Proton-induced motion in a molecular cup-and-ball zinc *funnel* complex

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ABSTRACT

A Zn(II)-*funnel* metal complex built around a calix[6]arene cavity can undergo a dramatic conformational change upon a protonic stress with the use of a primary amine intermediate. In the resting state, the strong amine ligand is bound to the Zn(II) cation and the hydroxyl arm is pending out of the cavity. Addition of an acid causes the protonation of the amine and the self-coordination of the hydroxyl arm into the calix cavity. This switch, which is fully reversible and operated with sequential additions of acid and base, is reminiscent at the molecular level, of a cup-and-ball toy.

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A molecular machine is defined as a functional system for which an external stimulus triggers a controlled, reversible and large amplitude molecular motion aiming at performing a task.[1] Such a device can be defined by the nature of the stimulus and the observed motion (conformational or configurational). Since the pioneer works by Sauvage and co-workers[2] and Stoddart and co-workers[3] on topologically nontrivial molecules, even more sophisticated systems have emerged.[1,4] Among the different stimuli, the most popular one is based on the control of the pH.[5] It necessitates the use of simple acid/base chemistry applied to large molecular structures. Besides translational and rotational motions most often found in catenanes and rotaxanes, the intramolecular recognition of a substrate by a cavity, reminiscent of a cup-and-ball device, offers another large conformational reorganization.[6,7] In the latter example, the conformational switch controls the opening/closing of a cavity for an exogenous ligand. We wish to report in this article a pH-switch of a cup-and-ball Zn(II) complex mediated by an exogenous primary amine.

For the last decade, we have been interested in the study of *funnel* complexes. These complexes are based on a calix[6]arene ligand presenting at the small rim some coordinating units.[8] Interestingly, the metal center (Zn(II), Cu(II) or Cu(I)) bound to this ligand has a labile coordination site oriented toward the inside of the calixarene cavity. In the case of Zn(II) complexes, this coordination site can be occupied by a solvent molecule (in the case of CH_3CN), a water molecule (in a non coordinating solvent such as $CHCl_3$) or an exogenous ligand (primary amine for instance).

We have recently described two Zn(II) complexes, [ZnL^{OH}]$(ClO_4)_2$ and [ZnL^{NH_2}]$(ClO_4)_2$, based on a calix[6]arene presenting one functional arm able at the large rim to interact intramolecularly with the metal center through the cavity (Scheme 1).[9] These complexes belong to the family of Ouroboros-like molecules.[10] We have shown that the amino and hydroxyl derivatives behave differently. For [ZnL^{NH_2}]$^{2+}$, the amino arm is strongly bound to the metal center in an *endo*-position either in $CHCl_3$ (a non-coordinating solvent) or in CH_3CN (a competitive coordinating solvent). Indeed, the *endo*-conformation is entropically stabilized and addition of 3–5 equiv of an exogenous primary amine RNH_2 does not allow to expulse the *endo*-bound arm. On the contrary, in the case of [ZnL^{OH}]$^{2+}$, both *endo*- and *exo*-conformations can be obtained as a function of the solvent nature or in the presence of a strong exogenous ligand (see Scheme 1). For instance, in pure CH_3CN, the *exo*-conformation greatly predominates (in a 97:3 ratio) while the *endo*-conformation is the only species present in $CHCl_3$. In a parent Zn(II) metal *funnel* complex deprived of a coordinating arm at the large rim, a large excess of alcohol exogenous ligand (ca. 60 equiv) is required to compete with the 3–5 equiv of water present in solution and form the host–guest adduct.[11] It proves again that the self-coordination (of an alcohol in this case) is strongly reinforced for entropic reason.

We were then interested in tuning the access for an exogenous substrate to the metal center by pH change. We first investigated an inclusion complex with a symmetrical calixarene complex [ZnX_6N_3]$(ClO_4)_2$ and a primary amine in CD_3CN (Fig. 1).[12] The formation of the inclusion complex was easily monitored by ^1H NMR spectroscopy. Indeed, the observation of three new resonances in the high field region revealed the presence of the amino guest

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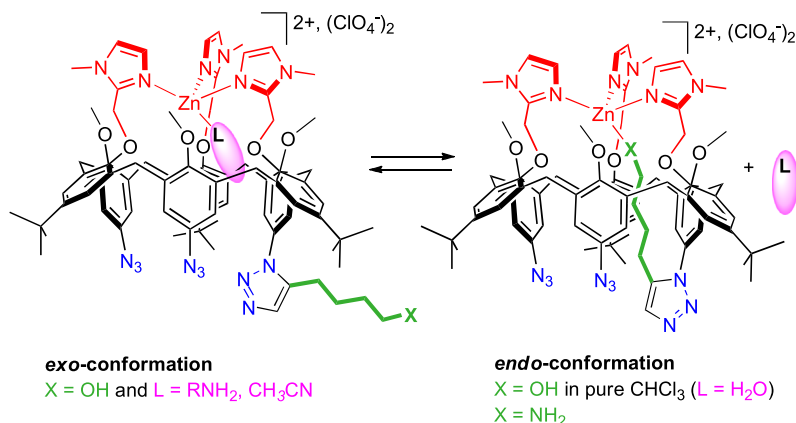
Scheme 1. Representation of the two complexes [ZnL^{OH}]$^{2+}$ and [ZnL^{NH_2}]$^{2+}$ in the two possible *endo-* and *exo-*conformations. For [ZnL^{NH_2}]$^{2+}$, only the *endo-*conformation is observed in any conditions.
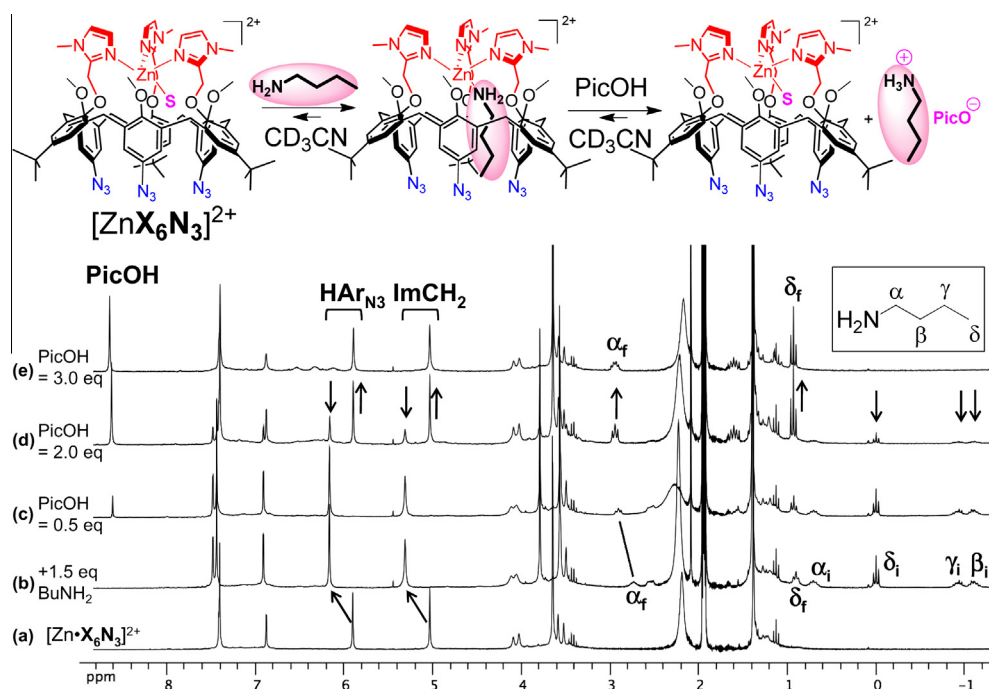

Figure 1. Top: equilibria mediated by the protonation of the inclusion complex with *n*-BuNH$_2$ (S = CD$_3$CN); bottom: ^{1}H NMR spectra (CD$_3$CN, 250 MHz, 300 K) of the starting acetonitrile complex (a), after addition of 1.5 equiv of *n*-BuNH$_2$ (b) and sequential addition of picric acid (c–e). (f) Refers to free *n*-BuNH$_2$ or *n*-BuNH$_3^+$ and (i) refers to encapsulated *n*-BuNH$_2$.

inside the cavity. The gradual addition of picric acid eventually led to the decoordination of the amine due to its protonation and the formation of the starting acetonitrile complex. In this case, the moderate addition of acid is sufficient to protonate the amine without affecting the imidazole coordination sphere around the Zn(II) cation.

We then tried to apply this first result onto the *endo* complex [ZnL^{NH_2}](ClO$_4$)$_2$. Ideally, protonation should induce a large conformational change from the *endo-*conformation to the *exo-*conformation and liberate the access of the metal cation for a guest ligand. However, the addition of 3 equiv of picric acid did not modify the ^{1}H NMR spectrum (Fig. 2b). After the addition of a larger excess of acid (7 equiv), the starting complex presenting the self-coordination of the amino arm was still present in solution but not as a single species anymore. Some new broad resonances appeared and were indicative of the presence of the free ligand obtained after the protonation of the imidazoles and decoordination of the Zn(II) cation (Fig. 2c).[13] Hence, the intramolecular

coordination of the amine to the Zn(II) center decreases dramatically its basicity so that the protonation first takes place at the imidazole site. This trend can be explained by the entropically reinforced coordination of the internal amino arm. This experiment showed that the stability of the complex was not sufficient to promote the selective protonation of the amine and consequently to induce its motion out of the cavity.

These two results prompted us to operate the molecular switch with the [ZnL^{OH}](ClO$_4$)$_2$ complex thanks to the intermediate of an exogenous amine. The molecular switch was monitored by ^{1}H NMR spectroscopy in a non coordinating solvent (CDCl$_3$). In this solvent, the complex is in the *endo-*conformation, as confirmed by the presence of two resonances in the high field region (Fig. 3a). These two peaks correspond to H$_\beta$ and H$_\gamma$ protons of the hydroxyl chain buried in the center of the calix cavity.[14] The hydroxyl group, in spite of the entropically favored intramolecular coordination, was quantitatively replaced by *n*-PrNH$_2$ (1.1 equiv) (Fig. 3b). Addition of 3 equiv of picric acid led to the protonation of the amine and the