(CuPPh_3)_3]^{5+}$, with G = *n*-heptylamine. Aromatic region of the ^{1}H NMR spectra for (a) $[L^{TNMe2}Zn(G)]^{2+}$, CD_3CN, 300 MHz; (b) $[L^{TNMe2}Zn(G)Cu(S)_3]^{5+}$, CD_3CN (S), 300 MHz; (c) $[L^{TNMe2}Zn(G)Cu_3]^{5+}$, CD_2Cl_2, 500 MHz; (d) $[L^{TNMe2}Zn(G)Cu_3]^{5+}$ + 3 PPh_3, CD_2Cl_2, 500 MHz. † = H_{Im}; □ = H_{ArTria}; ■ = H_{ArtBu}; ◇ = H_{Tria}; * = PPh_3 protons.

PPh_3) completes the coordination sphere to three-coordinate. They also indicate that $[L^{TNMe2}Zn(G)(Cu)_3]^{5+}$ is a selective system with respect to the coordination of these exogenous ligands. CO is a strong π-acceptor and thus displaces the equilibria in favor of the formation of Cu−CO bonds. But as a small ligand, it can fit in both environments, the large rim and the small rim, yielding a mixture of species. In contrast, PPh_3

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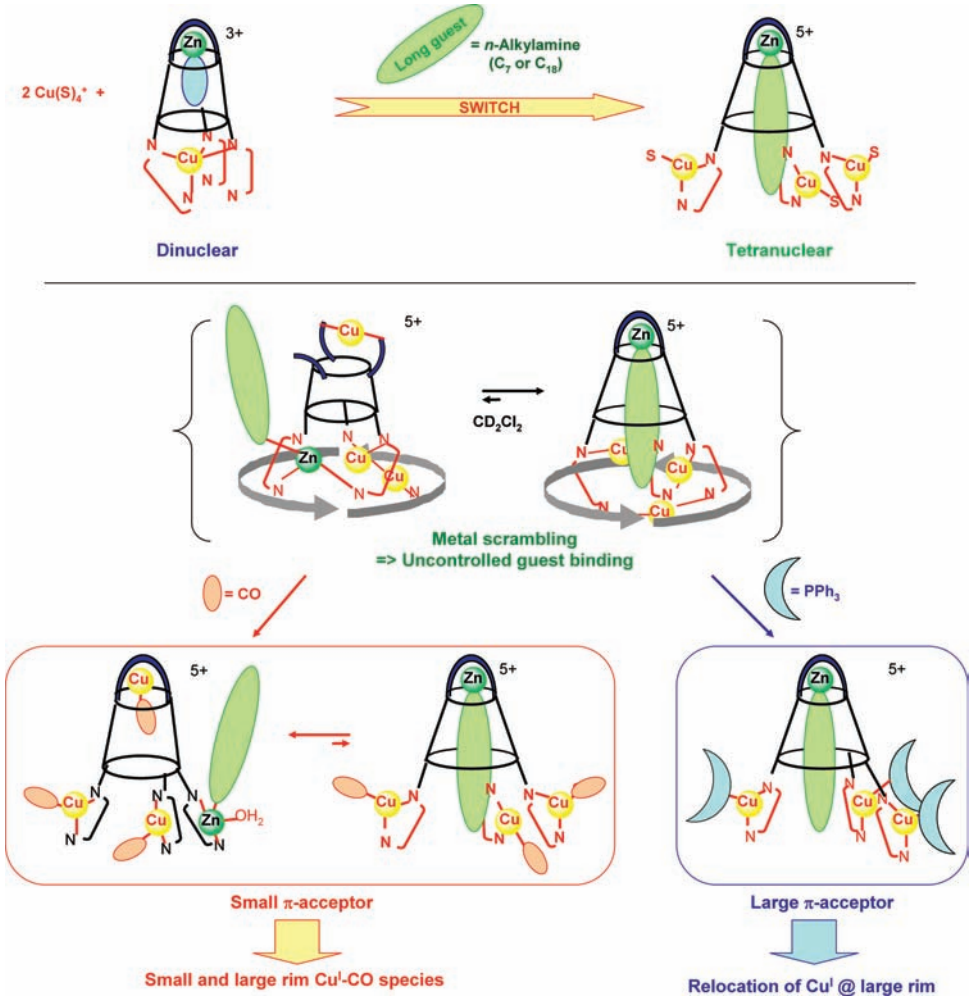
Scheme 4. (Top) Guest-Induced Selectivity in Heteropolymetallic Systems and Switch of Cu^{I} Binding Mode;[a] (Bottom) Cavity-Induced Steric Selectivity and Cu^{I} Relocation in Dichloromethane



[a]S stands for the solvent MeCN.

binding at the small rim is prevented as the cavity cannot accommodate it for sterical reasons. PPh_3 thus displaces the equilibria to maximize Cu–PPh_3 bond formation and forces Cu^{I} to relocate at the large rim, leading to a symmetrical C_{3v} adduct. This illustrates a size selectivity of the system between two π-acceptor ligands (Scheme 4, bottom).

Guest-Triggered Switch of the Cu^{I} Binding Mode. Two different well-defined types of Cu^{I} binding at the large rim have been observed so far. When the solvent MeCN (S) sits in the cavity of complex $[L^{TNMe2}Zn(S)]^{2+}$, the triazole groups at the large rim behave as a tridentate core for the coordination of a single Cu^{I}, and $[L^{TNMe2}Zn(S)Cu]^{3+}$ is the only detected species, even in the presence of excess Cu^{I}. In contrast, in the presence of heptylamine (G) endo-bound to Zn^{II}, coordination of Cu^{I} to $[L^{TNMe2}Zn(G)]^{2+}$ involves the bidentate triazole-dimethylamino chelate moieties, provided an exogenous ligand (MeCN, CO, or PPh_3) is present, and tetranuclear $ZnCu_3$ complexes are obtained. This suggests that the guest ligand plays a key role in the coordination mode of Cu^{I} at the large rim. Indeed, when heptylamine was added to a MeCN solution of $[L^{TNMe2}Zn(S)Cu]^{3+}$ containing an excess of Cu^{I} (two extra equivalents), the NMR signature of the tetranuclear complex, $[L^{TNMe2}Zn(G)Cu_3(S)_3]^{5+}$, was obtained (Figure 7). It highlights a switch of the Cu^{I} coordination mode from tridentate tris-triazole to bidentate triazole-dimethylamino induced by heptylamine binding to Zn^{II}. Hence, with a large guest, the cavity must open to accommodate it, and the preorganization of the tris-triazole core is lost for Cu^{I}. Consequently, the alternative bidentate triazole-dimethylamino coordination mode becomes the preferred one (Scheme 4, top). Similar behavior relative to the formation of $[L^{TNMe2}Zn(G)Cu_3(S)_3]^{5+}$ species was observed with other guest amines (G = octadecylamine; Figure S18).

■ DISCUSSION/CONCLUSION

The synthesis and coordination properties of a polytopic calix[6]arene ligand bearing coordination sites at both rims of its conic macrocycle were described. Ligand L^{TNMe2} displays a strong tris-imidazolyl coordination core at the small rim for a Td metal ion, provided a guest ligand favorably interacts within the calixarene cavity. Once coordinated to a Td metal ion thanks to a guest donor, the calixarene core is closed at the small rim. Interestingly, the degree of vicinity of the three remaining bidentate amino sites at the large rim depends on the cavity opening, which, in turn, is controlled by the guest ligand. Hence, the mono-Zn complex revealed to be a powerful building block for generating a variety of species with different

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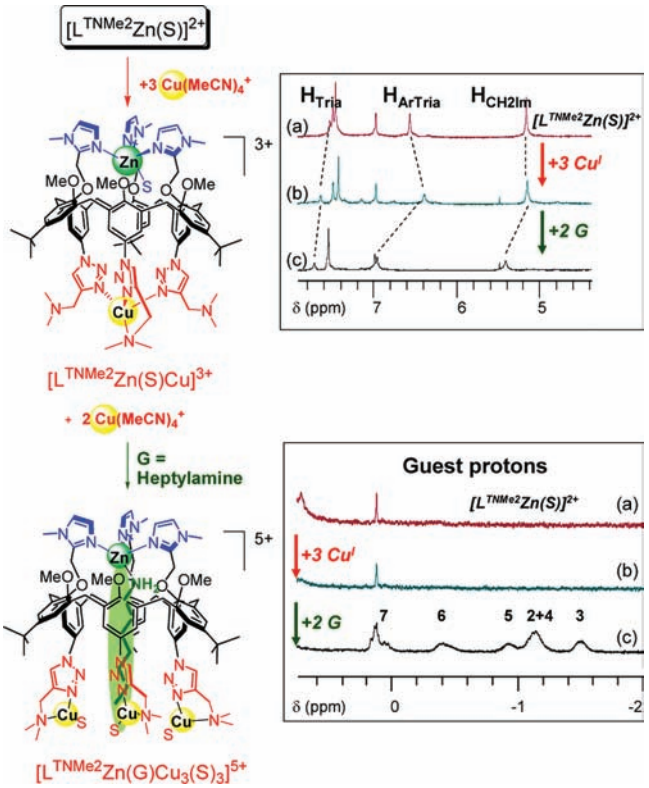

Figure 7. Guest-triggered switch of the Cu^{I} coordination mode at the large rim followed by ^{1}H NMR (CD_3CN, 250 MHz, 300 K). (a) $[L^{TNMe2}Zn(S)]^{2+}$; (b) $[L^{TNMe2}Zn(S)]^{2+}$ + 3 equiv of $Cu^{I}(MeCN)_4PF_6$; (c) $[L^{TNMe2}Zn(S)]^{2+}$ + 3 equiv of $Cu^{I}(MeCN)_4PF_6$ + 2 equiv of heptylamine.

functionalities. The major findings of this study are discussed below.

- *A host displaying a tunable (H^+) environment for guest binding* (Scheme 3). Once bound to the Zn^{II} cation, the tris-imidazole core becomes quite resistant to protonation. As a consequence, the mononuclear complexes $[L^{TNMe2}Zn(S)]^{2+}$ and $[L^{TNMe2}Zn(G)]^{2+}$ can be cleanly and selectively protonated at the large rim triazole-dimethylamino sites without loss of the metal ion or endo-bound guest alkylamine. This interestingly provides a polycationic environment around the guest alkyl moieties and opens routes for multipoint recognition.
- *Homo- and heterodinuclear metal complexes* (Scheme 3). The large rim donors can also be used for the selective complexation of a second Td metal ion such as Zn^{II} or Cu^{I}, thus closing the entrance of the cavity. Such a selectivity in favor of dinuclear species is possible only with a small guest ligand (MeCN) and has been previously highlighted by calorimetric determination of the thermodynamic parameters of coordination equilibria with the L^{TOAr} scaffold.[39] On the one hand, the small rim complexation was shown to be associated with a negative entropy variation, due to the freezing of the calixarene conformation by Zn^{II}; on the other hand, the positive entropy change associated with the coordination of a second Zn^{II} center at the large rim highlighted a well-preorganized tris-triazole trigonal core induced by the small rim complexation in MeCN. This explains why, in spite of the increased denticity at the large rim of L^{TNMe2}, homo- (Zn^{II}_2) and hetero- ($Zn^{II}Cu^{I}$) dinuclear complexes are favored at the expense of complexes of higher nuclearities with a small guest ligand (MeCN).
- *Heterotetranuclear complexes with controlled labile sites* (Scheme 4, bottom). Guest binding is required for the formation of the heterotetranuclear species. However, the presence of extra ligands is also required in order to stabilize Cu^{I} at the large rim, in the form of either solvent molecules (MeCN, Scheme 3) or exogenous ligands (CO, PPh_3). Addition of π-acceptor ligands to probe Cu^{I} coordination evidenced a size selectivity phenomenon. While CO stabilizes Cu^{I} at both small and large rim sites, the bulky PPh_3 drives Cu^{I} coordination back to the only site that is accessible to it, i.e., the large rim bidentate cores. This relocation of Cu^{I} yields $[L^{TNMe2}Zn(G)(Cu)_3(PPh_3)_3]^{5+}$ as a single species. The key features that allow the formation of such an unusual heterotetranuclear complex are the adequate denticity of the ligands grafted at the large rim that favors the binding of the metal ion of lower Lewis acidity (Cu^{I} vs Zn^{II}) and the receptor properties of the funnel. The long amino guest stabilizes the metal ion of higher Lewis acidity (Zn^{II}) at the small rim and allows the control of the environment at the large rim, disfavoring simultaneous binding of several triazole groups to the same metal ion.
- *Guest-induced switch of the metal ion binding modes* (Scheme 4, top). Inclusion of a long chain guest (e.g., G = *n*-heptylamine or octadecylamine) into the calixcone moves the triazole groups away from each other. This changes the coordination mode of Cu at the large rim from the *tris(triazole)* core to the bidentate *triazole-dimethylamine* sites. The nuclearity of the system consequently switches from di- to tetranuclear, as shown by the formation of a very unusual coordination complex, $[L^{TNMe2}Zn(G)Cu_3(S)_3]^{5+}$, in which up to five distinct components are self-assembled in a 3-fold symmetrical heteropolymetallic complex with site selectivity of Zn^{II} over Cu^{I}.

Interestingly, in $[L^{TNMe2}Zn(G)Cu_3(S)_3]^{5+}$, three Cu^{I} complexes are formed at the large rim of the calixarene, while the guest remains anchored in the cavity and dangling in the middle of them. Such an architecture is highly reminiscent of the active site of enzymatic systems.[40] Indeed, (i) copper centers are maintained in the vicinity of each other with nuclearity control, (ii) the copper site is located next to a substrate binding site (mimicked here by the conical Zn^{II} calix[6] complex), (iii) the substrate is held in place in a regioselective manner and preorganized toward the copper site, (iv) the supramolecular environment adapts to the substrate to optimize interactions through induced fit, like for many enzymes,[41,42] (v) substrate binding can trigger a change of the coordination number of the metal ion: in various mononuclear iron enzymes,[43−47] a switch from six- to five-coordinate of the ferrous center is observed upon substrate binding. This change is thought to prepare iron for O_2 activation next to the bound substrate and to protect the enzyme itself against self-hydroxylation.[48] We observed that the $[L^{TNMe2}Zn(G)Cu_3]^{5+}$ system was able to interact with carbon monoxide, which is an analogue of O_2 devoid of redox properties. We are now focusing our efforts on studying its behavior toward O_2, trying to identify putative transient Cu/O_2 adducts and thoroughly analyzing postoxygenation solutions. Indeed, guest preorganization toward such a transient species could lead, as in natural systems, to largely improved kinetics

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with respect to classical model systems and exquisitely tuned regioselectivity in oxidation.

■ ASSOCIATED CONTENT

Supporting Information

Experimental section: Synthesis and characterization (^{13}C, COSY, HSQC, MS) of ligand L^{TNMe2} and complexes $[L^{TNMe2}Zn(S)](ClO_4)_2$, $[L^{TNMe2}Zn(S)Zn](ClO_4)_4$, and $[L^{TNMe2}Zn(S)(H)_3](ClO_4)_5$. NMR spectra of host–guest adducts $[L^{TNMe2}Zn(G)](ClO_4)_2$ with G = *n*-alkylamine (C3, C7, C18). Titrations of $[L^{TNMe2}Zn(S)](ClO_4)_2$ by Zn^{II} and $HClO_4$, of $[L^{TNMe2}Zn(G)](ClO_4)_2$ by $HClO_4$, of T^{NMe2} by Cu^{I}, and of $[L^{TNMe2}Zn(G)](ClO_4)_2$ by Cu^{I} (G = *n*-octadecylamine). Infrared spectra of Cu^{I}-CO adducts. Full NMR spectra ($^{1}H/^{31}P$) of PPh_3 binding to $[L^{TNMe2}Zn(G)](ClO_4)_2$ with G = *n*-heptylamine. 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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