

4,7,10,23-Tetramethyl-17-oxa-1,4,7,10,13,23-hexaazabicyclo[11.7.5]pentacosane (L), a Two-Binding-Site Ligand for the Assembly of the $[\text{Zn}_2(\mu\text{-OH})_2]^{2+}$ Cluster

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The synthesis of the new macrobicyclic ligand 4,7,10,23-tetramethyl-17-oxa-1,4,7,10,13,23-hexaazabicyclo[11.7.5]pentacosane (L) is described. Its basicity and Zn^{2+} complexation have been studied by means of potentiometric titrations in 0.15 mol dm^{-3} NaClO_4 aqueous solution at 298.1 ± 0.1 K. L behaves as tetraprotic base for $\text{pH} > 2.5$. The crystal structure of $[\text{H}_3\text{L}](\text{ClO}_4)_3$ ($P\bar{1}$, $a = 10.358(3)$ Å, $b = 11.383(4)$ Å, $c = 14.858(3)$ Å, $\alpha = 105.24(2)^\circ$, $\beta = 95.26(2)^\circ$, $\gamma = 95.08^\circ$, $Z = 2$, $R = 0.0813$, $wR^2 = 0.1997$) evidences the formation of intramolecular H-bond networks, which stabilize the protonated forms. Mononuclear Zn^{2+} complexes are formed in aqueous solution, while both mono- and binuclear species are present in methanol. The dibridged binuclear $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}^{2+}$ species is almost the unique complex formed by L in presence of 2 equiv of the metal ion. The crystal structure of $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}(\text{ClO}_4)_2 \cdot \text{H}_2\text{O} \cdot 0.5\text{CH}_3\text{OH}$ ($P2_1/c$, $a = 8.552(2)$ Å, $b = 39.23(1)$ Å, $c = 11.419(3)$ Å, $\beta = 111.90(2)^\circ$, $Z = 4$, $R = 0.087$, $R_w = 0.091$) has been determined. Reaction of $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}^{2+}$ with various substrate molecules has been investigated: the binuclear complex recognizes chelating agents such as 2-hydroxypyridine and cytosine. The crystal structure of $\{[\text{Zn}_2(\mu\text{-OH})(2\text{-hydroxypyridinate})]\text{L}\}(\text{ClO}_4)_2$ ($P2_1/m$, $a = 11.796(3)$ Å, $b = 13.035(6)$ Å, $c = 14.842(3)$ Å, $\beta = 107.75(2)^\circ$, $Z = 2$, $R = 0.085$, $R_w = 0.083$) reveals that the chelating ligand binds a single metal center. The binuclear structure is retained in reactions with substrate molecules, suggesting the use of the $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}^{2+}$ species as a model for zinc-containing enzymes.

Introduction

The synthesis of tailored molecules for the recognition of chemical species is producing wide classes of macrocyclic and macropolycyclic structures.¹ In particular, special attention is being devoted to the search for ligands capable of promoting the assembly of polymolecular species.²

We have already presented in a recent communication³ a few details regarding the ability of the title ligand to assemble inside its tridimensional cavity the $[\text{Zn}_2(\mu\text{-OH})_2]^{2+}$ cluster, inducing selective reactions with substrate molecules. Special interest is being focused on metal complexes containing this cluster as model compounds for mimicking the active centers of zinc-containing enzymes such as phospholipase C from *Bacillus cereus* and bovine leucine aminopeptidase.^{4,5}

The ligand L is ideally composed of a monooxatriaia macrocycle overstructured by a triaza bridge. Both moieties of L are capable of binding transition metal ions, forming very stable complexes. Molecular modeling showed³ two metal ions coordinated within the two moieties should be forced about

3–3.5 Å from each other, reproducing the bimetallic structure presented by the active centers of the enzymes mentioned above.^{6,7} Furthermore, L occupies only few positions in the coordination spheres of the two metal ions, thus inducing binding of secondary ligands from the medium. The attainment of the $[\text{Zn}_2(\mu\text{-OH})_2]^{2+}$ complex fulfilled our expectations.

A principal problem connected with the proposed low-molecular-weight model systems for the dizinc(II) enzymes resides in the fact that their structures are composed of two zinc(II) complex subunits kept together by dibridging ligands and reactions with substrate molecules cleave the cluster separating the metal centers. The aim of the present work is the synthesis of a ligand capable of forming a “protected” $[\text{Zn}_2(\mu\text{-OH})_2]^{2+}$ cluster. We present here the synthesis of such a ligand, the assembly of $[\text{Zn}_2(\mu\text{-OH})_2]^{2+}$ inside its cavity, and the reactivity of the “protected” cluster toward substrate molecules.

Experimental Section

Materials. All chemicals were commercial products and were used as supplied unless otherwise noted.

Synthesis of the Compounds. 1,4,7,10-Tetramethyl-1,4,7,10,13,16-hexaazacyclooctadecane (1)⁸ and 3,3'-oxybis(propionyl) chloride (2)⁹ were prepared as already described. The procedure for the synthesis of L is summarized in Scheme 1.

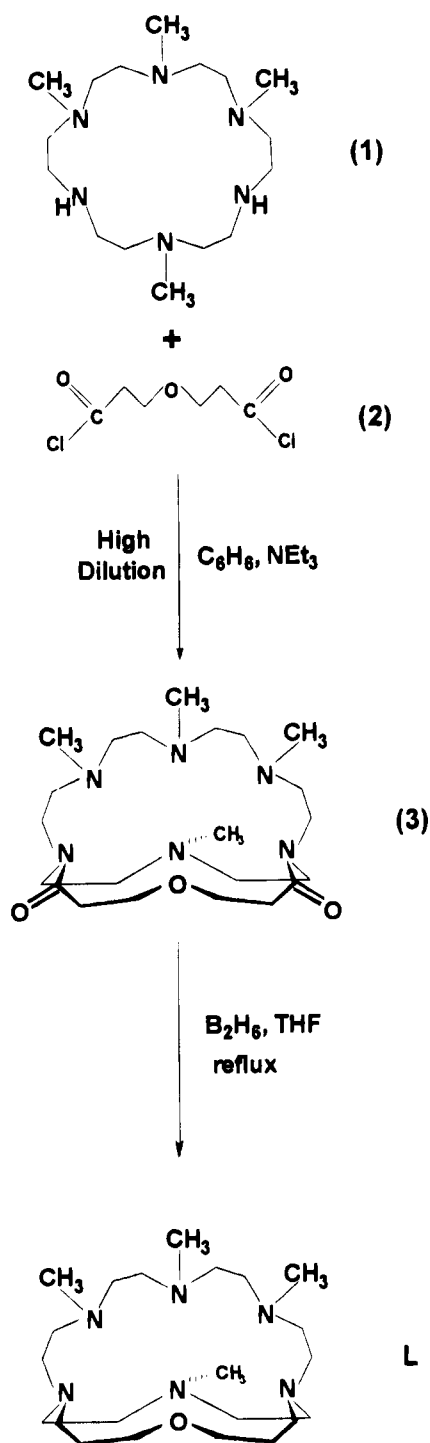
Bicyclic Diamide (3). A sample of 1 (2 g, 6.4 mmol) in dry benzene (250 cm^3) and a sample of 2 (1.45 g, 6.4 mmol) in dry benzene (250 cm^3) containing triethylamine (3 g, 28 mmol) were added simulta-

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Scheme 1



neously to dry benzene (250 cm³), with vigorous stirring, over a period of 7 h at room temperature. The reaction mixture was filtered, and the filtrate was evaporated to dryness under reduced pressure. The yellowish oil obtained was dissolved in the minimum quantity of chloroform, and the solution was chromatographed on neutral alumina (70–230 mesh, activity II–III), eluting with chloroform. The eluted fractions were collected and evaporated to dryness to obtain a colorless oil. Yield: 1.95 g (69%). Anal. Calcd for C₂₂H₄₄N₆O₃: C, 59.94; H, 10.10; N, 19.10. Found: C, 59.5; H, 10.2; N, 18.9.

4,7,10,13-Tetramethyl-17-oxa-1,4,7,13,23-hexaazabicyclo[11.7.5]-pentacosane (L). The reduction of **3** to **L** was carried out with diborane in dry THF. Diborane (0.05 mol) in dry THF (50 cm³) was added dropwise under an inert atmosphere to a cooled solution (20 cm³) of dry THF containing **3** (1.95 g, 4.4 mmol) over a period of 30 min. The cooling bath was removed, and the reaction mixture was allowed to warm to room temperature before being refluxed for 6 h. The solution

was then cooled to 0 °C, and the excess of diborane was destroyed with methanol (10 cm³) and water (5 cm³). The resulting suspension was evaporated to dryness, and the white solid obtained was dissolved in HCl (37%)–H₂O–MeOH (2:6:20 cm³) and refluxed for 4 h. The reaction mixture was treated with water (15 cm³) and the resulting solution filtered and made strongly alkaline with tetramethylammonium hydroxide. This solution was extracted with chloroform (5% 20 cm³), and the combined extracts were dried over sodium sulfate. The solvent was removed under reduced pressure to give a colorless oil. Anal. Calcd for C₂₂H₄₈N₆O₃: C, 66.46; H, 12.16; N, 21.13. Found: C, 66.2; H, 11.9; N, 21.0. ¹³C NMR, δ(CDCl₃): 27.04 (C8), 41.93 (C4), 43.24 (C12), 43.55 (C1), 50.69 (C7), 52.96 and 53.26 (C6 or C10), 55.67 (C3), 55.97 (C11, C5), 56.27 (C2), 67.05 (C9).

L·3HClO₄. The trihydroperchlorate was obtained in quantitative yield by adding 70% HClO₄ to an ethanolic solution containing the free amine. *Caution: perchlorate salts of organic ligands are potentially explosive; these compounds must be handled with great care!* The white solid formed was filtered off and recrystallized from water. Anal. Calcd for C₂₂H₅₁Cl₃N₆O₁₅: C, 37.00; H, 7.20; N, 11.77. Found: C, 37.4; H, 7.3; N, 11.8.

Crystals of this compound suitable for X-ray analysis were obtained by slow evaporation of a diluted aqueous solution.

[Zn₂(μ-OH)₂]L}(ClO₄)₂·H₂O·0.5CH₃OH. Crystals of the compound were obtained in quantitative yield by slow evaporation of methanolic solutions containing **L** and Zn(ClO₄)₂·6H₂O in 1:2 molar ratio. Anal. Calcd for C_{22.5}H₅₄Cl₂N₆O_{12.5}Zn₂: C, 33.35; H, 6.72; N, 10.37. Found: C, 33.4; H, 6.8; N, 10.5.

[Zn₂(μ-OH)(2-hydroxypyridinate)]L}(ClO₄)₂. Addition of equimolar quantities of 2-hydroxypyridine to methanolic solution of [Zn₂(μ-OH)₂]L}(ClO₄)₂·H₂O·0.5CH₃OH produced, after evaporation, crystals of the compound in almost quantitative yield. Anal. Calcd for C₂₇H₅₃Cl₂N₇O₁₁Zn₂: C, 38.00; H, 6.26; N, 11.49. Found: C, 38.3; H, 6.4; N, 11.6.

Potentiometric Measurements. Both protonation constants of **L** and equilibrium constants for complexation reaction were determined by pH-metric measurements (pH = -log [H⁺]) in 0.15 mol dm⁻³ NaClO₄ at 298.1 ± 0.1 K, by using the potentiometric equipment that has been already described.¹⁰ The reference electrode was an Ag/AgCl electrode in saturated KCl solution. The glass electrode was calibrated as a hydrogen concentration probe by titrating known amounts of HCl with CO₂-free NaOH solutions and determining the equivalent point by Gran's method,¹¹ which allows the determination of the standard potential *E*^o and the ionic product of water (p*K*_w = 13.73(1) at 298.1 K in 0.15 mol dm⁻³ NaClO₄). Ligand concentrations of 1 × 10⁻³–2 × 10⁻³ mol dm⁻³ were employed in protonation constant determinations, performing three titration experiments (about 100 data points each) in the pH range 2.5–10.5. Contrary to what observed for similar cryptand ligands, Zn²⁺ complexation by **L** is fast and can be studied by common pH-metric titrations. However the equilibrium attainment has been confirmed by batchwise measurements.¹² Three titrations (about 100 data points each) and a 20-solution batchwise experiment were performed. Metal and ligand concentrations were varied in the range 1 × 10⁻³–2 × 10⁻³ mol dm⁻³, the metal to ligand molar ratio ranging from 0.5 to 1.5.

The computer program SUPERQUAD¹³ was used to calculate equilibrium constants from emf data. All titrations for protonation or complexation reactions, respectively, were treated either as single sets or as separated entities, for each system, without significant variation in the values of the determined constants.

Crystallographic Data Collection and Refinement of the Structures. Crystallographic and experimental data for [H₃L](ClO₄)₃ (**a**), {[Zn₂(μ-OH)₂]L}(ClO₄)₂·H₂O·0.5CH₃OH (**b**), and {[Zn₂(μ-OH)(2-hydroxypyridinate)]L}(ClO₄)₂ (**c**) are summarized in Table 1. Prismatic

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Table 1. Crystallographic and Experimental Data for $[H_3L](ClO_4)_3$ (**a**), $\{[Zn_2(L)(\mu-OH)_2]\}(ClO_4)_2 \cdot H_2O \cdot 0.5CH_3OH$ (**b**), and $\{[Zn_2(L)(\mu-OH)(2\text{-hydroxypyridinate})]\}(ClO_4)_2$ (**c**)

	a	b	c
formula	$C_{22}H_{51}Cl_3N_6O_{13}$	$C_{22.5}H_{54}Cl_2N_6O_{12.5}Zn_2$	$C_{27}H_{53}Cl_2N_7O_{11}Zn_2$
mol wt	714.04	810.37	853.42
temp, °C	25	25	25
radiation, graphite monochromated	Cu K α	Cu K α	Mo K α
λ , Å	1.541 78	1.541 78	0.710 69
space gp	$P\bar{1}$	$P2_1/c$	$P2_1/m$
<i>a</i> , Å	10.358(3)	8.552(2)	11.796(3)
<i>b</i> , Å	11.383(4)	39.23(1)	13.035(6)
<i>c</i> , Å	14.858(3)	11.419(3)	14.842(3)
α , deg	105.24(2)	90	90
β , deg	95.26(2)	111.90(2)	107.75(2)
γ , deg	95.08(3)	90	90
<i>V</i> , Å ³	1671.5(8)	3554(2)	2173(1)
<i>Z</i>	2	4	2
<i>D</i> _{calcd} , mg/m ³	1.419	1.514	1.302
μ , mm ⁻¹	3.078	3.64	1.31
crystal size, mm	0.3 × 0.3 × 0.2	0.5 × 0.3 × 0.2	0.4 × 0.2 × 0.1
<i>R</i> ^a	0.0813	0.087	0.085
<i>wR</i> ² or <i>R</i> _w	0.1997 ^b	0.091 ^c	0.083 ^c

$$^a R = \sum ||F_o| - |F_c|| / \sum |F_o|, \quad ^b wR^2 = [\sum w(F_o^2 - F_c^2)^2 / \sum wF_o^4]^{1/2}, \quad ^c R_w = [\sum w(|F_o| - |F_c|)^2 / \sum w(F_o^2)]^{1/2}.$$

colorless crystals of **a** and **c** (approximate dimensions 0.3 × 0.3 × 0.2 mm and 0.4 × 0.2 × 0.1 mm for **a** and **c**, respectively) and a plate-shaped crystal of **b** (approximate dimensions 0.5 × 0.3 × 0.2 mm) were mounted on an Enraf-Nonius CAD4 X-ray diffractometer and used for data collections at room temperature. Graphite-monochromated Cu K α ($\lambda = 1.5418$ Å), for **a** and **b**, and Mo K α ($\lambda = 0.71069$ Å), for **c**. X-radiations were used.

Cell parameters for the three compounds were determined by least-squares refinement of diffractometer setting angles for 25 carefully centered reflections. The intensities of two standard reflections per compound were monitored during data collections: no loss of intensity was recognized. Totals of 4194 ($2\theta_{\max} = 129.9^\circ$), for **a**, 6464 ($2\theta_{\max} = 130^\circ$), for **b**, and 4159 ($2\theta_{\max} = 50^\circ$), for **c**, independent reflections were collected. Intensity data were corrected for Lorentz and polarization effects; absorption corrections were applied by the Stuart and Walker method¹⁴ once the structures were solved. Refinements were performed by means of the full-matrix least-squares method. The functions minimized were $\sum w(F_o^2 - F_c^2)^2$ for **a**, $w = 1/[\sigma^2(F_o^2) + (0.13P)^2]$ with $P = (\text{Max}(F_o^2, 0) + 2F_c^2)/3$ and $\sum w(|F_o| - |F_c|)^2$ with $w = 1/[\sigma^2(F) + 0.0002F^2]$ for **b**, and $w = 1/[\sigma^2(F) + 0.0006F^2]$ for **c**. Refinement calculations, carried out on a DEX 486-DX computer, were performed with the SHELX-93¹⁵ (**a**) and SHELX-76¹⁶ (**b**, **c**) programs, which use the analytical approximation for the atomic scattering factors and anomalous dispersion corrections for all the atoms from ref 17.

a. The compound crystallizes in the triclinic family, space group $P\bar{1}$, $Z = 2$. The structure was solved by means of the direct method of the SIR-92 program.¹⁸ Anisotropic temperature factors were used for the chlorine and the oxygen atoms belonging to the perchlorate anions. The hydrogen atoms bound to the carbon atoms of the ligand were included in calculated positions and their coordinates refined according to those of the linked atoms, with an overall thermal factor $U = 0.071$ Å². A final ΔF map allowed us to localize the H1, H3, and H5 acidic protons, which were introduced into the calculation and isotropically refined. One of the perchlorate anions showed a high degree of disorder. Two different models, with population parameters 0.53 and 0.47, were used for the Cl2 and O24 atoms, while the O21, O22, and O23 atoms, refined with population parameters 1, presented high values for the U_{11} term of the anisotropic temperature factors. The final agreement factors for 288 refined parameters were $R = 0.081$ (for 4018

unique observed reflections having $I > 2.0\sigma(I)$) and $wR^2 = 0.20$. No residual electron density was present in the last ΔF outside the range -0.37 to $+0.77$ e Å⁻³. Table 2 reports the final positional parameters and the isotropic or equivalent temperature factors, with estimated standard deviations, for all the non-hydrogen atoms.

b. Crystals of the compound belong to the monoclinic family, space group $P2_1/c$, $Z = 4$. The structure was solved by the Patterson technique.

The hydrogen atoms of the ligand molecule were introduced in calculated positions and refined according to their carrier atoms, with an overall temperature factor $U = 0.05$ Å². All non-hydrogen atoms were refined with anisotropic thermal parameters. A disordered methanol molecule was found near the crystallographic inversion center. Only the carbon and oxygen atoms of this solvent molecule were introduced and anisotropically refined with partial occupation factor 0.5. ΔF map, obtained in the last refinement step, did not allow us to localize the hydrogen atoms of the hydroxide ions and of the water molecule. Convergence was reached at $R = 0.087$, $R_w = 0.091$ for 4390 reflections with $I > 3.0\sigma(I)$ and 415 parameters. A final difference Fourier map showed no residual density outside -0.82 and $+0.77$ e Å⁻³.

Table 3 gives the final coordinates and the equivalent temperature factors for **b**.

c. Crystals of the compound belong to the monoclinic family, space group $P2_1/m$, $Z = 2$. The structure was solved by the Patterson technique.

Anisotropic thermal parameters were used for zinc, chlorine, nitrogen, and oxygen atoms. All the hydrogen atoms, bound to the carbon atoms, were introduced in calculated positions and their coordinates refined in agreement with those of the linked atoms, with a temperature factor $U = 0.05$ Å². A ΔF map, obtained in the last refinement step, did not allow us to localize the hydrogen atom belonging to the hydroxide ion. Convergence was reached at $R = 0.085$, $R_w = 0.083$ for 1564 reflections with $I > 3.0\sigma(I)$ and 182 parameters. A final difference Fourier map shows no residual density outside -0.50 and $+0.88$ e Å⁻³.

Table 4 gives the final coordinates and the isotropic or equivalent temperature factors for **c**.

NMR Spectroscopy. The 200.0 MHz ¹H NMR and 50.32 MHz ¹³C NMR spectra and ¹H-¹³C homonuclear and ¹H-¹³C heteronuclear 2D correlations in D₂O solutions at different pH values were recorded at 298 K on a Bruker AC-200 spectrometer. ¹H NMR spectra peak positions are reported relative to HOD at 4.75 ppm. Dioxane was used as the reference standard for ¹³C NMR spectra ($\delta = 67.4$ ppm). Zn^{2+} complexation was followed by means of NMR titrations adding a 5×10^{-3} mol dm⁻³ methanolic solution of $Zn(ClO_4)_2 \cdot 6H_2O$ to a 5×10^{-3} mol dm⁻³ solution of **L** in MeOD.

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Table 2. Positional Parameters ($\times 10^4$) and Equivalent or Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for $[\text{H}_3\text{L}](\text{ClO}_4)_3$ (Esd's in Parentheses)

atom	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>	<i>U</i> (eq)
C11	8072(3)	5105(2)	1966(2)	67(1)
O11	7080(11)	4664(11)	1254(7)	173(5)
O12	9300(8)	4987(8)	1617(7)	124(3)
O13	8017(10)	6357(9)	2389(7)	145(4)
O14	8011(10)	4471(10)	2681(7)	147(4)
Cl2	2738(12)	-167(10)	-17(8)	64(2)
Cl2'	2138(12)	-90(11)	-17(8)	51(2)
O21	2591(7)	-143(7)	908(5)	85(2)
O22	2073(11)	-1288(8)	-620(6)	134(4)
O23	2493(12)	832(10)	-282(7)	168(5)
O24	4081(14)	-118(14)	-101(12)	116(7)
O24'	863(20)	114(25)	9(16)	168(11)
Cl3	7573(2)	2591(2)	5458(2)	53(1)
O31	6643(9)	3406(7)	5492(9)	171(5)
O32	7040(10)	1720(9)	5858(7)	144(4)
O33	8760(8)	3211(7)	5988(6)	103(3)
O34	7698(9)	2027(13)	4568(6)	190(6)
N1	1215(7)	2909(6)	3221(5)	49(2)
C1	1846(10)	3846(9)	2794(7)	76(3)
C2	2830(9)	3391(9)	2166(7)	73(3)
N2	3943(7)	3010(6)	2651(5)	58(2)
C3	4745(10)	4038(9)	3340(7)	75(3)
C4	4745(9)	2390(8)	1960(6)	57(2)
C5	5599(9)	1522(8)	2307(7)	58(2)
N3	4867(7)	344(7)	2341(5)	46(2)
C6	3902(8)	498(8)	3055(6)	47(2)
C7	4495(8)	1007(8)	4065(6)	52(2)
C8	3463(9)	1326(8)	4728(6)	59(3)
O1	2843(6)	2293(5)	4513(4)	56(2)
C9	2136(10)	2905(9)	5238(7)	79(3)
C10	1625(11)	3940(10)	4944(8)	83(3)
C11	634(11)	3571(10)	4071(7)	82(3)
C12	192(9)	2063(8)	2481(7)	63(3)
C13	-542(9)	1060(8)	2784(6)	58(3)
N4	241(7)	93(6)	2889(5)	49(2)
C14	-248(10)	-468(9)	3603(7)	73(3)
C15	79(8)	-874(7)	1976(6)	52(2)
C16	881(8)	-1911(7)	2025(5)	47(2)
N5	1292(7)	-2508(7)	1078(5)	52(2)
C17	154(9)	-2925(9)	339(7)	72(3)
C18	2039(9)	-3573(9)	1089(7)	69(3)
C19	3279(8)	-3271(8)	1747(6)	56(2)
N6	4143(7)	-2270(6)	1608(5)	50(2)
C20	4740(10)	-2648(9)	727(7)	75(3)
C21	5148(9)	-1798(8)	2411(7)	61(3)
C22	5829(9)	-534(8)	2463(6)	55(2)
H1	2089(95)	2321(89)	3465(67)	107(34)
H5	1846(83)	-1935(79)	914(57)	73(28)
H3	4419(88)	-80(82)	1871(66)	73(32)

Results and Discussion

Description of the Structures. (a) $[\text{H}_3\text{L}](\text{ClO}_4)_3$. The molecular structure of $[\text{H}_3\text{L}](\text{ClO}_4)_3$ consists of $[\text{H}_3\text{L}]^{3+}$ cations and perchlorate anions. An ORTEP¹⁹ drawing of the $[\text{H}_3\text{L}]^{3+}$ cation is presented in Figure 1, and a list of bond lengths and angles is reported in Table 5.

The acidic protons, localized on N5 and on both bridge-head nitrogen atoms, seem to determine the overall conformation of the macrobicycle. In particular, the high charge density due to two protons on the bridge-head nitrogens forces these atoms into an *endo-exo* conformation. The H1 hydrogen atom gives rise to strong H-bonds with O1 and N2 at 1.7(1) and 2.5(1) Å, respectively, and to a weaker contact involving the lone pair of N4 (2.92(9) Å). The last intramolecular H-bond, together with those formed by H3 and H5 with N6 (H3, H5···N6 2.41(9), 2.61(9) Å, respectively), gives rise to a *gauche-trans-gauche-*

Table 3. Positional Parameters ($\times 10^4$) and Equivalent Displacement Parameters ($\text{\AA}^2 \times 10^3$) for $\{[\text{Zn}_2(\mu\text{-OH})_2\text{L}](\text{ClO}_4)_2\cdot\text{H}_2\text{O}\cdot 0.5\text{CH}_3\text{OH}$ (Esd's in Parentheses)

atom	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>	<i>U</i> (eq)
Zn1	2974(1)	1625(1)	5339(1)	48(1)
Zn2	1824(2)	1057(1)	3480(1)	61(1)
Cl1	6884(4)	1955(1)	1213(3)	91(2)
O11	5117(8)	1989(2)	522(6)	92(5)
O12	7633(12)	2743(3)	6429(18)	234(12)
O13	7269(15)	1806(5)	2354(10)	233(13)
O14	7575(17)	1771(6)	571(12)	287(17)
Cl2	-1148(5)	4428(1)	2439(4)	112(3)
O21	503(11)	4511(3)	3149(10)	144(8)
O22	-1339(12)	4088(2)	2565(10)	144(7)
O23	-1491(16)	4511(3)	1213(9)	165(10)
O24	-2274(15)	4596(4)	2866(13)	200(13)
O2	4106(6)	1269(1)	4543(4)	45(3)
O3	864(7)	1397(1)	4251(5)	58(3)
N1	3166(8)	2000(2)	3877(6)	55(4)
C1	1742(12)	2259(2)	3450(8)	68(5)
C2	1267(12)	2420(2)	4473(9)	73(6)
C3	365(10)	2192(2)	5069(8)	62(5)
O1	1511(6)	1981(1)	6023(5)	55(3)
C4	621(11)	1813(3)	6740(8)	66(6)
C5	1841(13)	1636(3)	7906(8)	74(6)
C6	2436(14)	1286(3)	7724(9)	78(6)
N2	3644(9)	1271(2)	7054(6)	62(5)
C7	5319(12)	1407(3)	7909(8)	73(6)
C8	6295(11)	1566(3)	7218(9)	73(6)
N3	5351(8)	1856(2)	6478(6)	58(4)
C03	5379(11)	2148(2)	7325(8)	65(5)
C9	6039(11)	1969(2)	5529(9)	69(6)
C10	4788(11)	2182(2)	4534(9)	68(6)
C11	3349(13)	1851(2)	2747(8)	70(6)
C12	1873(14)	1651(2)	1825(8)	78(6)
N4	2008(10)	1271(2)	1824(6)	69(5)
C04	3548(14)	1169(3)	1627(9)	87(7)
C13	477(15)	1152(3)	769(9)	92(7)
C14	156(16)	782(3)	944(10)	93(8)
N5	-77(11)	742(2)	2159(7)	75(5)
C05	-1767(15)	858(3)	2051(11)	103(9)
C15	208(16)	392(3)	2648(10)	91(8)
C16	762(17)	405(3)	4094(10)	98(8)
N6	2298(10)	618(2)	4653(7)	71(5)
C06	3852(17)	425(3)	4724(11)	105(9)
C17	2378(15)	713(3)	5947(9)	80(7)
C18	3915(12)	914(2)	6754(9)	73(6)
O	7511(13)	1147(3)	4711(9)	154(9)
O19	5091(69)	4952(12)	4263(69)	418(76)
C19	5870(76)	5163(11)	3277(42)	207(43)

gauche conformation of the N-C-C-N torsional angles belonging to the triaza bridge.

Strong intermolecular H-bond interactions are also shown by H3 and H5 with the O21 oxygen of a perchlorate anion (H3, H5···O21 2.25(9), and 2.12(8) Å, respectively).

(b) $\{[\text{Zn}_2(\mu\text{-OH})_2\text{L}](\text{ClO}_4)_2\cdot\text{H}_2\text{O}\cdot 0.5\text{CH}_3\text{OH}$. The molecular structure consists of dibridged $\{[\text{Zn}_2(\mu\text{-OH})_2\text{L}]^{2+}$ complex cations (ORTEP¹⁹ drawing in Figure 2), perchlorate anions, and water and methanol solvent molecules. Table 6 reports a list of selected bond distances and angles. The coordination environments of the Zn^{2+} cations define two binding moieties within the ligand **L**; the Zn1 metal ion is coordinated to the N₃O donor set of the 14-membered ring, while Zn2 is linked to the nitrogen atoms of the triaza bridge. The two hydroxo ions complete the coordination environment of both Zn^{2+} cations. The geometry around Zn1 is fairly distorted octahedral, while that around Zn2 is intermediate between a trigonal bipyramid, having O2 and N5 in axial positions, and a square pyramid, with the O3 atom in apical position. The $[\text{Zn}_2(\mu\text{-OH})_2]^{2+}$ cluster, assembled inside the cavity of the ditopic macrobicycle **L**, is planar, 0.007 Å for O3 being the largest deviation from the mean plane. This plane also contains the N3, N5, and O1

(19) Johnson, C. K. ORTEP. Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1971.

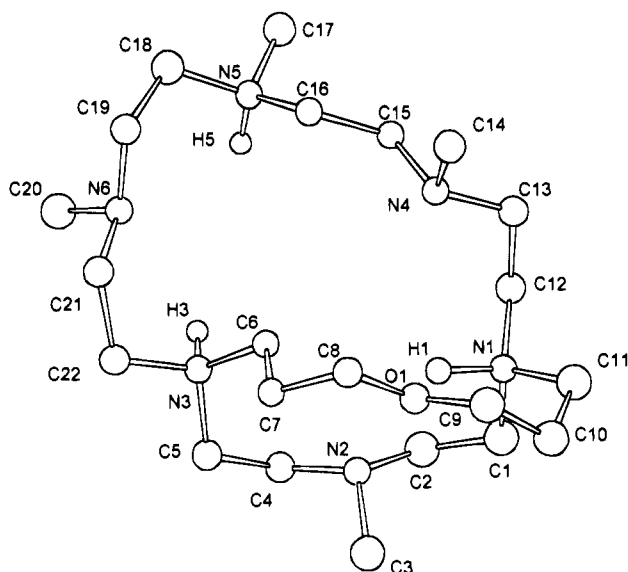


Figure 1. ORTEP¹⁹ drawing of the $[H_3L]^{3+}$ cation.

Table 4. Positional Parameters ($\times 10^4$) and Equivalent or Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for $\{[Zn_2(\mu-OH)(2\text{-hydroxypyridinate})]L\}(\text{ClO}_4)_2$ Esd's in Parentheses)

atom	x/a	y/b	z/c	U(eq)
Zn1	2225(2)	2500	-174(2)	52(2)
Zn2	2885(2)	2500	2262(2)	46(2)
C11	6855(6)	2500	1691(5)	91(5)
O11	7062(23)	2500	837(18)	206(8)
O12	7710(22)	2500	2464(22)	254(8)
O13	6173(19)	1687(12)	1737(12)	186(7)
C12	4711(6)	2500	6281(4)	82(4)
O21	5124(14)	2500	7244(11)	133(7)
O22	5719(19)	2500	5951(13)	191(8)
O23	4009(15)	1633(12)	5973(13)	181(7)
O2	3315(11)	2500	1151(8)	53(6)
O3	751(11)	2500	362(9)	56(6)
N7	318(14)	2500	-1173(12)	63(7)
C19	-32(19)	2500	-409(15)	56(5)
C20	-1259(20)	2500	-587(16)	70(5)
C21	-2024(21)	2500	-1471(15)	72(5)
C22	-1637(21)	2500	-2241(17)	78(6)
C23	-440(21)	2500	-2073(16)	74(5)
O1	4360(11)	2500	3417(9)	54(6)
N1	1442(16)	2500	2847(11)	62(7)
C01	1823(21)	2500	3884(16)	79(6)
C1	780(12)	1542(10)	2476(9)	54(4)
C2	1606(13)	642(12)	2689(11)	69(4)
N2	2576(10)	778(9)	2234(8)	60(6)
C3	2132(12)	406(11)	1249(9)	56(4)
C4	3001(12)	309(12)	661(9)	60(4)
N3	2459(10)	728(9)	-289(7)	53(6)
C03	1371(13)	148(12)	-818(10)	68(4)
C5	3299(14)	629(13)	-821(11)	76(4)
C6	4047(14)	1552(13)	-761(12)	86(5)
N4	3385(15)	2500	-1035(11)	61(7)
C04	2673(21)	2500	-2072(16)	78(6)
C7	3678(14)	179(12)	2770(10)	76(4)
C8	4368(14)	616(12)	3696(10)	73(4)
C9	5077(13)	1574(11)	3653(11)	71(4)

atoms (greatest deviation 0.03 \AA for O1 and N5). The Zn \cdots Zn separation is 2.982(2) \AA .

(c) $\{[Zn_2(\mu-OH)(2\text{-hydroxypyridinate})]L\}(\text{ClO}_4)_2$. The structure of $\{[Zn_2(\mu-OH)(2\text{-hydroxypyridinate})]L\}(\text{ClO}_4)_2$ consists of discrete $\{[Zn_2(\mu-OH)(2\text{-hydroxypyridinate})]L\}^{2+}$ complex cations (ORTEP¹⁹ drawing in Figure 3) and perchlorate anions. A list of selected bond distances and angles is reported in Table 7. The complex cation possesses a crystallographic symmetry plane containing the two metal ions, the chelated hydroxypyridinate group, the μ -hydroxo ion, and the O1, N1,

Table 5. Bond Lengths (\AA) and Angles (deg) for $[H_3L](\text{ClO}_4)_3$

C11-O11	1.362(9)	C5-N3	1.496(10)
C11-O13	1.407(9)	N3-H3	0.81(9)
C11-O12	1.421(8)	N3-C22	1.504(10)
C11-O14	1.435(9)	N3-C6	1.511(10)
C12-O23	1.335(13)	C6-C7	1.510(10)
C12-O22	1.427(14)	C7-C8	1.523(11)
C12-O21	1.391(12)	C8-O1	1.414(10)
C12-O24	1.40(2)	O1-C9	1.422(10)
C12'-O23	1.25(2)	C9-C10	1.483(13)
C12'-O24'	1.36(2)	C10-C11	1.518(13)
C12'-O22	1.41(2)	C12-C13	1.504(12)
C12'-O21	1.430(13)	C13-N4	1.457(10)
C13-O34	1.334(8)	N4-C14	1.479(11)
C13-O32	1.383(8)	N4-C15	1.490(10)
C13-O31	1.391(8)	C15-C16	1.516(11)
C13-O33	1.416(7)	C16-N5	1.510(10)
N1-H1	1.25(10)	N5-H5	0.93(9)
N1-C11	1.498(11)	N5-C17	1.487(11)
N1-C1	1.509(11)	N5-C18	1.498(11)
N1-C12	1.519(10)	C18-C19	1.496(12)
C1-C2	1.481(13)	C19-N6	1.456(10)
C2-N2	1.462(11)	N6-C21	1.460(10)
N2-C4	1.457(10)	N6-C20	1.477(11)
N2-C3	1.466(11)	C21-C22	1.525(11)
C4-C5	1.537(12)		
O11-C11-O13	110.2(8)	N2-C4-C5	113.8(7)
O11-C11-O12	110.5(7)	N3-C5-C4	114.3(7)
O13-C11-O12	107.8(6)	H3-N3-C22	99(6)
O11-C11-O14	111.9(7)	H3-N3-C5	119(7)
O13-C11-O14	107.9(6)	C22-N3-C5	109.0(7)
O12-C11-O14	108.3(6)	H3-N3-C6	102(7)
O23-C12-O22	114.6(10)	C22-N3-C6	113.1(7)
O23-C12-O21	116.8(10)	C5-N3-C6	114.0(7)
O22-C12-O21	108.6(9)	N3-C6-C7	115.1(7)
O23-C12-O24	98.8(11)	C6-C7-C8	112.1(7)
O22-C12-O24	109.8(11)	O1-C8-C7	108.1(7)
O21-C12-O24	107.3(11)	C8-O1-C9	113.2(7)
O23-C12'-O24'	96.0(13)	O1-C9-C10	107.0(8)
O23-C12'-O22	121.3(11)	C9-C10-C11	115.0(9)
O24'-C12'-O22	103.8(14)	N1-C11-C10	111.9(9)
O23-C12'-O21	119.8(10)	C13-C12-N1	115.6(7)
O24'-C12'-O21	105.3(12)	N4-C13-C12	113.4(7)
O22-C12'-O21	107.2(8)	C13-N4-C14	109.4(7)
O34-C13-O32	107.7(8)	C13-N4-C15	108.3(6)
O34-C13-O31	110.1(8)	C14-N4-C15	107.9(7)
O32-C13-O31	104.3(7)	N4-C15-C16	111.5(7)
O34-C13-O33	113.6(5)	N5-C16-C15	111.2(6)
O32-C13-O33	111.0(5)	H5-N5-C17	109(5)
O31-C13-O33	109.8(5)	H5-N5-C18	107(5)
H1-N1-C11	109(4)	C17-N5-C18	108.7(7)
H1-N1-C1	108(4)	H5-N5-C16	108(5)
C11-N1-C1	108.4(7)	C17-N5-C16	111.7(7)
H1-N1-C12	111(5)	C18-N5-C16	112.8(7)
C11-N1-C12	112.2(7)	C19-C18-N5	115.0(8)
C1-N1-C12	108.1(7)	N6-C19-C18	113.0(7)
C2-C1-N1	114.6(8)	C19-N6-C21	110.5(7)
N2-C2-C1	112.9(8)	C19-N6-C20	111.7(7)
C4-N2-C2	109.1(7)	C21-N6-C20	110.7(7)
C4-N2-C3	109.6(7)	N6-C21-C22	113.5(7)
C2-N2-C3	112.8(7)	N3-C22-C21	111.8(7)

and N4 atoms of the ligand, together with the C01 and C04 carbon atoms. The two zinc ions, 3.460(3) \AA apart, present different coordination spheres. Zn1 is bound to the nitrogen atoms of the triaza bridge, the two donor atoms of the 2-hydroxypyridinate group, and the bridging hydroxo ion in a distorted octahedral geometry. On the other hand, the Zn2 atom is coordinated to the N₃O donor set and to the bridging hydroxo ion. The rather irregular bond angle values around Zn2 determine a coordination polyhedron intermediate between a trigonal bipyramid, with the N2 and N2' symmetry-related atoms in apical positions, and a square pyramid, having O1 in an apical position.

Basicity Properties and Zn²⁺ Complexation in Aqueous Solution. Table 8 collects the equilibrium constants for H⁺

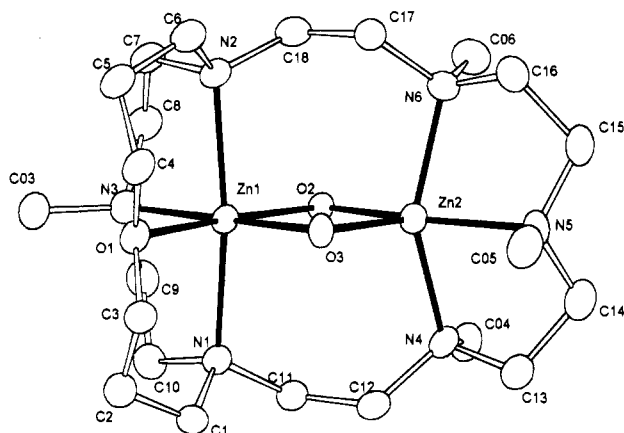


Figure 2. ORTEP¹⁹ drawing of the dibridged {[Zn₂(μ-OH)₂]L}²⁺ complex cation.

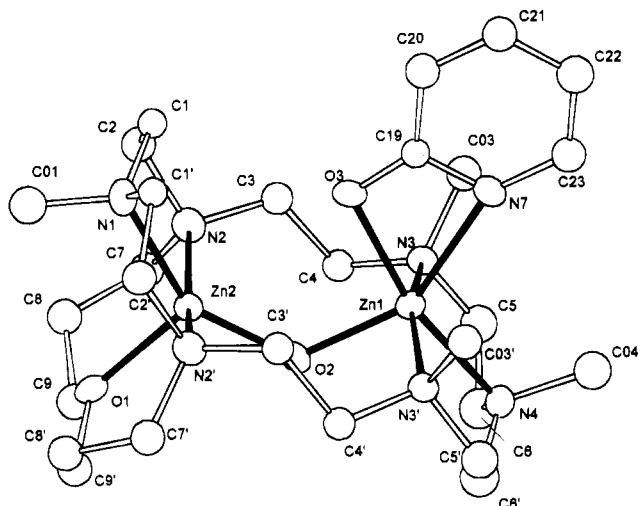


Figure 3. ORTEP¹⁹ drawing of the {[Zn₂(μ-OH)(2-hydroxypyridina-te)L]}²⁺ complexed cation.

Table 6. Selected Bond Lengths [Å] and Angles [deg] for {[Zn₂(μ-OH)₂]L}(ClO₄)₂·H₂O·0.5CH₃OH and e.s.d. in parentheses

Zn1–Zn2	2.982(2)	Zn1–N3	2.162(6)
Zn1–O2	2.092(5)	Zn2–O2	2.052(4)
Zn1–O3	1.983(5)	Zn2–O3	1.941(6)
Zn1–N1	2.277(7)	Zn2–N4	2.128(8)
Zn1–O1	2.203(6)	Zn2–N5	2.148(7)
Zn1–N2	2.293(7)	Zn2–N6	2.125(7)
N2–Zn1–N3	82.0(3)	O2–Zn1–N1	86.6(2)
O1–Zn1–N3	93.0(2)	O2–Zn1–O3	83.4(2)
O1–Zn1–N2	94.3(2)	N5–Zn2–N6	83.9(3)
N1–Zn1–N3	82.0(3)	N4–Zn2–N6	145.0(3)
N1–Zn1–N2	162.6(3)	N4–Zn2–N5	83.7(3)
N1–Zn1–O1	93.3(2)	O3–Zn2–N6	106.6(3)
O3–Zn1–N3	176.7(3)	O3–Zn2–N5	112.1(3)
O3–Zn1–N2	98.1(2)	O3–Zn2–N4	108.4(3)
O3–Zn1–O1	90.3(2)	O2–Zn2–N6	92.3(3)
O3–Zn1–N1	97.5(2)	O2–Zn2–N5	162.3(3)
O2–Zn1–N3	93.3(2)	O2–Zn2–N4	89.8(3)
O2–Zn1–N2	87.6(2)	O2–Zn2–O3	85.6(2)
O2–Zn1–O1	173.6(2)		

and Zn²⁺ binding by L potentiometrically determined in 0.15 mol dm⁻³ NaClO₄ at 298.1 K.

As can be seen, four out of the six tertiary amino groups of the macrobicyclic undergo protonation in the pH range investigated (2.5–10.5). The first aspect of the solution chemistry of L, which deserves to be evidenced, is the high basicity presented by the ligand in the first three protonation steps with respect to similar ligands also containing only tertiary amino groups.²⁰ On the other hand, a large drop in basicity is produced

Table 7. Selected Bond Lengths (Å) and Angles (deg) for {[Zn₂(μ-OH)(2-hydroxypyridina-te)L]}(ClO₄)₂ and Esd's in Parentheses

Zn2–Zn1	3.460(3)	Zn2–N4	2.14(2)
Zn2–O2	1.99(1)	Zn1–O2	1.87(1)
Zn2–O3	2.12(1)	Zn1–O1	2.04(1)
Zn2–N7	2.29(1)	Zn1–N1	2.13(2)
Zn2–N3	2.34(1)	Zn1–N2	2.27(1)
N3–Zn2–N4	81.1(3)	O2–Zn2–N7	148.3(6)
N3–Zn2–N3'	162.0(4)	O2–Zn2–O3	89.2(5)
N7–Zn2–N4	107.2(6)	N2–Zn1–N2'	162.1(5)
N7–Zn2–N3	93.9(3)	N1–Zn1–N2	82.2(3)
O3–Zn2–N4	166.2(6)	O1–Zn1–N2	96.1(3)
O3–Zn2–N3	98.9(3)	O1–Zn1–N1	103.9(6)
O3–Zn2–N7	59.1(6)	O2–Zn1–N2	93.9(3)
O2–Zn2–N4	104.6(6)	O2–Zn1–N1	145.6(6)
O2–Zn2–N3	91.0(3)	O2–Zn1–O1	110.6(6)

Table 8. Logarithms of the Protonation and Zn²⁺ Complexation Constants Determined for L in 0.15 mol dm⁻³ NaClO₄ at 298.1 K

reaction	log K
L + H ⁺ = LH ⁺	10.34(2) ^a
LH ⁺ + H ⁺ = LH ₂ ²⁺	8.93(2)
LH ₂ ²⁺ + H ⁺ = LH ₃ ³⁺	6.96(2)
LH ₃ ³⁺ + H ⁺ = LH ₄ ⁴⁺	2.08(2)
Zn ²⁺ + L = ZnL ²⁺	9.13(4)
ZnL ²⁺ + H ⁺ = ZnLH ³⁺	7.76(4)
ZnLH ³⁺ + H ⁺ = ZnLH ₂ ⁴⁺	6.87(4)
ZnL ²⁺ + OH ⁻ = ZnLOH ⁺	5.78(4)
ZnLOH ⁺ + OH ⁻ = ZnL(OH) ₂	2.97(5)

^a Values in parentheses are standard deviations in the last significant figures.

in the fourth step. With the aim of rationalizing this behavior, we determined the crystal structure of the H₃L(ClO₄)₃ salt containing the triprotonated H₃L³⁺ species. As previously discussed, the three H⁺ ions bind three amino groups in alternate positions, minimizing the electrostatic repulsion between positive charges, and give rise to the formation of an important intramolecular H-bond network with the remaining donor atoms. A similar arrangement of the triprotonated molecule in solution could explain both the high affinity of L for the first three protons and the reduced tendency to bind the fourth one, which should be necessarily located between contiguous ammonium groups.

Despite the high basicity of L only extensive protonation of the ligand inhibits the formation of Zn²⁺ complexes. In fact, as can be noted from Table 8 and Figure 4, the metal ion forms stable complexes with mono- and diprotonated L species. The equilibrium constants for the successive addition of H⁺ to ZnL²⁺ are significantly high, revealing that protonation occurs on a ligand moiety not involved in the coordination to the metal ion. This protonation behavior of the ZnL²⁺ complex coincides with the observed binucleating character of the ligand since the metal ion and the protons occupy two almost independent coordination sites. Thus, protonation of ZnL²⁺ strongly competes with the formation of binuclear species. As a matter of fact, similar complexes have not been detected in aqueous solutions and separation of zinc(II) hydroxide is observed from alkaline solutions containing Zn²⁺ and L in molar ratios greater than 1:1. At these pH values ZnL²⁺ produces mono- and bihydroxylated species. On the other hand, the highly stable [Zn₂(L)(μ-OH)₂]²⁺ complex is formed in alcoholic media.

Zn²⁺ Complexation in Methanol. The coordination of the Zn²⁺ ion by the macrobicyclic receptor has been followed by ¹H and ¹³C NMR titrations in MeOD. ¹H–¹H and ¹H–¹³C 2D

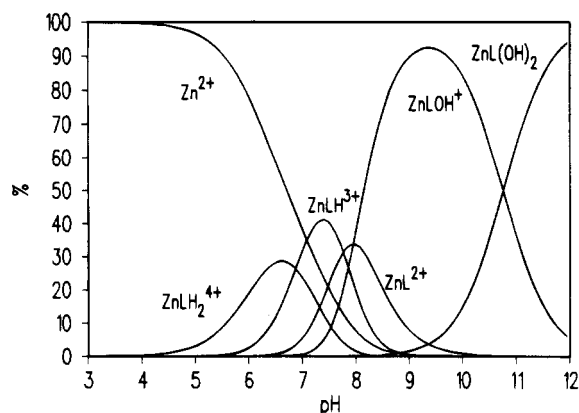


Figure 4. Calculated distribution diagram of the complexed species formed in the system Zn^{2+}/L . Metal and ligand concentrations: $1 \times 10^{-3} \text{ mol dm}^{-3}$.

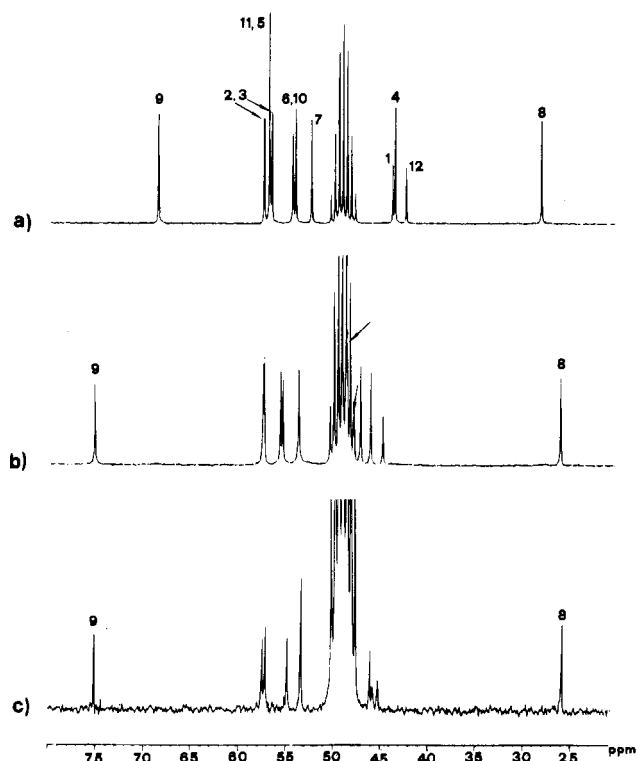
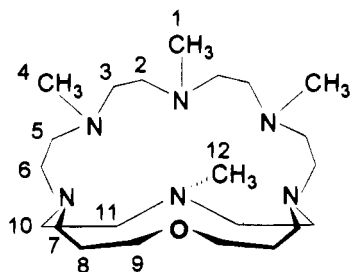


Figure 5. ^{13}C NMR spectra of **L** in MeOD, in absence of Zn^{2+} (a) and in presence of 1 (b) and 2 (c) equiv of the metal ion.

correlation experiments have been performed to assign all the signals.

The ^{13}C spectrum of a methanolic solution of **L** exhibits (Figure 5a) one peak at 68.4 ppm (C9), three signals in the range 44–42 ppm (roughly integrating 1:2:1 and assigned to the methyl groups), one peak at 28.1 ppm (C8), and seven resonances between 58 and 52 ppm, due to C7 and to the carbons of the ethylenic chains. These spectral features are indicative of a C_{2v} symmetry, averaged on the NMR time scale.



Upon the addition of 0.2 equiv of $Zn(ClO_4)_2$, a different set of signals appears in the NMR spectra, together with the resonances of the receptor, evidencing the presence in solution of a Zn^{2+} complex. On addition of further Zn^{2+} , the signals of this species are enhanced, while the resonance of **L** shows a clear decrease in intensity. When the $L:Zn^{2+}$ 1:1 molar ratio is reached, both 1H and ^{13}C **L** subpectra disappear, and the recorded ^{13}C spectrum can be reasonably due to a unique mononuclear Zn^{2+} complex (Figure 5b). It is noteworthy this complex and the ligand are slowly exchanging on the NMR time scale, suggesting the metal ion is deeply embedded into the macrobicyclic cavity.²¹ The signal assigned to C9, in α position with respect to the ethereal oxygen, shows a remarkable downfield shift (ca 7 ppm) upon complexation, indicating the involvement of the oxygen donor in the coordination to the metal ion. These data suggest that the Zn^{2+} ion could be coordinated by the 14-membered N_3O moiety of the ligand, similar to what is observed in the crystal structure of the mononuclear Zn^{2+} complex of an analogous macrobicyclic.¹²

Similar behavior was observed also for the formation of Zn^{2+} mononuclear complexes of **L** in aqueous solutions.

Upon addition of more than 1 equiv of Zn^{2+} in methanol, the 1H and ^{13}C spectra show a remarkable line broadening, attributable to the coordination of a second metal ion, which is rapidly exchanged between the binuclear and the mononuclear complexes.

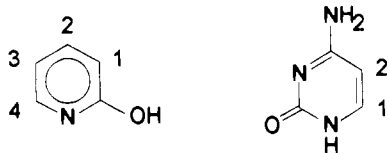
After the addition of 2 equiv, the ^{13}C spectrum (Figure 5c) shows again a C_{2v} time-averaged symmetry with sharp peaks at 75.1 (one signal, C9), at 47–45 (three resonances, the methyl groups), at 26.0 ppm (one peak, C8), and in the range 58–50 ppm (the remaining carbons). In accordance with the formation of a highly stable binuclear Zn^{2+} complex, further addition of Zn^{2+} does not affect the 1H and ^{13}C NMR spectra. It is worthy of note that the resonance of C9 does not shift with respect to the spectrum recorded with a 1:1 $Zn^{2+}:L$ molar ratio, confirming that the binding of the oxygen donor takes place in the first coordinative step.

Reaction with Substrate Molecules. The Zn–Zn distance (2.982 Å) in the $\{[Zn_2(\mu-OH)_2]L\}^{2+}$ complex is very similar to those observed in zinc-containing enzymes such as phospholipase C from *Bacillus cereus* (3.3 Å)⁶ and bovine leucine aminopeptidase (2.88 Å),⁷ where the two metal centers are bridged by hydroxo and/or carboxylate groups. In a recent paper, the structural properties of this enzymes as well as of a number of low-molecular-weight models were analyzed, leading to the general consideration that the Zn–Zn distances are primarily determined by the nature and the coordination mode of the bridging groups.⁴ For the specific case of $[Zn_2(\mu-OH)_2]^{2+}$ we observe the metal to metal separation is almost invariable (2.98–3.02 Å) in all the crystal structures containing the cluster.⁴

Although the nature of the primary ligand has poor effects on the structural properties of the $[Zn_2(\mu-OH)_2]^{2+}$ cluster, the ligand's preorganization is expected to influence its behavior toward reactions with further molecules. With regard to this aspect, we analyzed the interaction of a variety of mono- and bidentate substrates with the $\{[Zn_2(\mu-OH)_2]L\}^{2+}$ complex. The 1H NMR spectra of pyridine, phenol, 2-hydroxypyridine, 3-hydroxypyridine, 4-hydroxypyridine, and cytosine were recorded in the absence and in the presence of increasing amounts of the complex, both in MeOD and in $1 \times 10^{-1} \text{ mol dm}^{-3} NMe_4OH$ methanolic solution (where the substrates are deprotonated). Only in the case of cytosine and 2-hydroxypyridine have

(21) Bencini, A.; Bianchi, A.; Borselli, A.; Ciampolini, M.; Garcia-España, E.; Dapporto, P.; Micheloni, M.; Paoli, P.; Ramirez, J. A.; Valtancoli, B. *Inorg. Chem.* **1989**, *28*, 4279.

downfield shifts, relative to pure substrates' spectra, been observed in presence of $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}^{2+}$, indicating substrate interaction with the complex. For example, the ^1H NMR signals of 2-hydroxypyridine in methanol are displaced by 0.15 ppm (H1, H2) and 0.05 ppm (H3, H4) and those of cytosine by 0.22 ppm (H1) and 0.10 ppm (H2) in the presence of equimolar amounts of $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}^{2+}$.



In order to establish the binding mode of these secondary ligands, we determined the crystal structure of the $\{[\text{Zn}_2(\mu\text{-OH})\text{-}(2\text{-hydroxypyridinate})]\text{L}\}(\text{ClO}_4)_2$ compound whose description is presented in this paper. As already mentioned, 2-hydroxypyridinate acts as chelating ligand toward a single metal ion, removing a $\mu\text{-OH}$ bridge. Although the substrate coordination increases the Zn–Zn separation by about 0.5 Å, the integrity of the binuclear active center in the complex is conserved as a consequence of the two-binding-site nature of the primary ligand **L**, which forces the Zn^{2+} ions into close proximity. In this coordinative environment the bridging hydroxo groups play an important role in determining the selectivity of the dizinc(II) complex toward substrate recognition. In fact, the binding of

monodentate substrates to $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}^{2+}$ should occur either *via* the involvement of a sixth coordinative position on Zn^{2+} or by replacement of a bound donor. Both processes are generally not very favorable, from an energetic point of view, especially when occurring at the expense of highly stable species. On the other hand, coordination of a bidentate ligand occurs only when the energy lost due to the loss of a bridging hydroxo ligand is regained by the formation of appropriate chelated rings. Among the three isomers of hydroxypyridine only 2-hydroxypyridine presents the suitable bite.

The use of an appropriate macrocyclic molecule in the assembly of the $[\text{Zn}_2(\mu\text{-OH})_2]^{2+}$ cluster gives rise to the formation of a model compound for which (i) the binuclear structure is retained in reactions with substrate molecules and (ii) the high stability of the $\{[\text{Zn}_2(\mu\text{-OH})_2]\text{L}\}^{2+}$ complex increases the selectivity of the active center toward substrate recognition.

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Supplementary Material Available: Tables of crystallographic data, hydrogen positional parameters, and anisotropic thermal factors (4 pages). Ordering information is given on any current masthead page.

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