Synthesis and Coordination Properties of Highly Preorganised Polyamine Macrocycles

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Received August 6, 2001

Synthesis and characterisation of the new macrocyclic ligands **L1-L4** are reported. The ligands present one or two pentaamine moieties, each containing two piperazine rings, linked by benzene or anthracene spacers. Interaction of **L1** with H^+, Cu(II), Zn(II), Hg(II), and Pd(II) and of **L3** with H^+, and Cu(II) has been studied by potentiometric titrations in 0.15 mol dm^{-3} NaCl aqueous solution at 298.1 ± 0.1 K. The thermodynamic data suggest that in the metal complexes only three nitrogen donor atoms bind each metal ion. As a consequence of the low coordination number, these complexes are promising receptors for different molecules.

J. Heterocyclic Chem., **38**, 1273 (2001).

Introduction.

In the last few years special attention has been devoted to the design and synthesis of macrocyclic ligands because of the high degree of preorganization they can impose on metal coordination.[1-5] In particular, polyamine macrocycles may constitute an excellent basis for the study of molecular recognition of different kinds of substrates, such as inorganic or organic cations, anionic species, and neutral molecules [6,7]. Macrocyclic molecules containing two binding subunits linked by two spacers have received much attention since these compounds can form stable binuclear metal complexes [3]. From this point of view, much effort has been devoted to the synthesis of macrocyclic receptors containing two aromatic moieties as rigid spacers linking two binding subunits, such as polyamine chains [4,8-15]. Several ditopic macrocycles containing two equal polyamine moieties have been synthesised using 2 + 2 cyclization reactions. Their binuclear metal complexes have been shown to react with various molecules and ions and several assemblies containing two metal centres bridged by anionic species have been reported [16-18].

In previous works we have investigated the coordination properties of macrocyclic polyamines containing piperazine rings [4,19]. This unit is rigid and can introduce a certain degree of organisation in the macrocyclic framework. At the same time piperazine contains two nitrogens which can act as donors toward metals.

Aiming to get further insight into the binding properties of macrocycles containing piperazine rings we have synthesised the new ligands **L1-L4**, which possess one or two pentaamine moieties, each containing two piperazine rings, linked by benzene or anthracene spacers.

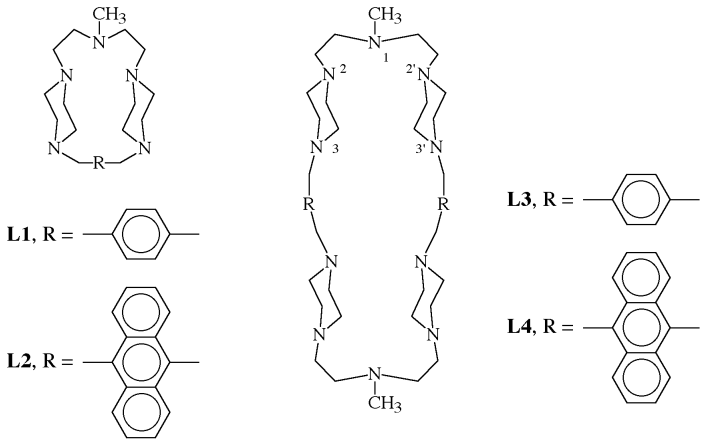


Figure 1. Ligand drawings.

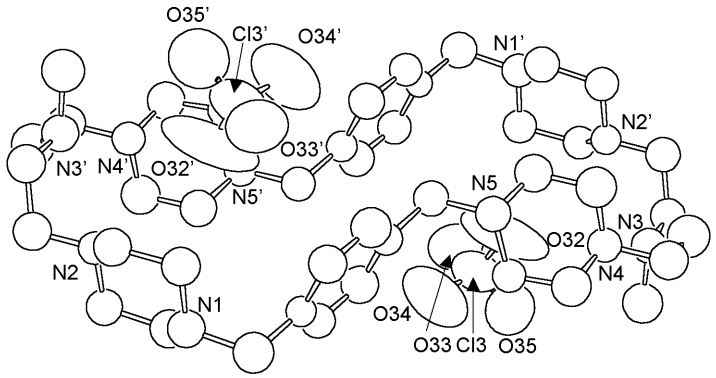
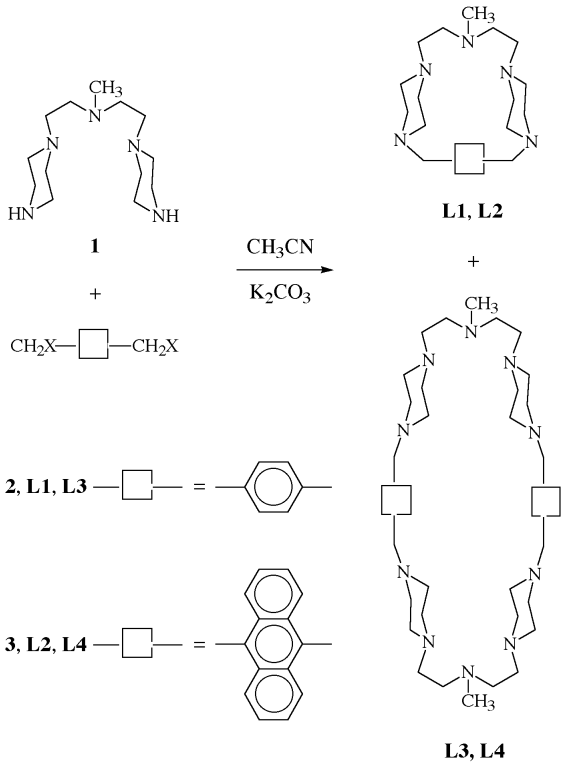


Figure 2. ORTEP drawing of the $[H_6\mathbf{L3}]^{6+}$ cation.

Scheme 1



The present work is done to attempt to understand the relationship between equilibrium constant for the binding of H^+ (basicity), Cu(II), Zn(II), Hg(II) and Pd(II) and the structural features of **L1** and **L3** (Figure 1) as a preliminary investigation of the reactivity of their dinuclear complexes with neutral or anionic substrates.

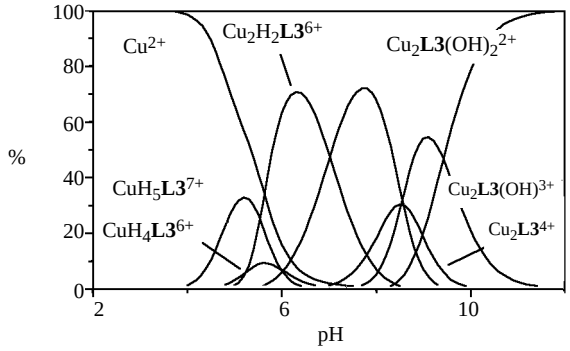


Figure 3. Distribution diagram of the complexed species formed in the system Cu/**L3** (0.15 mol dm^{-3} NaCl 298 K, $[Cu^{2+}] = 2 \times 10^{-3}$, [**L**] = 1×10^{-3} as a function of pH.

EXPERIMENTAL

Synthesis.

Materials.

All reagents and solvents were purchased from commercial sources and used as received unless otherwise noted.

Synthesis of the Compounds.

The precursor bis(2-piperazinylethyl)methylamine triperchlorate (**1**•3$HClO_4$) [19] and 9,10-bis-(chloromethyl)-anthracene [20] were prepared as already described.

Cyclophanes **L1** and **L3**.

The amine triperchlorate **1**•3$HClO_4$ (12.6 g, 0.023 mol) and K_2CO_3 (32 g, 0.23 mol) were suspended in refluxing CH_3CN (250 cm^3). To this mixture, a solution of *p*-dibromoxylene **2**

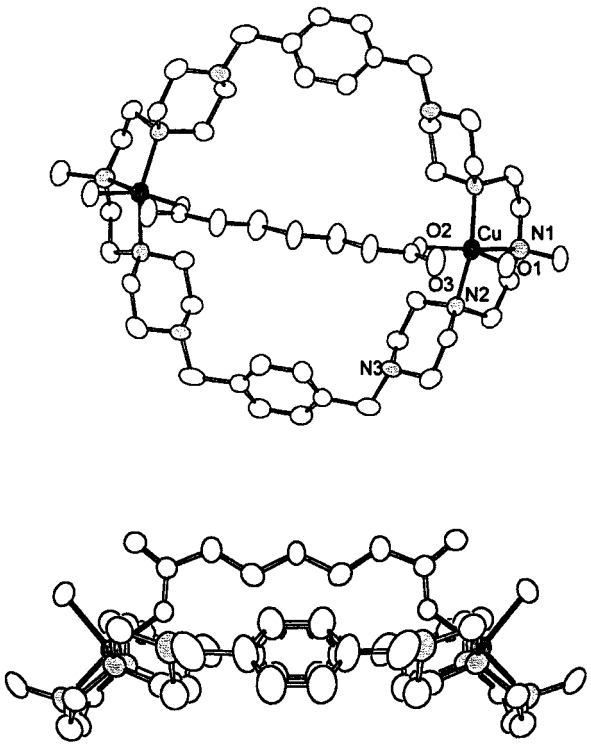


Figure 4. ORTEP drawing of the $\{[Cu_2\mathbf{L3}(H_2O)_2]\supset pimelate\}^{2+}$ cation [36].

Table 1

Crystal Data and Structure Refinement for $[H_6\mathbf{L3}](ClO_4)_6 \cdot 2H_2O$

Empirical formula	$C_{42}H_{80}Cl_6N_{10}O_{26}$
Formula weight	1353.86
Temperature	298 K
Wavelength	0.71069 Å
Crystal system, space group	monoclinic, $P2_1/n$
Unit cell dimensions	a = 11.311(6) Å alpha = 90 deg.
	b = 21.05(2) Å beta = 112.28(5) deg.
	c = 14.190(10) Å gamma = 90 deg.
Volume	3126(4) $Å^3$
Z, Calculated density	2, 1.438 Mg/m^3
Absorption coefficient	0.361 mm^{-1}
Final R indices [I>2sigma(I)]	R1 = 0.0849, wR2 = 0.2049
R indices (all data)	R1 = 0.1820, wR2 = 0.2374

* $R1 = \Sigma \,||Fo| - |Fc|| \,/\, \Sigma\, |Fo|$; $wR2 = [\Sigma w(Fo^2 - Fc^2)^2 \,/\, \Sigma\, wFo^4]^{1/2}$

(6 g, 0.023 mol) in CH_3CN (300 cm^3) was added dropwise over 6 hours. After the addition was completed, the suspension was refluxed for 48 hours and then filtered. The solution was evaporated under vacuum to yield the crude product, which was chromatographed on neutral alumina (activity II/III) eluting with $CHCl_3$/MeOH 100/1.5. The eluted fractions containing **L1** (R_f = 0.4) and **L3** (R_f = 0.6) were collected separately and evaporated to dryness to afford pure **L1** and **L3** as colourless oils (**L1** 0.8 g, 10 %; **L3** 2.3 g, 28%).

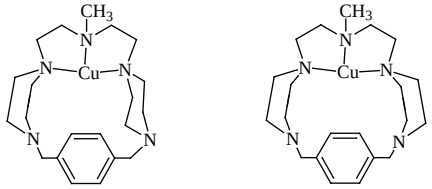


Figure 5. Two proposed coordination modes of Cu(II) in the $[Cu\mathbf{L1}]^{2+}$ complex. The structures drawn consider only the interactions of L1 and do not include additional water molecules or hydroxide ions at the remaining sites of Cu(II).

Table 2

Interatomic Distances Between Perchlorate or Water Oxygens atoms (Å) and Ligand Nitrogens

O32···N3'	3.48(3)
O32···N2	3.49(2)
O32···N4'	3.59(3)
N1...O1'(-x + 1/2, y + 1/2, -z – 1/2)	2.78(2)
N5..O13' (x + 1/2, -y - 1/2, z – 1/2)	2.86(2)
N5..O12' (x + 1/2, -y - 1/2, z – 1/2)	3.20(2)

L1 ^1H NMR (D_2O, pH = 3, 25 °C): 2.76 (s, 3H), 2.86 (m, 12H), 3.28 (m, 12H), 4.36 (s, 4H), 7.62 (s, 4H) ppm. ^{13}C NMR (D_2O, pH = 3, 25 °C): 41.3, 50.2, 51.6, 52.2, 53.5, 60.1, 131.4, 133.7 ppm. MS(FAB): 358 ($M+H^+$).

Anal. Calcd. for $C_{21}H_{35}N_5$: C, 70.55; H, 9.87; N, 19.59. Found: C, 70.6; H, 9.9; N, 19.6 %.

Table 3

Protonation Constants (log K) of **L1** and **L2** Determined by means of Potentiometric Measurements in 0.15 mol dm^{-3} NaCl Aqueous Solution, at 298.1 ± 0.1 K

Reaction	Log K	
	L1	**L3**
H + L = HL [a]	9.39(1) [b]	10.54(2)
HL + H = H_2L	7.91(2)	8.49(3)
H_2L + H = H_3L	6.59(3)	8.20(3)
H_3L + H = H_4L	2.47(7)	7.37(4)
H_4L + H = H_5L		6.93(3)
H_5L + H = H_6L		6.11(4)
H_6L + H = H_7L		5.98(5)
H_7L + H = H_8L		2.44(5)

[a] Charged omitted for clarity; [b] Values in parentheses are standard deviations on the last significant figure.

Table 4

Stability Constants (log K) of **L1** Determined by means of Potentiometric Measurements in 0.15 mol dm^{-3} NaCl Aqueous Solution, at 298.1 ± 0.1 K

Reaction	Log K			
	Cu(II)	Zn(II)	Hg(II)	Pd(II)
M + L = ML[a]	6.76(3) [b]	4.53(9)		
ML + OH = ML(OH)	6.06(4)	5.49(5)		
$ML(OH) + OH = ML(OH)_2$	4.36(8)	3.86(8)		
M + L + Cl = MLCl			21.28(3)	16.33(6)
MLCl + H = MLCl			6.32(3)	8.05(6)
MLCl + OH = MLCl(OH)			7.40(1)	
M + L + OH = ML(OH)				20.87(5)

[a] Charged omitted for clarity; [b] Values in parentheses are standard deviations on the last significant figure.

L3 ^{1}H NMR (D_2O, pH = 3, 25 °C): 2.95 (m, 30H), 3.40 (m, 24H), 4.43 (s, 8H), 7.64 (s, 8H) ppm. ^{13}C NMR (D_2O, pH = 3, 25 °C): 42.3, 50.4, 51.2, 52.3, 53.0, 60.7, 131.4, 133.3 ppm. MS(FAB): 716 ($M+H^+$)

Anal. Calcd. for $C_{42}H_{70}N_{10}$: C, 70.55; H, 9.87; N, 19.59. Found: C, 70.7; H, 10.1; N, 19.7 %

L1•3$HClO_4$.

The amine **L1** was dissolved in ethanol and treated with 65% perchloric acid to give the triperchlorate salt as a white solid in almost quantitative yield.

Anal. Calcd. for $C_{21}H_{38}N_5O_{12}Cl_3$: C, 38.28; H, 5.81; N, 10.63. Found: C, 38.3 ; H, 5.8; N, 10.6%.

CAUTION: *Perchlorate salts of metal complexes with organic ligands are potentially explosive; these compounds must be handled with great caution.*

Table 5

Stability Constants (log K) of the **L3** complexes with Cu(II) Determined by means of Potentiometric Measurements in 0.15 mol dm^{-3} NaCl Aqueous Solution, at 298.1 ± 0.1 K

Reaction	Log K
Cu + L = CuL [a]	9.3(1) [b]
CuL + H = CuHL	9.76(4)
$CuHL + H = CuH_2L$	7.91(6)
$CuH_2L + H = CuH_3L$	7.25(7)
$CuH_3L + H = CuH_4L$	6.62(4)
$CuH_4L + H = CuH_5L$	5.97(4)
$2Cu + L = Cu_2L$	8.1(1)
$Cu_2L + H = Cu_2HL$	8.58(4)
$Cu_2HL + H = Cu_2H_2L$	7.02(4)
$Cu_2L + OH = Cu_2L(OH)$	5.29(5)
$Cu_2L(OH) + OH = Cu_2L(OH)_2$	4.42(5)

[a] Charged omitted for clarity; [b] Values in parentheses are standard deviations on the last significant figure.

L3•7$HClO_4$.

The heptaperchlorate salt **L3**•7$HClO_4$ was obtained in an almost quantitative yield by treating the amine **L3** with 65% perchloric acid in ethanol.

Anal. Calc. for $C_{42}H_{77}N_{10}O_{28}Cl_7$: C, 35.57; H, 5.47; N, 9.88. Found: C, 35.6; H, 5.5; N, 10.0%.

Cyclophanes **L2** and **L4.**

The amine tripercholarate (**1**•3$HClO_4$) (21.0 g, 0.038 mol) and K_2CO_3 (52.5 g, 0.38 mol) were suspended in CH_3CN (500 cm^3) at room temperature. To this mixture, a solution of 9,10-bis-(chloromethyl)-anthracene **3** (10.5 g, 0.038 mol) in CH_3CN (500 cm^3) was added dropwise over 6-7 hours. The resulting yellow solid was filtered and dissolved in the minimum amount of chloroform and chromotographed on alumina (activity II/III) eluting with chloroform. The eluted fractions containing **L2** (R_f = 0.3) and **L4** (R_f = 0.6) were collected separately and evaporated to dryness to afford pure **L2** and **L4** as white solids. (**L2** 2.6 g, 15 %; **L4** 7.5 g, 43%).

L2 ^{1}H NMR ($CDCl_3$, 25 °C): 2.19 (s, 3H), 2.38 (m, 16H), 2.63 (m, 8 H), 4.36 (s, 4H), 7.40 (dd, 4H), 8.23 (dd, 4H) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): 42.1, 52.4, 53.6, 53.7, 54.6, 55.8, 124.6, 125.9, 129.7, 131.3 ppm. MS(FAB): 458 ($M+H^+$).

Anal. Calc. for $C_{29}H_{39}N_5$: C, 76.11; H, 8.59; N, 15.30. Found: C, 76.2; H, 8.6; N, 15.3 %.

L4 ^{1}H NMR ($CDCl_3$, 25 °C): 2.26 (s, 6H), 2.41 (m, 32H), 2.57 (m, 16H), 4.41 (s, 8H), 7.43 (dd, 8H), 8.46 (dd, 8H) ppm. ^{13}C NMR ($CDCl_3$, 25 °C): 43.3, 52.8, 53.6, 53.9, 54.3, 56.0, 124.9, 125.6, 130.1, 130.9 ppm. MS(FAB): 916 ($M+H^+$).

Anal. Calc. for $C_{58}H_{78}N_{10}$: C, 76.11; H, 8.59; N, 15.30. Found: C, 76.1; H, 8.6; N, 15.3 %.

X-ray Structures Analysis.

A colourless prismatic crystal of $[H_6\mathbf{L3}](ClO_4)_6$•$2H_2O$ was mounted on an Enraf-Nonius CAD4 X-ray diffractometer. Graphite monochromated Mo-Kα radiation was used for cell parameter determination and data collection. A summary of crystallographic data is reported in Table 1.

Cell parameters were determined by least-squares refinement of diffractometer setting angles of 25 carefully centered reflections. The crystals of the compound belong to the monoclinic family, space group $P2_1/n$ (Z = 2).

Intensities of two standard reflections were monitored during data collection to check the stability of the diffractometer and of the crystal: no loss of intensity was recognised. A total of 1804 reflections, to a limit of $2\theta = 40°$, were collected. Intensity data were corrected for Lorentz, polarisation and absorption (PSI-SCAN) effects.

The structure was solved by the direct methods of the SIR97 program [21]. Refinement was performed by means of the full-matrix least-squares method using the SHELXL97 program[22] which uses the analytical approximation for the atomic scattering factors and anomalous dispersion corrections from [23]. The function minimised was $\Sigma\, w(Fo^2 - Fc^2)^2$, with $w\text{-} = 1/[\sigma^2(Fo^2) + (aP)^2 + bP]$, where a and b are refined parameters and $P = (Fo^2 + 2\,Fc^2)/3$.

Anisotropic displacement parameters were used for oxygen and chlorine atoms, while isotropic thermal factors were used with carbon and nitrogen atoms. The hydrogen atoms were introduced in calculated position, and were allowed to ride on their neighbouring heavy atoms.

For 227 refined parameters, the final agreement factors were R1 = 0.0849 (for 815 reflections with I>2sigma(I)) and wR2 = 0.2374 (all data).

Crystal data, atomic coordinated and displacement parameters, full listing of bond distances and angles, have been deposed at the Cambridge Crystallografic Data Centre.

Emf Measurements.

All the pH metric measurements (pH = -log[H^+]) were carried out in degassed 0.15 mol dm^{-3} NaCl solutions, at 298.1 K, by using equipment and procedure which have already been described [24]. The combinated Ingold 405 S7/120 electrode was calibrated as a hydrogen concentration probe by titrating known amounts of HCl with CO_2-free NaOH solutions. The equivalent point was determined the by the Gran's method [25], which allows one to determine the standard potential E^o, and the ionic product of water (pK_w = 13.73(1) at 298.1 K in 0.15 mol dm^{-3} NaCl). In the measurements for the determination of the stability constants, the metal to ligand molar ratio was varied from 0.5 to 2 to verify the formation of polynuclear complexes. At least four measurements (about 150 data points for each one) were performed for each system in the pH range 2.5-10.5 and the relevant e.m.f. data were treated by means of the computer program HYPERQUAD [26] which furnished the equilibrium constants reported in Tables 3-5. Due to the high stability of the Hg(II) and Pd(II) complexes of polyammines **L1**, **L3**, competition between protonation of the free ligands and complex formation is not significant enough to derive the values of the stability constants, and competition with the formation of Hg(II) and Pd(II) chloro complexes was used. The stability constants for the formation of Hg(II) and Pd(II) chloro complexes were taken from references [27] and [28], respectively.

Results and Discussion.

Synthesis.

Piperazine, anthracene and benzene groups are good building blocks to form large receptors [4,19,20,29]. The insertion of such moieties in macrocyclic frameworks increases the rigidity and preorganization of the macrocycles, enhancing their selectivity in substrate binding. To this purpose we have synthesised the four new ligands **L1**-**L4** which simultaneously contain piperazine units and anthracene or *p*-phenylene moieties.

The procedure developed for the synthesis utilizes the simple starting material **1**, which can be obtained by tosylation of diethanolamine in high yields. [19] Reaction of **1** with *p*-dibromoxylene **2** or 9,10-bis-(chloromethyl)-anthracene **3** in 1:1 molar ratio was carried out in CH_3CN in the presence of M_2CO_3 (M= Li, Na, K, Cs) and gave, after separation by column chromatography, the cyclophanes **L1** and **L3** or **L2** and **L4,** respectively. The macrocycles were characterised by standard techniques. ESI mass spectrometry combined with ^1H and ^{13}C NMR measurements allow for the unequivocal assignment of compounds to the structures in Scheme 1. The yields of the reactions for **L1**-**L4** do not vary significantly with the use of different alkaline carbonates suggesting the absence of any template effect in the cyclizations.

It is of interest that the yields for the 2 + 2 cyclizations are remarkably larger than those of the 1+1 cyclizations. Alcock *et al* reported [30] the synthesis of two octaaza-macrocycles obtain by using 1,4-bis(3'-aminopropyl)piperazine in the cyclization reaction. The preferred chair conformation of the 1,4 piperazine ring and the consequent *trans* orientation of the two side arms bearing the NH_2 reactive functions was involved to explain the observed "two plus two" cyclization. In our case, the conformation of the piperazine rings does not seems to be responsible of the preferential 2 + 2 pathways. The preferred 2 + 2 cyclization are probably related to the presence of rigid spacers in both precursors (the piperazine unit in **1** and the *p*-phenylene and anthracene units in **2** and **3**). The absence of any cation-template effect contributes to support this hypothesis. Indeed, the same type of cyclization reaction, when carried out with linear, not reinforced, polyamine fragments yields only macrocycles by 1 + 1 cyclization reactions. [31]

In conclusion the reinforcement of one synthetic fragment, which represents a relatively small structural variation, has a profound influence on the reaction products.

Structure Analysis of $[H_6\mathbf{L3}](ClO_4)_6 \cdot 2H_2O$.

The molecular structure consists of hexaprotonated $[H_6\mathbf{L3}]^{6+}$ cations, lying around a crystallographic inversion centre with six disordered perchlorate anions and two water molecules. Figure 2 shows an ORTEP [32] drawing of the cation and two symmetry related perchlorate anions interacting with the polyammonium groups of the macrocycle. The overall conformation of the macrocycle is S-shaped, with parallel phenyl rings. Both piperazine rings are in chair conformation.

Six out of the ten nitrogen atoms (N2, N3, N4 and the centrosymmetric ones) are in the *endo* conformation, while N1, N1', N5 and N5' adopt an *exo* conformation, due to the chair conformation of the piperazine units. Although we were not able to localise the six protonation sites in the structure refinement, the analysis of the ligand conformation and of the N$\cdots$O interatomic distances suggests that four protons are bonded to the N1, N1', N5 and N5' nitrogens. In fact, Table 2 clearly shows that the interatomic distances between N1 and N5 and the oxygen atoms of perchlorate anions or water molecules are significantly shorter than those between N2, N3 and N4 and the oxygen atoms of the perchlorate anions.

Assigning position of the remaining two protons cannot be confidently made. Weaker interaction, however, are also found between the N2, N3 and N4 nitrogens and the O32 perchlorate anion, which are probably electrostatic in nature.

Solution Chemistry.

The coordination properties of **L1** and **L3** toward H^+, Cu(II), Zn(II), Hg(II) and Pd(II) were studied in 0.15 mol dm^{-3} NaCl aqueous solutions at 298.1 K by means of potentiometric measurements. Low solubility of the ligands **L2** and **L4** did not allow us to perform similar study with them.

The protonation constants for **L1** and **L3** are reported in Table 3. The values obtained are in agreement with the general behaviour observed for polyamine macrocycles [33].

Metal Complexes.

Cu(II) and Zn(II) Coordination.

The stability constants for **L1** and **L3** towards Cu(II) and Zn(II) are reported in Tables 4 and 5, respectively. As expected, **L3** forms both mono- and dinuclear Cu(II) complexes in aqueous solution. The mononuclear $[Cu\mathbf{L3}]^{2+}$ complex exhibits a marked tendency to protonation forming all the protonated species from $[CuH\mathbf{L3}]^{3+}$ to $[CuH_5\mathbf{L3}]^{7+}$. The stepwise addition constants

(log K) of the protons to the [Cu**L3**]$^{2+}$ species have high values indicating that the protonations occur on amine functions not involved in metal ion coordination.

It is to be noted that the stability constant (logK = 9.3) for the [Cu**L3**]$^{2+}$ complex is lower than those previously found for triaza ligands (for instance, log K = 12.16 for Cu(II) complex of 2,5,8-trimethyl-2,5,8-triazanonane) where the metal is coordinated by three tertiary nitrogens connected by ethylenic chains, [34] and much lower than that found for 1,4,7,10-tetrazabicyclobicyclo[8.2.2]tetradecane (logK = 21.5), where two nitrogens of the piperazine unit are bound to the metal [35]. It is seems likely than in the [Cu**L3**]$^{2+}$ complex the metal is coordinated by the methylated nitrogen N1 and by one adjacent nitrogen of each piperazine ring (N2 and N2' in Figure 1). This feature can be explained by considering that in the ligand both piperazine rings are in the chair conformation, as shown by the crystal structure of its hexaperchlorate salt. Coordination of the second piperazine nitrogen (N3 and N3') would involve the interconversion of the piperazine rings from the chair to the boat conformation, which is an expensive process from an energetic point of view. Indeed the two conforms are about 29 kJ mol^{-1} apart in energy [4], which means about five logarithmic units in the value of the stability constant, and thus reorganisation of the piperazine ring strongly reduced the thermodynamic ability of **L3** to bind the metal ion.

The equilibrium constant for the binding of the second Cu(II) ion by [Cu**L3**]$^{2+}$ to give binuclear complex [Cu_2**L3**]$^{4+}$ (log K = 8.1) is similar to that determined for the formation of [Cu**L3**]$^{2+}$. This behaviour is clearly depicted by the distribution diagram of the species formed as a function of pH reported in Figure 3. For 2:1 Cu(II):**L3** molar ratios, the formation of the monometallic complex is depressed and only protonated [Cu(H$_x$**L3**)]$^{(2+x)+}$ (x = 4, 5) complexes are formed in low percentages at acidic pH's, while the binuclear species are largely prevalent in solution in a wide pH range. All these observations agree with the involvement of the two identical ligand moieties in the coordination of each Cu(II) ion in the binuclear complex, as actually shown by the crystal structure of the {[Cu_2**L3**(H_2O)$_2$]⊃pimelate}$^{2+}$ (see below). Finally in the [Cu_2**L3**]$^{4+}$ species both metal ions are coordinated by only three nitrogens completing their coordination requirement with water molecules, which undergo to facile deprotonation at alkaline pH values giving mono- and dihydroxylated species. The equilibrium constants for the addition of the first and the second OH$^-$ anions to [Cu_2**L3**]$^{4+}$ are similar (see Table 5) suggesting that the hydroxide anions in [Cu_2**L3**$(OH)_2$]$^{2+}$ are located on two separate metal centres.

These experimental data suggest that in the [Cu_2**L3**]$^{4+}$ complex only three nitrogen donor atoms bind each Cu(II). As a consequence of the low coordination number, these complexes behave as receptors for molecules of anionic species, forming "cascade complexes". Crystallisation of methanol/butanol solutions containing $Cu(ClO_4)_2$, **L3**, and sodium pimelate in 2:2:1 molar ratio allows to isolate crystals of the complex {[Cu_2**L3**-$(H_2O)_2$]⊃pimelate}$(ClO_4)_2$.[36] The crystal structure of this complex (Figure 4), previously reported [36], confirms that the ligand involves only three out of five nitrogen atoms of each moiety in the binding of metal ions inducing the formation of cascade complex with the difunctional pimelate anion.

Ligand **L1** displays a more rigid and stiffened structure than **L3**, due to the simultaneous presence of two piperazine rings and an aromatic unit within its small cyclic framework. With the purpose of analysing the effect of such molecular rigidity on the binding features of **L1**, we decided to carry out a potentiometric study in aqueous solutions on the interaction of this macrocycle with Cu(II), Zn(II), Hg(II) and Pd(II) and the results are reported in Table 4. The most interesting finding is the markedly lower stability of the Cu(II) complex of **L1** compared to the mononuclear Cu(II) complex with **L3**. A preliminary molecular mechanics calculation shows that in the absence of metal ion, **L1** contains the two piperazine rings in the chair conformation. Most likely, binding of Cu(II) leads to an interconversion of one or both piperazine rings from the chair to the boat conformation (Figure 5), as already observed in the Cu(II) complexes with reinforced tetraazamacrocycles [35]. This structural feature can explain the lower stability constant of the [Cu**L1**]$^{2+}$ complex compared with the mononuclear **L3**. The facile deprotonation of the coordinated water molecules to give hydroxo complexes at neutral or slightly alkaline pH values confirm the low number of nitrogen donors involved in metal coordination.

The coordination properties of **L1** toward Zn(II) are similar to those found for Cu(II), the most significant difference being the lower stability of the [Zn**L1**]$^{2+}$ complex which is usually observed in Zn(II) complexes with polyamines.

Hg(II) and Pd(II) Coordination.

In Table 4 are shown the stability constants for the formation of Hg(II) and Pd(II) complexes with **L1** determined by potentiometry at 298.1 ± 0.1 K in 0.15 mol dm^{-3} NaCl. The high stability of these complexes made necessary the use of competing procedures to determine the relevant equilibrium constants since hydrogen ions do not compete significantly with the metal ions in the pH range 2.5-10.5. Competition of **L1** with chloride ions for the coordination of Hg(II) and Pd(II) was used.

As far as the stability constant of [Pd**L1**Cl]$^+$ complex is concerned some general features can been outlined. First of all it is to be noted that the stability of this species is markedly lower than those reported for tertiary triamine ligands (for instance log K = 24.9 for the Pd(II) complex with 2,5,8-trimethyl-2,5,8-triazanonane [37]). Furthermore the equilibrium constant for the addition of H$^+$ to the [Pd**L1**Cl]$^+$ complex is significantly high, revealing that protonation occurs on a nitrogen atom not involved in the metal coordination. This observation indicates that the metal ion is probably coordinated by the methylated nitrogen and by one nitrogen of each adjacent piperazine ring and one chloride anion with typical square geometry. This is confirmed by the electronic spectrum of the complex which displays a band at 350 nm typical of a square planar N_3PdCl chromophore [37]. This binding mode would involve, once again, interconversion of one or two piperazine rings from the chair conformation to the less energetically favoured boat conformation, thus explaining the observed low stability constant of the [Pd**L1**Cl]$^+$ complex.

Similar consideration can be made for the Hg(II) complexes. The stability constant value accounts for a Hg(II) ion coordinated by only three nitrogens in the [Hg**L1**Cl]$^+$ complex [38]. The most interesting finding is the big gap in the stability between the complexes of Hg(II) and those of Cu(II) and Zn(II) which would allow the selective recognition of this ion.

Acknowledgements.

Financial support by the Italian Ministero dell'Università e della Ricerca Scientifica e Tecnologica, within the program COFIN 2000, and by Italian Research Council (CNR) is gratefully acknowledged and by Spanish DGCYT BQU2000-1424.

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