



# Highly selective complexation of metal ions by the self-tuning tetraazacalixpyridine macrocycles

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## ABSTRACT

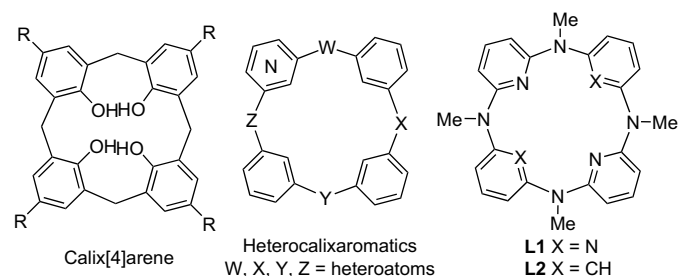
By means of UV–vis and  $^1\text{H}$  NMR titrations and X-ray crystallography, complexation of tetramethylazacalix[4]pyridine **L1** and tetramethylazacalix[2]arene[2]pyridine **L2** with metal ions was studied. While no interaction was observed with alkali and alkaline earth metal ions, both ligands have been found to act as powerful and selective macrocyclic hosts to complex a number of transition and heavy metal ions. Due to the intrinsic nature of the bridging nitrogen atoms that can adopt different electronic configurations and form varied degrees of conjugations with their adjacent pyridine rings, tetramethylazacalix[4]pyridine **L1** regulated its conformation and cavity structure to best fit the guest metal ion species, yielding a 1:1 square planar **L1**– $\text{M}^{n+}$  complex with binding constants  $\log K_{1:1}$  ranging from 2.7(1) to 8.2(8).

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## 1. Introduction

The design and synthesis of powerful and highly selective macrocyclic receptors for metal ions have continuously been one central focus of the study in supramolecular host–guest interaction and molecular recognition because of their importance and applications in ion transport, chemosensing and imaging, metalloenzyme mimics, catalysis and nuclear waste treatment.<sup>1</sup> So far, a large number of macrocyclic host molecules have been developed for the complexation of metal ions,<sup>2</sup> and among them, calixarenes and their derivatives<sup>3</sup> are a type of well known ligands. For example, the parent calix[4]arene (Fig. 1) and their functionalized derivatives that bear various chelating segments or a crown ether moiety have been extensively investigated to interact with metal species including alkali, alkaline earth, transition and heavy metal ions.<sup>4</sup> To seek for versatile synthetic receptors and therefore to establish new supramolecular systems, the heteroatom bridged calix(hetero)aromatics (Fig. 1), a new generation of synthetic macrocyclic host molecules after calixarenes, have been devised in recent years.<sup>5</sup> The binding studies,<sup>6</sup> though they are very limited, have indicated that these novel macrocyclic molecules are interesting and potentially useful ligands in the recognition of metal ions and neutral molecules. Very recently, we have demonstrated that the introduction of heteroatoms, particularly the amino nitrogen atoms as the bridge linkages in calix(hetero)aromatics

such as calix[*n*]pyridines, leads to different conformations with fine bridge-tuned macrocyclic cavities, thanks to the bridging amino nitrogen atoms that can adopt  $\text{sp}^2$  and/or  $\text{sp}^3$  hybrid configurations and form different degrees of conjugation with the neighbouring pyridines.<sup>6,7</sup> More interestingly, the formation of different conformations of various cavity sizes of the methylazacalix[4]pyridine was determined or induced by the guest species when forming a host–guest complex.<sup>6</sup> We envisioned that, as the multinitrogen-containing macrocyclic molecules, the self-regulating and fine tunable cavity azacalixpyridines **L1** and **L2** (Fig. 1) might exhibit novel and unique properties in the recognition of metal ions. Herein, we report the interactions of tetramethylazacalix[4]pyridine **L1** and tetramethylazacalix[2]arene[2]pyridine **L2** with metal ions.<sup>8</sup> Both macrocyclic compounds are versatile and powerful ligands to complex transition and heavy metal ions in a selective manner.



**Figure 1.** Structures of calix[4]arene, heterocalixaromatics including tetramethylazacalix[4]pyridine **L1** and tetramethylazacalix[2]arene[2]pyridine **L2**.

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## 2. Results and discussion

The interaction of tetramethylazacalix[4]pyridine ligand **L1**, which was prepared according to our previous report,<sup>6a,9</sup> with metal ions was first studied by means of electronic absorption spectrophotometric method. No spectral change was observed when it was treated with alkali and alkaline earth metal ions. Interaction with some transition and heavy metal ions (Table 1), however, led to remarkable changes of the electronic absorption spectrum of **L1** (Figs. S1–S9). As a representative of UV–vis titration experiments, the spectral changes of tetramethylazacalix[4]pyridine **L1** upon addition of Cu<sup>2+</sup> at 298 K are shown in Figure 2. With the addition of Cu<sup>2+</sup>, for example, the absorbance at 310 nm increased and slightly shifted to 319 nm, while the absorbance at 278 nm decreased. The equilibrium between **L1** and Cu<sup>2+</sup> was evidenced by the observation of two isosbestic points at 242.5 and 299.5 nm, respectively. The Job plot indicated the formation of the 1:1 complex between **L1** and all metal ions interacted (insets in Figs. 2 and S1–S9). The binding constants (log K<sub>1:1</sub>) for **L1**–metal ion complexes were calculated by a nonlinear least-square fit of the titration data using a Hyperquad2003 program.<sup>10</sup> They, along with ΔG<sub>298 K</sub> values, are summarized in Table 1.

As indicated by the results in Table 1, while showing no affinity towards to alkali and alkaline earth metal ions, tetramethylazacalix[4]pyridine **L1** acted as a powerful and selective ligand in complexation with transition and heavy metal ions. It formed the most stable complex with Cu<sup>2+</sup>, followed by Cu<sup>+</sup>, Zn<sup>2+</sup> and Co<sup>2+</sup> with log K<sub>1:1</sub> values being 8.2(3), 6.2(0), 5.7(8) and 5.6(2), respectively. While the binding with Pd<sup>2+</sup> [log K<sub>1:1</sub> 4.9(1)], Cr<sup>3+</sup> [log K<sub>1:1</sub> 4.7(9)] and Fe<sup>2+</sup> [log K<sub>1:1</sub> 4.6(6)] was also strong and effective, the interaction with Hg<sup>2+</sup>, Ag<sup>+</sup> and Pb<sup>2+</sup> appeared weak, giving the binding constant (log K<sub>1:1</sub>) in the range of 2.7(1) to 3.9(2). Surprisingly, no interaction between **L1** and Cd<sup>2+</sup>, Mn<sup>2+</sup> and Ni<sup>2+</sup> ions was observed, as the addition of these metal ions to **L1** solution did not cause any change of the electronic absorption spectrum of **L1**.

Using the same UV–vis spectrophotometric titration method, the interaction of tetramethylazacalix[2]arene[2]pyridine **L2**<sup>6a,7</sup> with metal ions was also investigated. Interestingly, on the basis of Job plot experiments, **L2** also formed 1:1 complexes with several metal ions, and no 2:1 complexation was observed (Figs. S10–S15). The binding constants (log K<sub>1:1</sub>) and ΔG<sub>298 K</sub> for **L2**–M<sup>n+</sup> complexes are compiled in Table 2. Noticeably, in comparison with tetramethylazacalix[4]pyridine **L1**, tetramethylazacalix[2]arene[2]pyridine **L2** displayed higher selectivity in complexing with transition and heavy metal ions. No interaction was observed between **L2** and metal ions

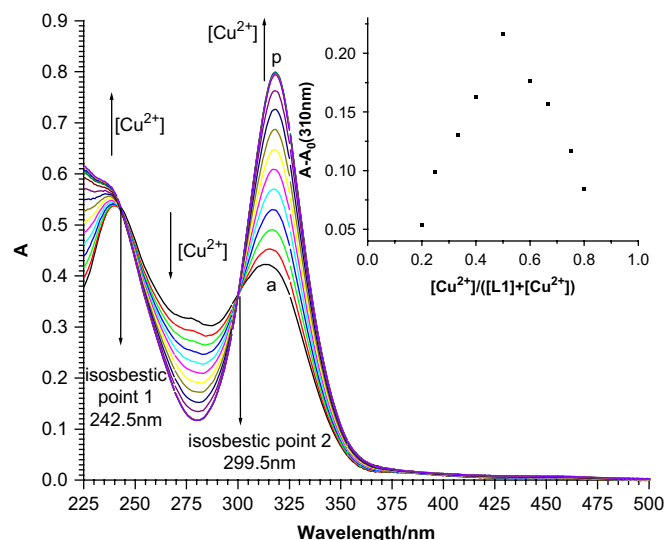
**Table 1**  
Binding constants (log K<sub>1:1</sub>) and ΔG<sub>298 K</sub> for 1:1 complexation between **L1** and metal ions at 298 K<sup>a,b</sup>

<b>L1</b> –M <sup>n+</sup>	Alkali	Alkaline earth	Cr <sup>3+</sup>	Mn <sup>2+</sup>	Fe <sup>2+</sup>
log K <sub>1:1</sub> (M <sup>-1</sup> )	— <sup>c</sup>	— <sup>c</sup>	4.79±0.02	— <sup>c</sup>	4.66±0.00
ΔG <sub>298 K</sub> <sup>0</sup> (kJ mol <sup>-1</sup> )	—	—	-27.4±0.1	—	-26.6±0.0
<b>L1</b> –M <sup>n+</sup>	Co <sup>2+</sup>	Ni <sup>2+</sup>	Cu <sup>+</sup>	Cu <sup>2+</sup>	Zn <sup>2+</sup>
log K <sub>1:1</sub> (M <sup>-1</sup> )	5.62±0.01	— <sup>c</sup>	6.20±0.03	8.23±0.07	5.78±0.00
ΔG <sub>298 K</sub> <sup>0</sup> (kJ mol <sup>-1</sup> )	-32.1±0.0	—	-35.4±0.2	-47.0±0.4	-33.0±0.0
<b>L1</b> –M <sup>n+</sup>	Ag <sup>+</sup>	Cd <sup>2+</sup>	Hg <sup>2+</sup>	Pb <sup>2+</sup>	Pd <sup>2+</sup>
log K <sub>1:1</sub> (M <sup>-1</sup> )	3.72±0.00	— <sup>c</sup>	3.92±0.01	2.71±0.01	4.91±0.01
ΔG <sub>298 K</sub> <sup>0</sup> (kJ mol <sup>-1</sup> )	-21.2±0.0	—	-22.4±0.1	-15.5±0.1	-28.0±0.0

<sup>a</sup> UV–vis titration experiments were conducted in a mixture acetonitrile and water (4:21, v/v) at 298 K.

<sup>b</sup> Perchlorate salts were used, except Cu(CH<sub>3</sub>CN)<sub>4</sub>PF<sub>6</sub>, CrCl<sub>3</sub> and PdCl<sub>2</sub>.

<sup>c</sup> The spectral changes are too small for accurate determination.



**Figure 2.** UV–vis spectral changes of **L1** [2.075×10<sup>-5</sup> M in a mixture of acetonitrile and water (4:21, v/v)] in response to the addition of Cu<sup>2+</sup> ion at 298 K. The concentrations of Cu<sup>2+</sup> for curves a–p are 0, 2.08, 4.15, 6.23, 8.30, 10.38, 12.45, 14.53, 16.60, 18.68, 20.75, 24.90, 29.05, 33.20, 37.35, and 41.50×10<sup>-6</sup> mol dm<sup>-3</sup>. Inset: Job plot showing a 1:1 **L1**–Cu<sup>2+</sup> complex ([**L1**]+[Cu<sup>2+</sup>]=4.500×10<sup>-5</sup> M in a mixture of acetonitrile and water (18:7, v/v)).

such as Mn<sup>2+</sup>, Co<sup>2+</sup>, Ni<sup>2+</sup>, Zn<sup>2+</sup>, Ag<sup>+</sup>, Cd<sup>2+</sup> and Pb<sup>2+</sup> in addition to alkali and alkaline earth metal ions. The binding constants (log K<sub>1:1</sub>) ranged only from 3.4(9) for **L2**–Hg<sup>2+</sup> to 4.9(4) for **L2**–Pd<sup>2+</sup>.

Though the molecular structures of the complexes of tetramethylazacalix[4]pyridine **L1** and tetramethylazacalix[2]arene[2]pyridine **L2** with anions<sup>6a</sup> and neutral molecules such as aromatic and aliphatic diols and monoals<sup>6c</sup> have been systematically studied, only one solid state structure of metal complex was reported. In a communication,<sup>9</sup> the X-ray molecular structure of **L1**–Zn<sup>2+</sup> complex was reported.<sup>9</sup> To understand the binding of macrocyclic ligands **L1** and **L2** with metal ions at the molecular level, and also to shed light on the selectivity of the ligands in the complexation with metal ions, the molecular structures of the complexes were studied. No single crystals were successfully cultivated from the complexes between **L2** and metal cations. Fortunately, however, we were able to obtain high quality single crystals of the complexes between tetramethylazacalix[4]pyridine **L1** and Fe<sup>2+</sup> and Co<sup>2+</sup> ions by slow evaporation of solvent from a solution of tetramethylazacalix[4]pyridine **L1** and a metal salt. The molecular structures of the

**Table 2**  
Binding constants (log K<sub>1:1</sub>) and ΔG<sub>298 K</sub> for 1:1 complexation between **L2** and metal ions at 298 K<sup>a,b</sup>

<b>L2</b> –M <sup>n+</sup>	Alkali	Alkaline earth	Cr <sup>3+</sup>	Mn <sup>2+</sup>	Fe <sup>2+</sup>
log K <sub>1:1</sub> (M <sup>-1</sup> )	— <sup>c</sup>	— <sup>c</sup>	4.81±0.01	— <sup>c</sup>	4.61±0.01
ΔG <sub>298 K</sub> <sup>0</sup> (kJ mol <sup>-1</sup> )	—	—	-27.4±0.0	—	-26.3±0.1
<b>L2</b> –M <sup>n+</sup>	Co <sup>2+</sup>	Ni <sup>2+</sup>	Cu <sup>+</sup>	Cu <sup>2+</sup>	Zn <sup>2+</sup>
log K <sub>1:1</sub> (M <sup>-1</sup> )	— <sup>c</sup>	— <sup>c</sup>	4.27±0.00	4.43±0.01	— <sup>c</sup>
ΔG <sub>298 K</sub> <sup>0</sup> (kJ mol <sup>-1</sup> )	—	—	-24.4±0.0	-25.3±0.0	—
<b>L2</b> –M <sup>n+</sup>	Ag <sup>+</sup>	Cd <sup>2+</sup>	Hg <sup>2+</sup>	Pb <sup>2+</sup>	Pd <sup>2+</sup>
log K <sub>1:1</sub> (M <sup>-1</sup> )	— <sup>c</sup>	— <sup>c</sup>	3.49±0.02	— <sup>c</sup>	4.94±0.01
ΔG <sub>298 K</sub> <sup>0</sup> (kJ mol <sup>-1</sup> )	—	—	-19.9±0.1	—	-28.2±0.1

<sup>a</sup> UV–vis titration experiments were conducted in a mixture of acetonitrile and water (4:21, v/v) at 298 K.

<sup>b</sup> Perchlorate salts were used, except Cu(CH<sub>3</sub>CN)<sub>4</sub>PF<sub>6</sub>, CrCl<sub>3</sub> and PdCl<sub>2</sub>.

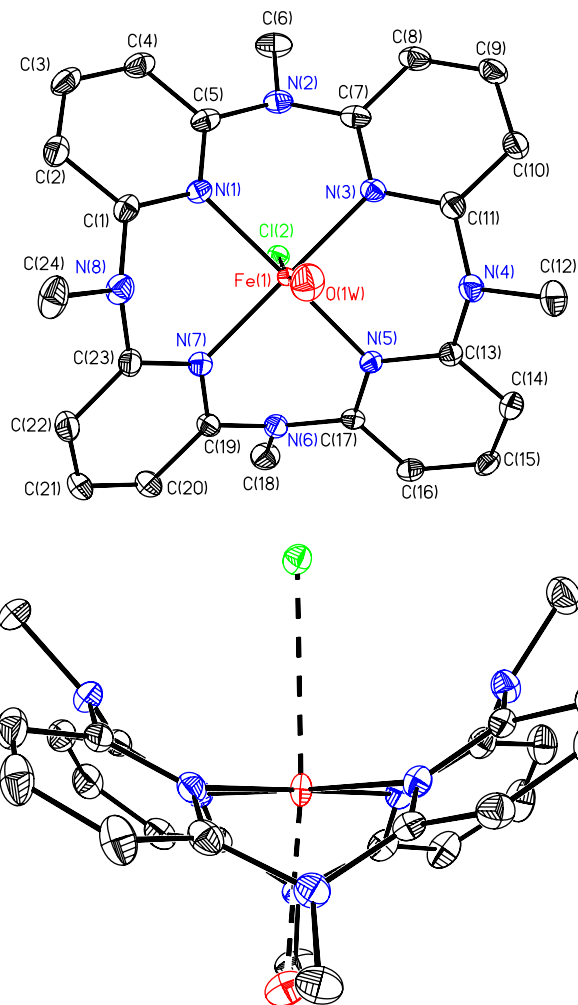
<sup>c</sup> The spectral changes are too small for accurate determination.

**Table 3**  
Crystallographic data for complexes **L1**-Fe<sup>2+</sup> and **L1**-Co<sup>2+</sup>

Complex	<b>L1</b> ·FeCl <sub>2</sub> ·3H <sub>2</sub> O	<b>L1</b> ·Co(NO <sub>3</sub> ) <sub>2</sub> ·CH <sub>2</sub> Cl <sub>2</sub> ·H <sub>2</sub> O
Empirical formula	C <sub>24</sub> H <sub>24</sub> Cl <sub>2</sub> FeN <sub>8</sub> O <sub>3</sub>	C <sub>25</sub> H <sub>25</sub> Cl <sub>2</sub> CoN <sub>10</sub> O <sub>7</sub>
M <sub>r</sub>	599.26	707.38
Crystal size (mm <sup>3</sup> )	0.79×0.27×0.03	0.53×0.20×0.14
Crystal system	Monoclinic	Monoclinic
Space group	P2(1)/c	C2/c
a [Å]	13.834(3)	18.411(4)
b [Å]	12.062(2)	13.055(3)
c [Å]	15.667(3)	13.538(3)
α [°]	90.00	90.00
β [°]	92.49(3)	115.64(3)
γ [°]	90.00	90.00
V [Å <sup>3</sup> ]	2611.7(9)	2933.5(10)
d [g/cm <sup>3</sup> ]	1.524	1.602
Z	4	4
T [K]	293(2)	293(2)
R1, wR2 I>2σ(I)	0.0767, 0.2237	0.0697, 0.1939
R1, wR2 (all data)	0.1099, 0.2453	0.0929, 0.2040
Quality of fit	1.011	1.024
CCDC No.	666979	666978

complexes were determined by X-ray diffraction analysis, and the crystallographic data and the selected bond lengths and angles are listed in Tables 3 and 4, respectively.

As illustrated in Figures 3 and 4, tetramethylazacalix[4]pyridine **L1** acted as a square planar tetradentate ligand to form a 1:1 complex with the guest ion Fe<sup>2+</sup> and Co<sup>2+</sup> in the solid state. A few structural features of the complexes are worth addressing. Firstly, in both cases of the complexes between **L1** and Fe<sup>2+</sup> and Co<sup>2+</sup> ions, four pyridine nitrogen atoms coordinated equatorially to the metal centre to form a square planar geometry. The same binding pattern was reported in the complexation of host **L1** to zinc ion.<sup>9</sup> The bond lengths between nitrogen and Fe<sup>2+</sup> and Co<sup>2+</sup> ions ranged from 1.983 Å to 2.001 Å, and bond angles around metal ions (∠N-M<sup>2+</sup>-N) were around 90.00° (Table 4). Secondly, a water molecule acted as the fifth ligand to coordinate to cobalt at the axial position with a bond distance of 2.171 Å, giving a five-coordinated square pyramid cobalt complex. Additionally, in the crystal structure of the **L1**-Fe<sup>2+</sup> complex, both a water molecule and a chloride anion were located at the axial positions of both-sides of the N<sub>4</sub>Fe plane. The distances between oxygen and Fe<sup>2+</sup> and between chloride and Fe<sup>2+</sup> were 2.642 and 3.061 Å,



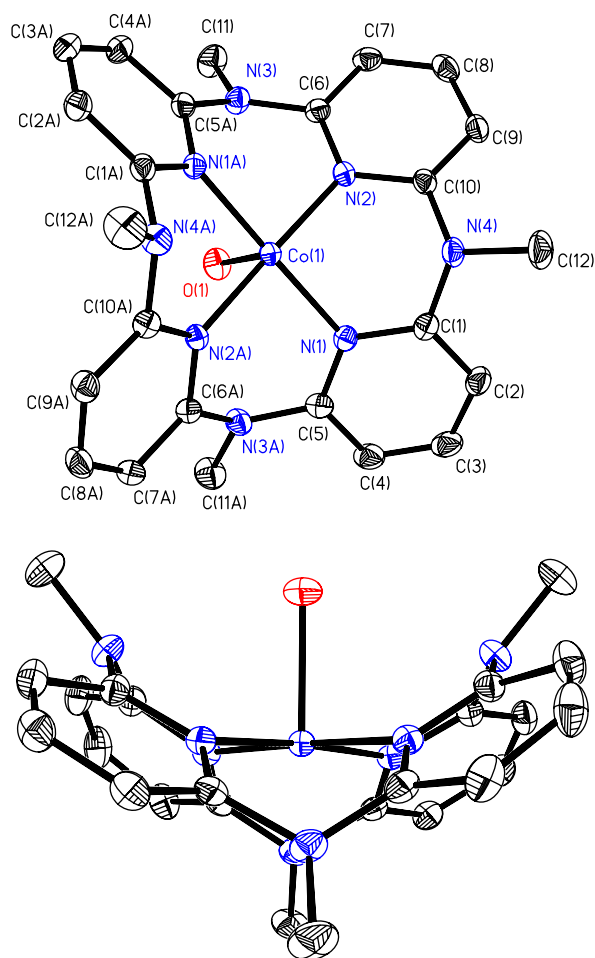
**Figure 3.** X-ray molecular structure of **L1**-Fe<sup>2+</sup> complex: top (left) and side (right) views.

**Table 4**  
Selected bond lengths (Å) and bond angles (°) with estimated standard deviations (esd's) in parentheses for complexes **L1**-Fe<sup>2+</sup> and **L1**-Co<sup>2+</sup>

<b>L1</b> -Fe <sup>2+</sup>	C(5)-N(2)	1.393	C(23)-N(8)	1.415	Fe(1)-N(3)	1.983
	N(2)-C(7)	1.390	N(8)-C(1)	1.409	Fe(1)-N(5)	2.001
	C(11)-N(4)	1.418	N(3)-N(5)	2.834	Fe(1)-N(7)	1.991
	N(4)-C(13)	1.398	N(5)-N(7)	2.805	Fe(1)-O(1W)	2.642
	C(17)-N(6)	1.394	N(7)-N(1)	2.807	Fe(1)-Cl(2)	3.061
	N(6)-C(19)	1.387	Fe(1)-N(1)	1.985		
	∠N(1)-N(3)-N(5)	89.81	∠N(1)-Fe(1)-O(1W)	87.13		
	∠N(3)-N(5)-N(7)	89.61	∠N(3)-Fe(1)-O(1W)	85.85		
	∠N(5)-N(7)-N(1)	90.53	∠N(5)-Fe(1)-O(1W)	94.11		
	∠N(7)-N(1)-N(3)	90.00	∠N(7)-Fe(1)-O(1W)	93.12		
	∠N(1)-Fe(1)-N(3)	90.28	∠N(1)-Fe(1)-Cl(2)	91.81		
	∠N(3)-Fe(1)-N(5)	90.70	∠N(3)-Fe(1)-Cl(2)	87.77		
	∠N(5)-Fe(1)-N(7)	89.25	∠N(5)-Fe(1)-Cl(2)	87.06		
	∠N(7)-Fe(1)-N(1)	89.80	∠N(7)-Fe(1)-Cl(2)	93.26		
<b>L1</b> -Co <sup>2+</sup>	C(6)-N(3)	1.397	N(1)-N(2)	2.750	Co(1)-N(1)	1.927
	N(3)-C(5)	1.395	N(2)-N(1A)	2.695	Co(1)-N(2)	1.926
	C(1)-N(4)	1.408	N(1A)-N(2A)	2.750	Co(1)-O(1)	2.171
	N(4)-C(10)	1.413	N(2A)-N(1)	2.695		
	∠N(1)-N(2)-N(1A)	90.07	∠N(1)-Co(1)-N(2)	91.09		
	∠N(2)-N(1A)-N(2A)	89.90	∠N(2)-Co(1)-N(1A)	88.79		
	∠N(1A)-N(2A)-N(1)	90.07	∠N(1)-Co(1)-O(1)	91.37		
	∠N(2A)-N(1)-N(2)	89.90	∠N(2)-Co(1)-O(1)	92.54		

respectively. Finally, it is interesting to address that in all metal complexes, the tetramethylazacalix[4]pyridine ligand **L1** adopted a saddle conformation with an approximate *D*<sub>2h</sub> symmetry (Figs. 3 and 4). Careful scrutiny of the bond lengths and angles of the bridging nitrogen atoms (Table 4) revealed that all linking nitrogen atoms adopted an electronic configuration in-between sp<sup>2</sup> and sp<sup>3</sup>, and each bridging nitrogen atom formed partial conjugation with its adjacent two pyridine rings. The parent tetramethylazacalix[4]pyridine **L1**, however, as reported in our previous paper,<sup>6a</sup> adopted a 1,3-alternate conformation with a *C*<sub>2v</sub> symmetry, and the bridging nitrogen atoms formed sp<sup>2</sup> electronic configuration and form full conjugation with one of the neighbouring pyridine rings. The formation of different conformations of different electronic configurations and conjugation states of the bridging nitrogen atoms in the absence and presence of a guest metal ion reflected the uniqueness of the nitrogen bridged calix[4]pyridine in host-guest interactions. In other words, due to the intrinsic nature of bridging nitrogen atoms that can change their electronic configurations and conjugation systems with their adjacent pyridine rings, tetramethylazacalix[4]pyridine **L1** is able to self-regulate its conformation and therefore cavity structures to achieve the most effective interaction with the presence of guest species.

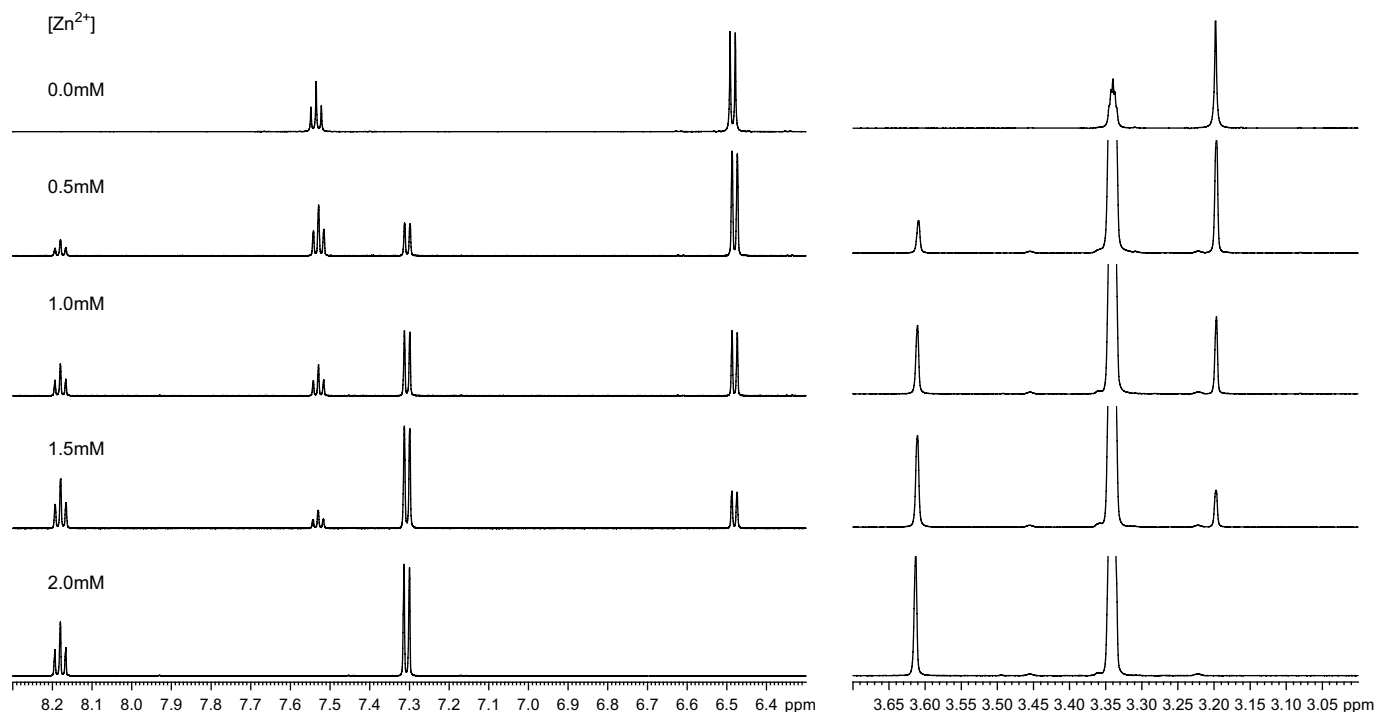
To shed further light on the dynamic aspect of complexation and the structure of host-M<sup>n+</sup> complexes in solution, <sup>1</sup>H NMR titration and the variable temperature <sup>1</sup>H NMR spectroscopy study were



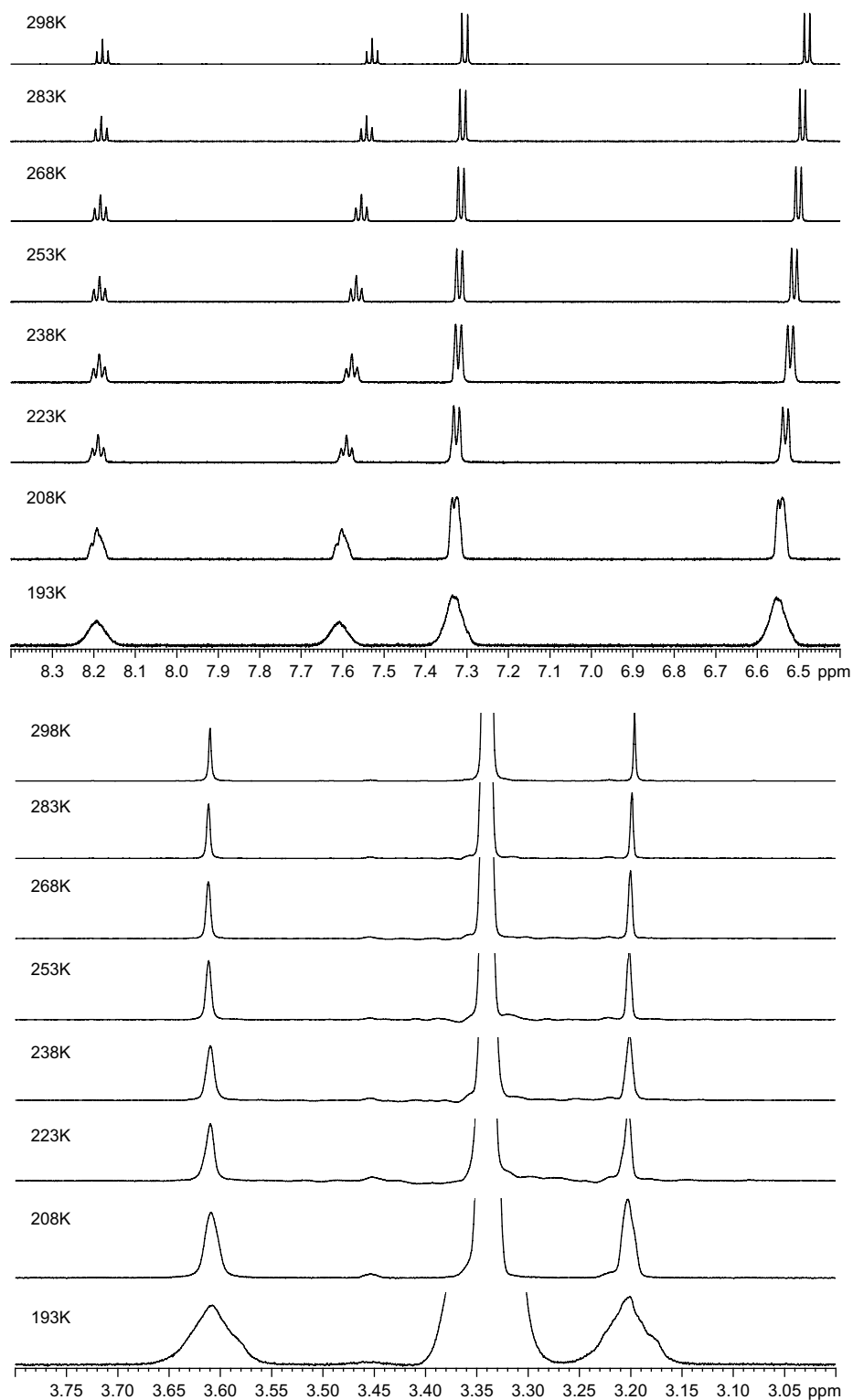
**Figure 4.** X-ray molecular structure of **L1**-Co<sup>2+</sup> complex: top (left) and side (right) views.

conducted. Zn<sup>2+</sup> ion was chosen as the guest metal ion species in <sup>1</sup>H NMR study because it formed diamagnetic complex with **L1**. As illustrated in Figure 5, tetramethylazacalix[4]pyridine **L1** exhibits one set of signals corresponding to protons on pyridine ring and bridging methyl moieties in its <sup>1</sup>H NMR spectrum. Upon the addition of Zn<sup>2+</sup>, however, a new set of resonance signals of both aromatic and aliphatic protons appeared downfield relative to the signals of the parent macrocyclic ring. When the ratio of host to guest reached 1:1, all proton signals corresponding to free **L1** disappeared, only the proton signals of **L1**-Zn<sup>2+</sup> were observed. It indicated the formation of a very stable **L1**-Zn<sup>2+</sup> complex in solution, and the exchange between **L1** and **L1**-Zn<sup>2+</sup> was slow on the NMR time scale. The observation of simple <sup>1</sup>H NMR spectrum, viz. only one pair of coupled triplet (8.18 ppm) and doublet (7.31 ppm) signals along with one singlet signal (3.61 ppm), and the drastic downfield shift of both aromatic and aliphatic proton signals (Fig. 5) suggested that the **L1**-Zn<sup>2+</sup> complex in solution assembled the same molecular structure as that in the solid state Fig. 6 lists actually the NMR spectra.<sup>9</sup> The variable temperature <sup>1</sup>H NMR spectra of a mixture of **L1** and Zn<sup>2+</sup> in a 2 to 1 ratio showed slight downfield shift of the proton signals of the parent ligand when the temperature was decreased (Fig. S6). Following the literature methods,<sup>11</sup> the activation energy for the formation of **L1**-Zn<sup>2+</sup> complex at 298 K was determined as 55.8 kJ M<sup>-1</sup> (see Supplementary data).

The selectivity of binding of calixpyridine derivatives **L1** and **L2** towards metal ions is intriguing. It is most probably a result of the nature of pyridine ligand that macrocyclic molecules **L1** and **L2** do not interact with alkali and alkaline earth metal ions because alkali and alkaline earth metal ions are hard acid species. On the basis of the binding model both in solution and in solid state aforementioned, tetramethylazacalix[4]pyridine **L1** acted as a tetradentate ligand to display stronger binding power towards transition and heavy metal ions than its bidentate tetramethylazacalix[2]arene[2]pyridine counterpart **L2**. In the case of binding with divalent metal ions of the first transition series, tetramethylazacalix[4]pyridine **L1** followed in general the



**Figure 5.** <sup>1</sup>H NMR spectra of **L1** (2 mM) in CD<sub>3</sub>OD in the absence and presence of Zn<sup>2+</sup> at 298 K.



**Figure 6.** The partial  $^1\text{H}$  NMR spectra of **L1** (2 mM) in  $\text{CD}_3\text{OD}$  in the presence of  $\text{Zn}^{2+}$  (1 mM) at different temperatures.

Irving–Williams order,<sup>12</sup> giving binding constants in the order of  $\text{Fe}^{2+} < \text{Co}^{2+} < \text{Cu}^{2+} > \text{Zn}^{2+}$ . The observation of no interaction between **L1** and  $\text{Mn}^{2+}$ ,  $\text{Ni}^{2+}$  and  $\text{Cd}^{2+}$  was not expected. Based on the 1:1 **L1**– $\text{M}^{n+}$  complexation model and the comparison of the sizes of ionic radii between the interacted and not interacted,  $\text{Ni}^{2+}$ ,  $\text{Cd}^{2+}$ , and  $\text{Mn}^{2+}$  would be strongly interacted by macrocyclic host molecule **L1**. Although it remains difficult at the

current stage to provide a rationale, the mismatch between the ligand and these metal ions in terms of electronic and geometric effects might be responsible for less effective interaction. The higher selectivity towards metal ion binding of tetramethylazacalix[2]arene[2]pyridine **L2** than tetramethylazacalix[4]pyridine **L1** is most probably attributable to the bidentate nature of the former macrocyclic host molecule.

### 3. Conclusion

In summary, we have demonstrated that tetramethylazacalix[4]pyridine **L1** and tetramethylazacalix[2]arene[2]pyridine **L2** are powerful and selective macrocyclic ligands to metal ions. While no interactions at all were observed with alkali and alkaline earth metal ions, they formed 1:1 complexes with some transition and heavy metal ions giving binding constants ( $\log K_{1:1}$ ) in the range of 2.7(1) to 8.2(8). In both the solution and the solid state, tetramethylazacalix[4]pyridine **L1** acted as a square planar tetradentate ligand to form complex with metal ion. The high binding ability and good selectivity of tetramethylazacalix[4]pyridine **L1** originated most probably from the intrinsic nature of the bridging nitrogen atoms that can adopt different electronic configurations and form varied degrees of conjugations with their adjacent pyridine rings. In other words, tetramethylazacalix[4]pyridine **L1** can regulate its conformation and cavity to best fit the guest ion species. Applications of the complexes of macrocyclic tetraazacalix[4]pyridine derivatives with various metal ions in molecular recognition and, particularly, in supramolecular catalysis are actively investigated in this laboratory and will be reported in due course.

### 4. Experimental

**Caution!** The complexes between organic ligands and perchlorate salts of metals are potentially explosive. Only very small amounts of these materials should be used and prepared, and they must be handled with caution.

Macrocyclic ligands, tetramethylazacalix[4]pyridine **L1** and tetramethylazacalix[2]arene[2]pyridine **L2**, were prepared from the stepwise fragment coupling approaches starting from 2,6-dibromopyridine, 2,6-diaminopyridine and *m*-phenylenediamine following our previous study.<sup>6a</sup> Metal salts with purity over 97% were purchased from commercial sources (see [Supplementary data](#)).

The electronic absorption spectral titration was performed at room temperature on a UV-2401PC UV–vis spectrometer. The stoichiometry of the complexes was determined by means of the Job plot experiments. Binding constants ( $\log K_{1:1}$ ) were obtained using Hyperquad2003 program. <sup>1</sup>H NMR spectra of tetramethylazacalix[4]pyridine complex with Zn<sup>2+</sup> in CD<sub>3</sub>OD solution were recorded on a Bruker AV600FT NMR spectrometer using solvent signal at 3.34 ppm as an internal standard.

Single crystals were obtained by refluxing a mixture of **L1** and a metal salt [Co(NO<sub>3</sub>)<sub>2</sub> and FeCl<sub>2</sub> (5 equiv)] in CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>OH (1:1, v/v) solution for 0.5 h. After cooling to 10 °C and slow evaporation of the solvent, single crystals of complexes **L1**–Co<sup>2+</sup> and **L1**–Fe<sup>2+</sup> suitable for X-ray diffraction studies were obtained, respectively. A crystal of the complex mounted on a glass capillary was used for data collection at 20 °C on a Rapid Auto

(Rigaku 2001) diffractometer. The crystallographic data are listed in Table 3.

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### Supplementary data

Electronic supplementary data available: UV–vis and <sup>1</sup>H NMR titrations. Supplementary data associated with this article can be found in the online version, at [doi:10.1016/j.tet.2008.10.100](https://doi.org/10.1016/j.tet.2008.10.100).

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