

# Synthesis and Ligational Properties of Two New Binucleating Oxa–Aza Macrocyclic Receptors

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Synthesis and characterization of the two new macrocyclic ligands 1,4,7,16,19,22-hexaza-10,13,25,28-tetraoxacyclotriacontane (**L1**) and 1,4,7,16,19,22,25-heptaza-10,13,28,31-tetraoxacyclotriacontane (**L2**) are reported. Both of them contain two polyamine units separated by two eight-atom dioxo bridges. The basicity constants and the formation constants of their complexes with Cu(II) and Zn(II) have been determined by potentiometric measurements in aqueous solution (298.1 K,  $I = 0.15 \text{ mol dm}^{-3}$ ). Both **L1** and **L2** form mono- and dinuclear complexes in aqueous solution. In the  $[\text{ML1}]^{2+}$  and  $[\text{ML2}]^{2+}$  ( $M = \text{Zn}^{2+}$  or  $\text{Cu}^{2+}$ ) complexes, the metal ion is coordinated by only one polyamine moiety. The binuclear complexes show a marked tendency to form mono- and dihydroxo species in aqueous solution. The high values of the constants for the addition of the first hydroxide group to the dinuclear species suggest that in the  $[\text{M}_2\text{L1}(\text{OH})]^{3+}$  and  $[\text{M}_2\text{L2}(\text{OH})]^{3+}$  species the OH<sup>-</sup> group bridges the two metal centers. This thermodynamic result is confirmed by the crystal structure of the  $[\text{Zn}_2\text{L1}(\mu\text{-OH})(\text{ClO}_4)_3 \cdot 0.5\text{EtOH}]$  compound (**a**) (space group *Pbca*,  $a = 14.289(4) \text{ \AA}$ ,  $b = 15.617(6) \text{ \AA}$ ,  $c = 33.862(8) \text{ \AA}$ ,  $V = 7556(4)$ ,  $Z = 8$ ,  $R = 0.0612$ ,  $wR^2 = 0.1780$ ) which shows the hydroxide ion bridging the two Zn(II) cations (Zn<sup>••</sup>–Zn distance 3.5 Å). In the crystal structure of  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (**b**) (space group *P2<sub>1</sub>/a*,  $a = 8.550(6) \text{ \AA}$ ,  $b = 17.854(6) \text{ \AA}$ ,  $c = 12.090(3) \text{ \AA}$ ,  $\beta = 102.23(4)^\circ$ ,  $V = 1804(2)$ ,  $Z = 2$ ,  $R = 0.0520$ ,  $wR^2 = 0.1618$ ) each metal ion is coordinated by one triamine unit and by two isothiocyanate ions in a distorted square pyramidal arrangement. Finally, in the crystal structure of  $[\text{Cu}_2\text{L1}(\text{NCS})_4]\text{Na}_2\text{S}_2$  (**c**) (space group *P2<sub>1</sub>/a*,  $a = 8.492(3) \text{ \AA}$ ,  $b = 17.740(4) \text{ \AA}$ ,  $c = 13.016(3) \text{ \AA}$ ,  $\beta = 94.54(3)^\circ$ ,  $V = 1954.7(9)$ ,  $Z = 2$ ,  $R = 0.1101$ ,  $wR^2 = 0.3105$ ) the two metal ions exhibit a coordination environment almost equal to that found for (**b**), but the  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  units are joined by NCS<sup>-</sup>–Na<sup>+</sup>–(S–S)<sup>2-</sup>–Na<sup>+</sup> interactions giving rise to a tridimensional polymeric structure.

## Introduction

In the last few years a variety of Zn(II) and Cu(II) complexes with synthetic ligands have been used in biomimetic zinc<sup>1</sup> or copper chemistry.<sup>2</sup>

A number of zinc enzymes with multinuclear metal sites are known to be responsible for the hydrolysis of the phosphate ester bond in a variety of low molecular weight metabolites and nucleic acid.<sup>3</sup> Alkaline phosphatase contains two Zn(II),<sup>3,4</sup> while in the phospholipase C there are three Zn(II) ions per each reactive subunit, two of which are in close proximity (3.3 Å).<sup>5</sup> In both cases the two Zn(II) show a different coordination environment and seem to work cooperatively. Furthermore, a zinc-bound water molecule plays a fundamental role in the hydrolytic mechanism, which involves the nucleophilic attack of a hydroxide anion to the phosphorous center, with the subsequent cleavage of the P–O bond. In the case of the

phospholipase C the two Zn(II) ions at 3.3 Å are connected by a bridging OH<sup>-</sup> or H<sub>2</sub>O group. It seems likely that hydrolytic cleavage is strongly influenced by the generation of L–Zn(II)–OH species from H<sub>2</sub>O-bound Zn(II) complexes, *i.e.*, by the pK<sub>a</sub> of the coordinated water molecule.

In order to obtain further information on such hydrolytic mechanism, a variety of Zn(II) complexes with macrocyclic receptors has been recently used as model systems for the above enzymes.<sup>6–8</sup> Particularly, macrocycles containing two binding polyamine subunits linked by two bridges are known to form dinuclear complexes with metal cations and can be used to force two metal ions at close distance. The distance between the two metal ions is determined by the length and flexibility of the two bridges. Moreover, the chemical properties of the metal centers depend on the ligational properties of the two chelating sites. In particular, when the binding sites contain three or four amine groups, the macrocycle can bind a variety of transition metal ions and the resulting complexes are characterized by unsaturated coordination spheres. Consequently, these complexes behave as receptors for molecules or anionic species, forming "cascade" complexes.<sup>9</sup>

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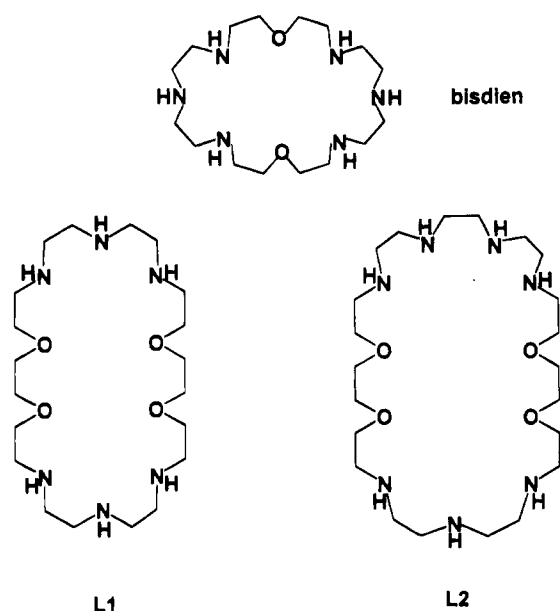
<sup>‡</sup> University of Urbino.

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- (1) Koike, T.; Kajitani, S.; Nakamura, I.; Kimura, E.; Shiro, M. *J. Am. Chem. Soc.* **1995**, *117*, 1210–1219 and references therein.
- (2) Karlin, K. D. *Science* **1993**, *261*, 701–708 and references therein.
- (3) (a) Coleman, J. E. In *Zinc Enzymes*; Birkauser: Boston, MA, 1986; Chapter 4, pp 49–58. (b) Coleman, J. E.; Gettins, P. In *Zinc Enzymes*; Birkauser: Boston, MA, 1986; Chapter 6, pp 77–96. (c) Vallee, B. L.; Auld, D. S. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 2715–2719.
- (4) (a) Wyckoff, H. W.; Handschumaker, M.; Murthy, H. M. K.; Sowadski, J. M. *Adv. Enzymol.* **1983**, *55*, 453. (b) Coleman, J. E. *Annu. Rev. Biophys. Biomol. Struct.* **1992**, *21*, 441–483.
- (5) (a) Hough, E.; Hansen, L. K.; Birknes, B.; Jynge, K.; Hansen, S.; Hardvik, A.; Little, C.; Dodson, E.; Derewenda, Z. *Nature* **1989**, *338*, 357–360. (b) Burley, S. K.; David, P. R.; Taylor, A.; Lipscomb, W. N. *Proc. Natl. Acad. Sci. U.S.A.* **1990**, *87*, 6878–6882.

- (6) (a) Koike, T.; Kimura, E. *J. Am. Chem. Soc.* **1991**, *113*, 8935–8941. (b) Koike, T.; Kimura, E.; Nakamura, I.; Hashimoto, Y.; Shiro, M. *J. Am. Chem. Soc.* **1992**, *114*, 7338–7345. (c) Kimura, E.; Nakamura, I.; Koike, T.; Shionoya, M.; Kodama, Y.; Ikeda, T.; Shiro, M. *J. Am. Chem. Soc.* **1994**, *116*, 4764–4771.
- (7) Chaudhuri, P.; Atockheim, C.; Wiegand, K.; Deck, W.; Gregorzic, R.; Vahrenkamp, H.; Nuber, B.; Weiss, J. *Inorg. Chem.* **1992**, *31*, 1451–1457.
- (8) Chin, J. *Acc. Chem. Res.* **1991**, *24*, 145–152 and references therein.
- (9) Lehn, J. M. *Pure Appl. Chem.* **1980**, *52*, 2441–2449.

Chart 1



Among macrocyclic molecules,<sup>10</sup> oxa-aza macrocycles have been widely studied in the last few years.<sup>11</sup> The macrocycle 1,4,7,13,16,19-hexaza-10,22-dioxacyclotetracosane (bisdien, Chart 1), containing two diethylene triamine units separated by two five-atom diethyl ether chains, is one of the most extensively studied binucleating macrocyclic receptors.<sup>12,13</sup> It can form both mono- and dinuclear complexes and the stability of its mono-nuclear species as well as its binucleating tendency have been nicely discussed by Martell and co-workers in terms of disposition of the donors, ligand flexibility, and metal ions' stereochemical requirements. Furthermore, its binuclear complexes have been shown to react with various molecules or ions and several assemblies containing two metal centers bridged by anionic species have been reported. In bisdien, the simplest example of bridge between two metal centers is the hydroxide ion, which forms bridging complexes with great facility.<sup>13</sup>

Furthermore, even without the involvement of metal cations, protonated species of this macrocycle are effective receptors for negative substrates and can also catalyze hydrolytic reactions and syntheses of nucleotides, such as ATP.<sup>14</sup>

In this context, it appeared of interest to develop this study with new macrocyclic receptors containing two polyamine subunits connected by two polyoxa bridges. In this paper we report on the synthesis of two new macrocyclic molecules, 1,4,7,16,19,22-hexaza-10,13,25,28-tetraoxacyclotriacosane (**L1**, Chart 1) and 1,4,7,16,19,22,25-heptaza-10,13,28,31-tetraoxacyclotriacosane (**L2**). The former contains two triamine units separated by two eight-atom dioxo bridge; the latter presents two different chelating units (a triamine and a tetraamine moieties) linked by the same eight-membered chains.

The present work tries to rationalize the relations between the coordination characteristics toward  $H^+$  (basicity),  $Cu^{2+}$ , and  $Zn^{2+}$  and the structural features of **L1** and **L2**, as a preliminary investigation on the reactivity of their dinuclear complexes toward neutral or anionic substrates.

### Experimental Section

**Synthesis of the Compounds.** *N,N',N''*-tris(*p*-tolylsulfonyl)diethylenetriamine (**1**, Scheme 1) and *N,N',N'',N'''*-tetrakis(*p*-tolylsulfonyl)-triethylenetetraamine (**5**) were prepared as already described.<sup>15,16</sup> 9,12,15-Tris(*p*-tolylsulfonyl)-9,12,15-triaza-3,6,18,21-tetraoxatricosane-1,23-diol (**3**) was obtained by following a modified procedure of the method reported by Mertes.<sup>17</sup> 2-[2-(2-Chloroethoxy)ethoxy]ethanol (**2**) was purchased from Aldrich. The 200.0 MHz  $^1H$  and 50.32 MHz  $^{13}C$  NMR spectra were recorded at 298 K on a Bruker AC-200 spectrometer. Peak positions are reported relative to TMS. ESI mass spectra have been recorded on a TSQ 700 Finnigan mat apparatus.

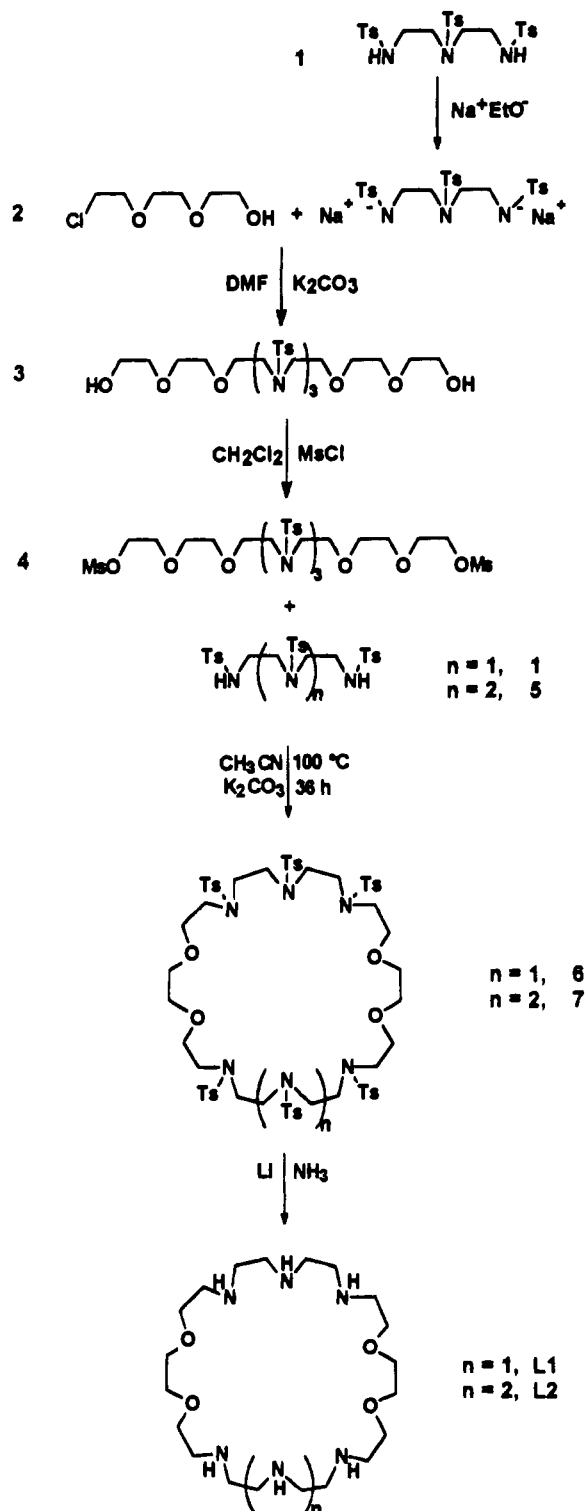
**9,12,15-Tris(*p*-tolylsulfonyl)-9,12,15-triaza-3,6,18,21-tetraoxatricosane-1,23-diol (**3**).** All reactions were carried out in a nitrogen atmosphere. A solution of sodium (1.24 g, 0.054 mol) in dry ethanol (50 cm<sup>3</sup>) was added to a solution of **1** (13.9 g, 0.025 mol) in dry ethanol (50 cm<sup>3</sup>). The resulting suspension was refluxed for *ca.* 30 min, and then the solvent was evaporated under reduced pressure. The solid residue was dissolved in dry DMF (80 cm<sup>3</sup>), and  $K_2CO_3$  (27.2 g, 0.2 mol) was added. To the resulting suspension, heated at 145 °C, was added 2-[2-(2-chloroethoxy)ethoxy]ethanol (**2**) (50 g, 0.3 mol), with stirring over a period of *ca.* 2 h. The reaction mixture was kept at 145 °C for a further 2 h. After being cooled at room temperature, the suspension was poured into ice-water and the precipitate was collected by suction and washed with water. The crude product was purified by chromatography on a neutral alumina column (70–230 mesh, activity I), eluting with chloroform. The eluted fractions were collected and evaporated to dryness to obtain **3** as a viscous oil. Yield: 17.8 g (87%).  $^{13}C$  NMR ( $CDCl_3$ ):  $\delta$  21.5, 49.2, 49.3, 49.6, 61.7, 70.0, 70.2, 70.3, 72.4, 127.8, 130.4, 136.1, 136.4 ppm. Anal. Calcd for  $C_{37}H_{55}N_3O_{12}S_3$ : C, 53.54; H, 6.68; N, 5.06. Found C, 53.1; H, 6.8; N, 5.0.

**1,23-Bis(methylsulfoxy)-9,12,15-tris(*p*-tolylsulfonyl)-9,12,15-triaza-3,6,18,21-tetraoxatricosane-1,23-diol (**4**).** A solution of **3** (17.8 g, 0.021 mol) and triethylamine (10.8 g, 0.11 mol) in 120 cm<sup>3</sup> of anhydrous methylene chloride was cooled at –20 °C. To this solution was added dropwise over a period of 2 h, with stirring, a solution of methanesulfonyl chloride (12.3 g, 0.11 mol) in 80 cm<sup>3</sup> of methylene chloride. The reaction mixture was kept at –10 °C for 30 min and then was allowed to warm up to room temperature. The resulting suspension was washed twice with a 0.1 mol dm<sup>–3</sup> NaOH aqueous solution and then with water. The organic phase was dried over  $Na_2SO_4$  and evaporated to dryness to obtain **4** as a yellowish oil. Yield: 17.1 g (81%).  $^{13}C$  NMR ( $CDCl_3$ ):  $\delta$  22.1, 38.2, 49.6, 49.8, 50.1, 69.5, 69.9, 70.4, 70.8, 71.0, 127.8, 130.4, 136.1, 136.4, 144.2 ppm. Anal.

- (10) (a) Lehn, J. M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89–112. (b) Lindoy L. F., Ed.; *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge Univ. Press: Cambridge, England, 1989. (c) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1991**, *91*, 1721–2085.
- (11) (a) Gokel, G. W. *Crown Ethers and Cryptands*; Monographs in Supramolecular Chemistry, Stoddart J. F., Ed.; The Royal Society of Chemistry: Cambridge, England, 1992. (b) Bradshaw, J. S. *Aza-crown Macrocycles*; Wiley: New York, 1993. (c) Guerriero, P.; Tamburini, S.; Vigato, P. A. *Coord. Chem. Rev.* **1995**, *110*, 17–243.
- (12) (a) Coughlin, P. K.; Dewan, J. C.; Lippard, S. J.; Watanabe, E.; Lehn, J. M. *J. Am. Chem. Soc.* **1979**, *101*, 265–266. (b) Coughlin, P. K.; Lippard, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3228–3229.
- (13) (a) Motekaitis, R. J.; Martell, A. E.; Lecomte, J. P.; Lehn, J. M. *Inorg. Chem.* **1983**, *22*, 609–614. (b) Comarmond, J.; Dietrich, B.; Lehn, J. M.; Louis, R. *J. Chem. Soc., Chem. Commun.* **1985**, 74–76. (c) Motekaitis, R. J.; Martell, A. E. *J. Chem. Soc., Chem. Commun.* **1988**, 915–916. (d) Motekaitis, R. J.; Martell, A. E. *J. Am. Chem. Soc.* **1988**, *110*, 8059–8064. (e) Motekaitis, R. J.; Martell, A. E.; Murase, I.; Lehn, J. M.; Hosseini, M. H. *Inorg. Chem.* **1988**, *27*, 3630–3636. (f) Motekaitis, R. J.; Martell, A. E. *Inorg. Chem.* **1991**, *30*, 694–700. (g) Motekaitis, R. J.; Martell, A. E. *Inorg. Chem.* **1992**, *31*, 5534–5542. (h) Motekaitis, R. J.; Martell, A. E. *Inorg. Chem.* **1994**, *33*, 1032–1037 and references therein.
- (14) (a) Hosseini, M. W.; Lehn, J. M.; Mertes, M. P. *Helv. Chim. Acta* **1983**, *66*, 2454–2466. (b) Hosseini, M. W.; Lehn, J. M.; Maggiora, L.; Mertes, M. P.; Mertes, K. B. *J. Am. Chem. Soc.* **1985**, *107*, 909–916. (c) Hosseini, M. W.; Lehn, J. M.; Maggiora, L.; Mertes, M. P.;

- Mertes, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 537–544. (d) Hosseini, M. W.; Lehn, J. M.; Jones, K. C.; Plute, K. E.; Mertes, M. P.; Mertes, K. B. *J. Am. Chem. Soc.* **1989**, *109*, 6330–6335. (e) Hosseini, M. W.; Blacker, A. J.; Lehn, J. M. *J. Am. Chem. Soc.* **1990**, *110*, 3896–3904. (f) Mertes, M. P.; Mertes, K. B. *Acc. Chem. Res.* **1990**, *23*, 413–418 and references therein.
- (15) Richman, J. E.; Atkins, T. J. *J. Am. Chem. Soc.* **1974**, *96*, 2268–2270.
- (16) Bencini, A.; Bianchi, A.; Garcia-Espana, E.; Giusti, M.; Micheloni, M.; Paoletti, P. *Inorg. Chem.* **1987**, *26*, 681–684.
- (17) Qian, L.; Sun, Z.; Mertes, M. P.; Mertes, K. B. *J. Org. Chem.* **1991**, *56*, 4904–4907.

Scheme 1



Calcd for  $C_{39}H_{59}N_3O_{16}S_6$ : C, 53.55; H, 6.68; N, 5.06. Found C, 53.1; H, 6.8; N, 5.0.

**1,4,7,16,19,22-Hexakis(*p*-tolylsulfonyl)-1,4,7,16,19,22-hexaza-10,13,25,28-tetraoxacyclotriacontane (6).** To a refluxing suspension of **1** (8.6 g, 0.015 mol) and of  $K_2CO_3$  (21 g, 0.15 mol) in 150 cm<sup>3</sup> of acetonitrile, was added, over a period of ca. 6 h, a solution of **4** (15 g, 0.015 mol) in 100 cm<sup>3</sup> of acetonitrile. The reaction mixture was maintained at reflux for 2 h. After the reaction mixture was cooled to room temperature, the resulting suspension was filtered and evaporated under reduced pressure to give a yellowish oil, which was dissolved in the minimum quantity of  $CH_2Cl_2$  and chromatographed on neutral alumina (70–230 mesh, activity I), with an eluent of  $CH_2Cl_2$ –ethyl acetate (100:5). The eluted fractions were collected and evaporated to

dryness to obtain a colorless solid. (4.5 g, 22%). Mp 71–72 °C. <sup>13</sup>C NMR ( $CDCl_3$ ):  $\delta$  21.5, 48.9, 49.0, 49.6, 70.0, 70.2, 127.3, 127.5, 129.8, 135.6, 136.0, 143.4, 143.5 ppm. Anal. Calcd for  $C_{62}H_{82}N_6O_{16}S_6$ : C, 54.77; H, 6.08; N, 6.18. Found C, 54.5; H, 6.0; N, 6.1.

**1,4,7,16,19,22-Hexaza-10,13,25,28-tetraoxacyclotriacontane (L1).** On a suspension of **6** (4 g, 0.0029 mol) in diethyl ether (30 cm<sup>3</sup>) and methanol (1 cm<sup>3</sup>) cooled at –70 °C, ammonia (300 cm<sup>3</sup>) was condensed. When small bits of lithium were added (ca. 10 mg each piece), the reaction mixture became blue. The addition was continued until the suspension kept the blue color for at least 3 min.  $NH_4Cl$  (12 g, 0.2 mol) was added in small portions, and the reaction mixture was allowed to stand up to room temperature. Evaporation of ammonia gave a white solid residue, which was treated with 3 mol dm<sup>3</sup> HCl (300 cm<sup>3</sup>). The resulting suspension was washed with chloroform (3 × 100 cm<sup>3</sup>) and the aqueous layer filtered and evaporated to dryness under reduced pressure to give a white solid. This product was dissolved in the minimum amount of water and the resulting solution was made alkaline with concentrated NaOH. This solution was extracted with  $CHCl_3$  (6 × 100 cm<sup>3</sup>). The organic layer was dried over anhydrous  $Na_2SO_4$  and evaporated under reduced pressure, affording the macrocycle **L1** as a colorless oil. (0.5 g, 39%). <sup>1</sup>H NMR ( $CDCl_3$ ):  $\delta$  3.11 (8H, t), 3.33 (8H, t), 3.43 (8H, t), 3.83 (8H, s), 3.90 (8H, t) ppm; <sup>13</sup>C NMR:  $\delta$  44.9, 47.3, 48.0, 66.1, 70.5 ppm. Anal. Calcd for  $C_{20}H_{46}N_6O_4$ : C, 55.27; H, 10.67; N, 19.34. Found C, 55.0; H, 10.8; N, 19.1.

**L1·4.5HClO<sub>4</sub>.** The perchlorate salt was obtained in a quantitative yield by adding 70%  $HClO_4$  to an ethanolic solution containing the free amine. The white solid formed was filtered off and washed with ethanol. Anal. Calcd for  $C_{20}H_{50.5}N_6O_{22}Cl_{4.5}$ : C, 27.09; H, 5.74; N, 9.48. Found C, 27.0; H, 5.8; N, 9.1. MS (ESI) ( $m/z$ ): 218 [ $m + 2/2$ ], 435 [ $m + H^+$ ], 535 ( $m + HClO_4$ ), 635 ( $m + 2HClO_4$ ), 735 ( $m + 3HClO_4$ ).

*Caution!* Perchlorate salts of organic ligands are potentially explosive; these compounds must be handled with great caution.

**1,4,7,16,19,22,25-Heptakis(*p*-tolylsulfonyl)-1,4,7,16,19,22,25-heptaza-10,13,28,31-tetraoxacyclotritriacontane (7).** This compound was synthesized from **5** (13.6 g, 0.018 mol) and **4** (17.5 g, 0.018 mol) by following the procedure reported for **6**. Yield: 3.7 g (13.4%). Anal. Calcd for  $C_{71}H_{93}N_7O_{18}S_7$ : C, 54.77; H, 6.02; N, 6.30. Found C, 54.3; H, 5.9; N, 6.2.

**1,4,7,16,19,22,25-Heptaza-10,13,28,31-tetraoxacyclotritriacontane (L2).** This macrocycle was obtained from **7** (3.7 g, 0.0024 mol) as described for **L1**. Yield: 0.45 g (20%). <sup>1</sup>H NMR ( $CDCl_3$ ):  $\delta$  3.12 (4H, t), 3.23 (4H, s), 3.35 (8H, t), 3.46 (12H, m), 3.88 (8H, s) 3.95 (8H, t) ppm; <sup>13</sup>C NMR:  $\delta$  44.6, 45.0, 46.0, 47.6, 48.0, 48.3, 66.2, 66.3, 70.6 86.1 ppm. Anal. Calcd for  $C_{22}H_{51}N_7O_4$ : C, 55.31; H, 10.76; N, 20.52. Found C, 54.9; H, 10.9; N, 20.3.

**L2·5HClO<sub>4</sub>.** The pentaperchlorate salt was obtained in a quantitative yield by adding 70%  $HClO_4$  to an ethanolic solution containing the free amine. The white solid formed was filtered off and washed with ethanol. Anal. Calcd for  $C_{22}H_{56}N_7O_{24}Cl_5$ : C, 26.96; H, 5.76; N, 10.00. Found C, 27.1; H, 5.8; N, 9.9. MS (ESI) ( $m/z$ ): 483 ( $m + H^+$ ), 583 ( $m + HClO_4$ ), 683 ( $m + 2HClO_4$ ), 783 ( $m + 3HClO_4$ ).

**Synthesis of the Complexes.** [ $Zn_2L1(\mu-OH)(ClO_4)_3 \cdot 0.5EtOH$ ]. A solution of  $Zn(ClO_4)_2 \cdot 6H_2O$  (20.6 mg, 0.054 mmol) in ethanol (5 cm<sup>3</sup>) was added to a methanolic solution (5 cm<sup>3</sup>) of **L1** (12.0 mg, 0.027 mmol). To the resulting solution was added butanol (10 cm<sup>3</sup>). Crystals of the complex suitable for X-ray analysis were obtained by slow evaporation at room temperature of this solution. Yield: 18 mg (73%). Anal. Calcd for  $C_{21}H_{50}N_6O_{13.5}Cl_3Zn_2$ : C, 27.57; H, 5.54; N, 9.24. Found C, 27.7; H, 5.6; N, 9.2.

[ $Cu_2L1(NCS)_4$ ]. A solution of  $Cu(ClO_4)_2 \cdot 6H_2O$  (37.2 mg, 0.1 mmol) in methanol (10 cm<sup>3</sup>) was added to a methanolic solution (10 cm<sup>3</sup>) of **L1** (21.7 mg, 0.05 mmol). To the resulting blue solution were added KSCN (19.4 mg, 0.2 mmol) and butanol (10 cm<sup>3</sup>). Blue crystals of the complex suitable for X-ray analysis were obtained by slow evaporation at room temperature of this solution. Yield: 32 mg (78%). Anal. Calcd for  $C_{24}H_{46}N_{10}O_4S_4Cu_2$ : C, 35.02; H, 5.63; N, 17.00. Found C, 34.9; H, 5.6; N, 16.9.

[ $Cu_2L1(NCS)_4 \cdot Na_2S_2$ ]. A solution of  $Cu(ClO_4)_2 \cdot 6H_2O$  (37.2 mg, 0.1 mmol) in methanol (10 cm<sup>3</sup>) was added to a methanolic solution (10 cm<sup>3</sup>) of **L1** (21.7 mg, 0.05 mmol). To the resulting blue solution were added NaSCN (16.1 mg, 0.2 mmol) and butanol (10 cm<sup>3</sup>). Blue crystals

**Table 1.** Crystal Data and Structure Refinement Data for  $[\text{Zn}_2\text{L1}(\mu\text{-OH})](\text{ClO}_4)_3 \cdot 0.5\text{EtOH}$  (a),  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (b), and  $[\text{Cu}_2\text{L1}(\text{NCS})_4] \cdot \text{Na}_2\text{S}_2$  c

	a	b	c
empirical formula	$\text{C}_{21}\text{H}_{50}\text{Cl}_3\text{N}_6$	$\text{C}_{24}\text{H}_{46}\text{Cu}_2$	$\text{C}_{24}\text{H}_{46}\text{Cu}_2\text{N}_{10}$
fw	903.76	794.03	904.12
temp, K	298	298	298
wavelength, Å	0.71069	0.71069	0.71069
cryst syst	orthorhombic	monoclinic	monoclinic
space group	<i>Pbca</i>	<i>P2<sub>1</sub>/a</i>	<i>P2<sub>1</sub>/a</i>
a, Å	14.289(4)	8.550(6)	8.492(3)
b, Å	15.617(6)	17.854(6)	17.740(4)
c, Å	33.862(8)	12.090(3)	13.016(3)
$\beta$ , deg		102.23(4)	94.54(3)
V, Å <sup>3</sup>	7556(4)	1804(2)	1954.7(9)
Z	8	2	2
$D_c$ , Mg/m <sup>3</sup>	1.589	1.462	1.536
$\mu$ , mm <sup>-1</sup>	1.558	1.455	1.475
$R[I > 2\sigma(I)]^a$	0.0612	0.0520	0.1101
wR <sup>2</sup> <sup>b</sup>	0.1780	0.1618	0.3105
a, b	0.1190, 0	0.0835, 0	0.0617, 60.73

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

of the complex suitable for X-ray analysis were obtained by slow evaporation at room temperature of this solution. The resolution of the crystal structure of this compound revealed the presence of the  $\text{S}_2^{2-}$  anion. Yield: 9 mg (10%). Anal. Calcd for  $\text{C}_{24}\text{H}_{46}\text{N}_{10}\text{O}_4\text{S}_6\text{Na}_2\text{Cu}_2$ : C, 30.88; H, 4.97; N, 14.50. Found C, 30.7; H, 5.0; N, 14.4.

Subsequent elemental analysis on NaSCN used revealed that it contained  $\text{Na}_2\text{S}_2$  (about 3%).

**X-ray Structure Analysis.** Analyses on single crystals of  $[\text{Zn}_2\text{L1}(\mu\text{-OH})](\text{ClO}_4)_3 \cdot 0.5\text{EtOH}$  (a),  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (b) and  $[\text{Cu}_2\text{L1}(\text{NCS})_4] \cdot \text{Na}_2\text{S}_2$  (c) were carried out with an Enraf-Nonius CAD4 X-ray diffractometer that uses an equatorial geometry; a summary of crystal data is reported in Table 1.

A prismatic colorless crystal of a and blue parallelepiped-shaped crystals of b and c (approximated dimensions  $0.2 \times 0.4 \times 0.5$  mm,  $0.3 \times 0.3 \times 0.6$  mm and  $0.2 \times 0.2 \times 0.3$  mm for a, b, and c, respectively) were mounted on the diffractometer and used for data collections at room temperature with graphite-monochromated Mo K $\alpha$  radiation. Cell parameters were determined by least-squares refinement of diffractometer setting angles for 25 carefully centered reflections. Intensities of two standard reflections per compound were monitored during data collections: no loss of intensity was recognized.

A total of 3595 ( $2\theta_{\text{max}} = 44^\circ$ ), 3970 ( $2\theta_{\text{max}} = 50^\circ$ ) and 2508 ( $2\theta_{\text{max}} = 44^\circ$ ) reflections were collected for a, b, and c, respectively. Intensity data were corrected for Lorentz and polarization effects; absorption corrections were applied, once the structures were solved, by the Walker and Stuart method.<sup>18</sup>

The structures were solved by the Patterson method which showed the heavy atom positions in all structures. Subsequent Fourier maps showed all non-hydrogen atoms. Refinements were performed by means of the full-matrix least-squares technique. The function minimized was  $\sum w(F_o^2 - F_c^2)^2$  with  $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]^2$  and  $P = (F_o^2 + 2F_c^2)/3$ , where a and b are adjustable parameters (their final values are reported in Table 1).

All calculations, carried out on a DEX 486-DX computer, were performed with the SHELX-76<sup>19</sup> and the SHELXL-93<sup>20</sup> programs which use the analytical approximation for the atomic scattering factors and anomalous dispersion corrections for all atoms from ref 21.

**$[\text{Zn}_2\text{L1}(\mu\text{-OH})](\text{ClO}_4)_3 \cdot 0.5\text{EtOH}$  (a).** The compound crystallizes in the orthorhombic family, space group *Pbca* ( $Z = 8$ ).

Three peaks in the electron density map were found near the inversion center. They were attributed to a disordered ethanol molecule and introduced as carbon atoms with fixed population parameters 0.5.

**Table 2.** Atomic Coordinates ( $\times 10^4$ ) and Equivalent Isotropic Displacement Parameters ( $\text{Å}^2 \times 10^3$ ) for  $[\text{Zn}_2\text{L1}(\mu\text{-OH})](\text{ClO}_4)_3 \cdot 0.5\text{EtOH}$  (a)

atom	x/a	y/b	z/c	U(eq)
Zn1	-488(1)	1365(1)	3623(1)	55(1)
Zn2	885(1)	-466(1)	3839(1)	59(1)
C11	890(2)	737(2)	1488(1)	82(1)
O11	1419(7)	1459(6)	1417(4)	156(5)
O12	1431(8)	141(7)	1684(4)	155(5)
O13	92(7)	900(9)	1682(5)	187(6)
O14	642(15)	394(11)	1140(4)	252(10)
C12	1937(2)	3361(2)	2784(1)	71(1)
O21	1465(7)	2730(5)	2561(3)	105(3)
O22	2771(9)	3586(8)	2635(4)	172(6)
O23	1353(10)	4104(7)	2817(4)	179(6)
O24	2022(6)	3091(6)	3180(3)	110(3)
C13	1276(3)	1682(3)	4813(1)	99(1)
O31	1483(13)	2003(10)	5157(4)	247(9)
O32	474(14)	1231(23)	4814(6)	244(13)
O33	1098(18)	2142(15)	4503(7)	224(12)
O34	2014(21)	1528(21)	4613(13)	279(20)
O35	1602(41)	816(16)	4805(9)	331(23)
O1	371(5)	655(4)	3898(2)	53(2)
N1	907(6)	-1449(5)	3446(3)	66(3)
C1	1042(10)	-2246(8)	3672(4)	95(4)
C2	547(11)	-2242(9)	4065(5)	109(5)
N2	641(7)	-1436(7)	4273(3)	91(3)
C3	1418(15)	-1372(11)	4553(5)	141(7)
C4	2265(14)	-1114(12)	4400(6)	157(8)
N3	2178(7)	-387(6)	4149(3)	76(3)
C5	2973(9)	-312(9)	3890(4)	90(4)
C6	2840(8)	400(9)	3592(4)	91(4)
O2	2044(5)	205(4)	3366(2)	67(2)
C7	1864(8)	867(8)	3081(4)	80(4)
C8	1125(8)	650(8)	2802(3)	78(4)
O3	228(5)	669(5)	2988(2)	68(2)
C9	-506(9)	642(9)	2701(4)	93(4)
C10	-1416(9)	612(9)	2927(4)	89(4)
N4	-1531(6)	1293(6)	3227(3)	67(3)
C11	-1659(9)	2173(8)	3062(4)	93(4)
C12	-729(9)	2629(9)	3008(5)	107(5)
N5	-71(7)	2508(5)	3328(3)	75(3)
C13	-50(11)	3187(9)	3647(6)	120(6)
C14	-805(11)	3133(9)	3915(5)	114(5)
N6	-917(7)	2249(6)	4077(3)	77(3)
C15	-1867(9)	2081(8)	4222(4)	92(4)
C16	-1922(10)	1199(10)	4366(4)	108(5)
O4	-1757(5)	623(5)	4054(2)	66(2)
C17	-1729(9)	-230(8)	4190(4)	91(4)
C18	-1712(8)	-845(8)	3864(4)	85(4)
O5	-856(5)	-832(4)	3650(2)	66(2)
C19	-809(8)	-1498(8)	3353(4)	82(4)
C20	122(9)	-1473(7)	3167(4)	80(4)
C21	590(36)	-224(43)	71(15)	187(18)
C23	693(28)	-977(28)	-126(12)	157(14)
C22	182(47)	540(36)	-10(16)	198(20)
H1	628(52)	868(50)	4077(24)	22(27)

High degree of disorder affects a perchlorate anion: the best model found consists of five oxygen atoms around the C13 atom with population parameters normalized to four (population parameter 1 for O31 and 0.75 for the remaining oxygen atoms).

Anisotropic displacement parameters were used with all non-hydrogen atoms except the carbon atoms of the solvent molecule (C21, C22, and C23). The significantly high displacement parameters found for the C3, C4, C13, and C14 carbon atoms are probably due to poorly solved double positions.

The hydrogen atoms belonging to the ligand were introduced in calculated positions with an overall temperature factor  $U = 0.113(7)$  Å<sup>2</sup>. The H1 atom of the hydroxo ion was localized in the  $\Delta f$  map, introduced in the calculation and isotropically refined. The final agreement factors for 459 refined parameters, corresponding to the atomic coordinates listed in Table 2, were  $R = 0.0612$  (for 2329 observed reflections with  $I > 2\sigma(I)$ ) and  $wR^2 = 0.1780$ .

**$[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (b).** Crystals of the compound belong to the

(18) Walker, N.; Stuart, D. D. *Acta Crystallogr., Sect. A* **1983**, *39*, 158-166.

(19) Sheldrick, G. M. SHELX-76, Program for Crystal Structure Determination. University of Cambridge Cambridge, England, 1976.

(20) Sheldrick, G. M. SHELXL-93. University of Göttingen, 1993.

(21) *International Tables for X-ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. IV.

**Table 3.** Atomic Coordinates ( $\times 10^4$ ) and Equivalent Isotropic Displacement Parameters ( $\text{\AA}^2 \times 10^3$ ) for  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (b)

atom	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>	<i>U</i> (eq)
Cu	5239(1)	-97(1)	2488(1)	45(1)
N1	6808(6)	-949(3)	2923(4)	31(1)
C1	8060(8)	-888(4)	2245(6)	62(2)
C2	8415(7)	-78(4)	2105(5)	59(2)
N2	6881(6)	310(3)	1683(4)	48(1)
C3	6865(8)	1135(4)	1823(5)	55(2)
C4	5156(8)	1367(4)	1521(6)	57(2)
N3	4257(6)	957(3)	2227(4)	50(1)
C5	2491(8)	978(4)	1797(7)	67(2)
C6	1809(8)	1741(4)	1760(6)	67(2)
O1	2067(5)	2090(2)	2834(4)	56(1)
C7	858(8)	1921(4)	3454(6)	65(2)
C8	1166(8)	2325(4)	4538(6)	62(2)
O2	2481(5)	1966(2)	5273(4)	59(1)
C9	2798(9)	2260(4)	6400(6)	64(2)
C10	3901(8)	1701(4)	7086(5)	56(2)
N4	3712(7)	-616(3)	917(4)	60(2)
C11	2734(9)	-1070(4)	891(5)	59(2)
S1	1396(3)	-1701(2)	835(2)	121(1)
N5	3970(7)	-349(3)	3579(5)	61(2)
C12	3107(7)	-443(3)	4181(5)	45(1)
S2	1854(3)	-562(1)	4978(2)	88(1)

**Table 4.** Atomic Coordinates ( $\times 10^4$ ) and Equivalent Isotropic Displacement Parameters ( $\text{\AA}^2 \times 10^3$ ) for  $[\text{Cu}_2\text{L1}(\text{NCS})_4]\cdot\text{Na}_2\text{S}_2$  (c)

atom	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>	<i>U</i> (eq)
Cu	6015(3)	-243(2)	2720(2)	49(1)
Na	5950(9)	-3095(4)	692(5)	38(2)
S3	5323(14)	-4394(8)	246(7)	163(5)
N1	5136(25)	-906(14)	1327(16)	72(6)
C1	4548(38)	-1480(15)	1151(20)	79(9)
S1	3672(11)	-2295(4)	854(7)	104(3)
N2	4254(24)	-376(11)	3598(15)	64(6)
C2	3421(27)	-451(12)	4199(16)	45(6)
S2	2144(8)	-576(4)	5064(5)	76(2)
N3	5202(21)	805(10)	2237(13)	52(5)
C3	6390(28)	1135(13)	1590(17)	56(6)
C4	7970(31)	896(12)	2050(17)	65(8)
N4	8028(18)	69(10)	2135(13)	48(5)
C5	9336(27)	-294(16)	2769(21)	75(8)
C6	8928(26)	-1073(13)	2994(19)	59(7)
N5	7360(20)	-1054(10)	3465(13)	51(5)
C7	6646(33)	-1817(16)	3536(22)	91(10)
C8	7478(28)	-2285(15)	4314(21)	72(8)
O1	7443(20)	-1951(9)	5273(14)	71(5)
C9	8441(30)	-2287(18)	6049(21)	84(9)
C10	8397(32)	-1926(16)	6996(22)	83(9)
O2	7017(20)	-2016(9)	7487(14)	70(5)
C11	6974(29)	-1638(16)	8452(17)	74(9)
C12	6347(33)	-792(15)	8346(18)	75(8)

monoclinic family, space group  $P2_1/a$ . The molecule lies around a crystallographic inversion center ( $Z = 2$ ).

All non-hydrogen atoms were anisotropically refined, while the hydrogen atoms were introduced in calculated positions with an overall thermal parameter  $U = 0.056(4) \text{\AA}^2$ . The final agreement factors for 200 refined parameters, corresponding to the atomic coordinates listed in Table 3, were  $R = 0.052$  (for 1611 observed reflections with  $I > 2\sigma(I)$ ) and  $wR^2 = 0.1618$ .

$[\text{Cu}_2\text{L1}(\text{NCS})_4]\cdot\text{Na}_2\text{S}_2$  (c). Crystals of the compound belong to the monoclinic family, space group  $P2_1/a$ . Both complex macrocycle and disulfur anion lie around crystallographic inversion centers ( $Z = 2$ ).

All non-hydrogen atoms were anisotropically refined, while the hydrogen atoms were introduced in calculated positions with an overall thermal parameter  $U = 0.093(17) \text{\AA}^2$ . The high value of the displacement parameter of the sulfur atom in the disulfide ion could be due to positional disorder. The final agreement factors for 218 refined parameters, corresponding to the atomic coordinates listed in Table 4, were  $R = 0.1101$  (for 1095 observed reflections with  $I > 2\sigma(I)$ ) and  $wR^2 = 0.3105$ . The remarkably high values of the agreement factors are not unexpected in view of the poor quality data and the disorder shown by the sulfur atom belonging to the disulfur anion.

**Emf Measurements.** All potentiometric measurements were carried out in  $0.15 \text{ mol dm}^{-3}$  NaCl at  $298.1 \pm 0.1 \text{ K}$ , in the pH range 2.5–10, by using the equipment that has been already described.<sup>22</sup> 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  $\text{CO}_2$ -free NaOH solutions and determining the equivalent point by the Gran method<sup>23</sup> which allows one to determine the standard potential  $E^\circ$ , and the ionic product of water ( $pK_w = 13.73$  in  $0.15 \text{ mol dm}^{-3}$  NaCl at  $298.1 \pm 0.1 \text{ K}$ ). At least three measurements were performed for each system (100 data points each measurements). 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. The computer program SUPERQUAD<sup>24</sup> was used to calculate both protonation and stability constants from emf data. The titration curves for each system were treated either as a single set or as separated entities without significant variations in the values of the stability constants. Finally all the measurements for both protonation and complexation were merged together, and the equilibrium constants for protonated and complexed species were simultaneously refined to give the final values.

## Results and Discussion

**Synthesis.** The diol **3** was obtained in good yields by reaction of **1**<sup>15</sup> with 2-[2-(2-chloroethoxy)ethoxy]ethanol (**2**) by using drastic conditions (DMF,  $145 \text{ }^\circ\text{C}$ , large excess of base). Milder conditions leads to **3** in small yields. The methylsulfonyl derivative **4** was obtained by using standard methods.<sup>15,16,17</sup> Reaction of **4** with compounds **1** and **5** in  $\text{CH}_3\text{CN}$  in the presence of  $\text{K}_2\text{CO}_3$ , a modification of the method of Richman and Atkins,<sup>15</sup> affords the tosylated macrocycles **6** and **7**, respectively. **4**, which contains a triaza moiety, is a versatile precursor for oxa-aza macrocyclic receptors. In fact, the same synthetic procedure can produce other macrocyclic molecules containing a triaza moiety by substitutions of **1** or **5** in the cyclization, thus originating macrocycles characterized by two oxa bridges that link two different binding moieties. Finally, the removal of the protecting tosyl groups was carried out by employing Li in liquid  $\text{NH}_3$ <sup>25</sup> as the cleavage of ether linkages could take place by using alternative acidic detosylation methods.<sup>15</sup>

Binuclear Cu(II) and Zn(II) complexes of **L1** can be obtained in solution by adding  $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  or  $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  to a solution of the ligand, with 1:2 ligand to metal molar ratio. In the case of Zn(II), solid  $[\text{Zn}_2\text{L1}(\mu\text{-OH})](\text{ClO}_4)_3 \cdot 0.5\text{EtOH}$  (a) was isolated from an ethanol/butanol solution. The binuclear Cu(II) complex can react with  $\text{SCN}^-$ , forming the  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (b) compound, which was isolated as a crystalline solid. This behavior is indicative of the tendency of these binuclear complexes to coordinate further species from the medium and can be ascribed to the unsaturated coordination sphere of the metal in the  $[\text{M}_2\text{L1}]^{4+}$  complexes (*vide infra*). Finally, in the synthesis of the Cu(II) complex, by using NaSCN containing  $\text{Na}_2\text{S}_2$  as an impurity, the  $[\text{Cu}_2\text{L1}(\text{NCS})_4]\cdot\text{Na}_2\text{S}_2$  (c) compound was isolated.

**Description of the Structures.**  $[\text{Zn}_2\text{L1}(\mu\text{-OH})](\text{ClO}_4)_3 \cdot 0.5\text{EtOH}$  (a). The crystal structure consists of  $[\text{Zn}_2\text{L1}(\mu\text{-OH})]^{3+}$  complex cations, perchlorate anions and disordered ethanol molecules. An ORTEP<sup>26</sup> drawing of the  $[\text{Zn}_2\text{L1}(\mu\text{-$

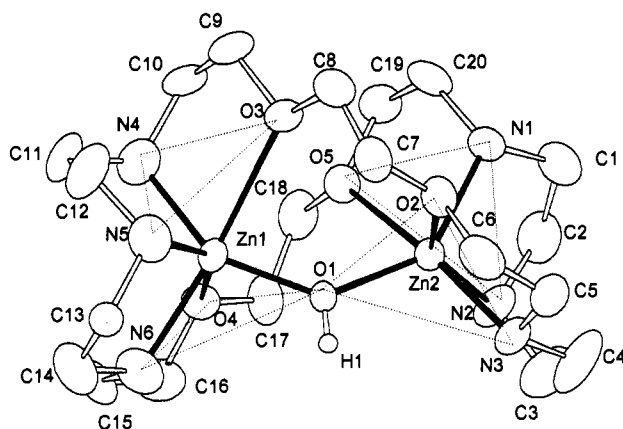
(22) Bianchi, A.; Bologni, L.; Dapporto, P.; Micheloni, M.; Paoletti, P. *Inorg. Chem.* **1984**, *23*, 1201–1205.

(23) (a) Gran, G. *Analyst (London)*, **1952**, *77*, 661–663. (b) Rossotti, F. J.; Rossotti, H. *J. Chem. Educ.* **1965**, *42*, 375–378.

(24) Gans, P.; Sabatini, A.; Vacca, A. *J. Chem. Soc., Dalton Trans.* **1985**, 1195–1200.

(25) Lehn, J. M.; Montavon, F. *Helv. Chim. Acta* **1976**, *59*, 1566–1582.

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



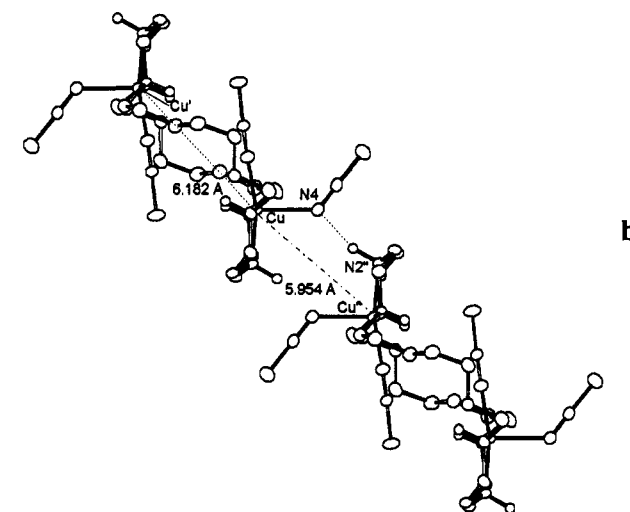
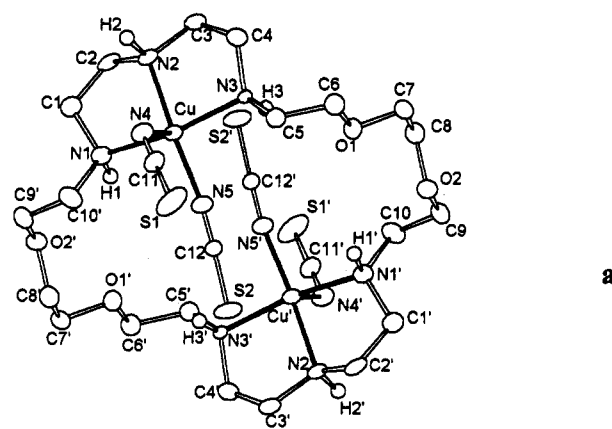
**Figure 1.** ORTEP drawing of the  $[\text{Zn}_2\text{L1}(\mu\text{-OH})]^{3+}$  cation. The dashed lines evidence the basal faces of the trigonal prismatic coordination geometries of the metal cations

**Table 5.** Selected Bond Lengths (Å) and Angles (deg) for  $[\text{Zn}_2\text{L1}(\mu\text{-OH})](\text{ClO}_4)_3 \cdot 0.5\text{EtOH}$  (a)

Zn1—O3	2.617(7)	Zn2—O2	2.531(7)
Zn1—O4	2.600(7)	Zn2—O5	2.631(7)
Zn1—O1	1.898(7)	Zn2—O1	1.908(7)
Zn1—N4	2.007(9)	Zn2—N1	2.033(9)
Zn1—N5	2.130(9)	Zn2—N2	2.14(1)
Zn1—N6	2.156(9)	Zn2—N3	2.128(9)
N6—Zn1—O4	71.8(3)	O2—Zn2—O5	123.6(2)
N5—Zn1—O4	146.2(2)	N3—Zn2—O5	162.4(3)
N4—Zn1—O4	80.3(3)	N3—Zn2—O2	73.7(3)
O3—Zn1—O4	123.3(2)	N2—Zn2—O5	81.9(3)
O3—Zn1—N6	164.3(3)	N2—Zn2—O2	146.6(3)
O3—Zn1—N5	81.6(3)	N1—Zn2—O5	72.0(3)
O3—Zn1—N4	73.7(3)	N1—Zn2—O2	83.5(3)
O1—Zn1—O4	85.1(3)	O1—Zn2—O5	82.0(3)
O1—Zn1—O3	84.8(3)	O1—Zn2—O2	86.5(3)
O1—Zn1—N4	140.8(3)	O1—Zn2—N1	140.1(3)
O1—Zn1—N5	122.6(3)	O1—Zn2—N2	121.0(4)
N4—Zn1—N5	86.6(4)	N1—Zn2—N2	85.3(4)
O1—Zn1—N6	102.0(3)	O1—Zn2—N3	103.3(3)
N4—Zn1—N6	107.5(4)	N1—Zn2—N3	110.7(4)
N5—Zn1—N6	82.9(3)	N2—Zn2—N3	81.0(4)

$\text{OH})]^{3+}$  cation is reported in Figure 1. Selected bond lengths and angles are reported in Table 5.

The two metal centers, 3.543(2) Å apart from each other, are linked by a hydroxide ion (Zn1—O1—Zn2 137.1(5)°) and show analogous coordination environments. The bond distances and angular values are in the range usually found in other  $\text{Zn}_2(\mu\text{-OH})$  bridges.<sup>7,27,28</sup> Zn1 is coordinated by N4, N5, N6, and O1. Further weak interactions between the Zn1 atom and the ethereal oxygens O3 and O4 are observed (Zn1—O3 2.617(7) Å and Zn1—O4 2.600(7) Å). The coordination geometry results in a distorted trigonal prism with the basal faces determined by O3, N4, N5 and by O1, O4, N6. Analogously, the coordination environment of the Zn2 is trigonal prismatic, determined by O1, N1, N2, N3 and by the remaining O2, O5 ethereal oxygen atoms (Zn2—O2 = 2.531(7) Å and Zn2—O5 = 2.631(7) Å). The basal faces are described by O5, N1, N2 and O1, O2, N3. The resulting overall conformation of the ligand is screw-shaped. A weak hydrogen bond network involves some oxygen atoms belonging to the perchlorate anions and the H1, H3, H4, H5, and H6 atoms (H1···O32 2.57(9) Å, H1···O33 2.55(8) Å,



**Figure 2.** ORTEP drawings of the  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  complex: (a) top view; (b) side view showing the intermolecular hydrogen bonding and the intramolecular and intermolecular  $\text{Cu}\cdots\text{Cu}$  distances.  $\text{Cu}\cdots\text{Cu}\cdots\text{Cu}''$  angle = 170.01(2)°. The primed atoms are related by the following symmetry transformation:  $1 - x, -y, 1 - z$ .

**Table 6.** Selected Bond Lengths (Å) and Angles (deg) for  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (b)

Cu—N5	1.930(5)	Cu—N3	2.057(5)
Cu—N2	2.007(5)	Cu—N4	2.264(6)
Cu—N1	2.023(5)		
N5—Cu—N2	165.6(2)	N1—Cu—N3	162.6(2)
N5—Cu—N1	94.9(2)	N5—Cu—N4	99.8(2)
N2—Cu—N1	84.5(2)	N2—Cu—N4	94.5(2)
N5—Cu—N3	92.7(2)	N1—Cu—N4	98.2(2)
N2—Cu—N3	84.2(2)	N3—Cu—N4	95.8(2)

H3···O34 2.49(4) Å, H3···O35 2.19(3) Å, H5···O24 2.39(1) Å, H6···O33 2.42(3) Å).

$[\text{Cu}_2\text{L1}(\text{NCS})_4]$  (b). The structure of the compound consists of binuclear  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  complex molecules, resulting from the binding of two  $\text{Cu}(\text{NCS})_2$  units into the macrocycle **L1**. Two ORTEP<sup>26</sup> drawings of the complex are reported in Figure 2. Selected bond lengths and angles for the coordination environment are reported in Table 6. Each molecule lies around a crystallographic inversion center.

The three adjacent nitrogen atoms of the macrocycle and those belonging to the two thiocyanate ions are involved in metal coordination. The arrangement of the two thiocyanates in the coordination of the metal center is different. One thiocyanate ion (N4—C11—S1) is directed outside the cavity of the ligand, while the other (N5—C12—S2) almost inside the cavity. Cu and S2' are not in contact (Cu—S2' 3.703(3) Å).

(27) (a) Bazzicalupi, C.; Bencini, A.; Bianchi, A.; Fusi, V.; Paoletti, P.; Valtancoli, B. *J. Chem. Soc., Chem. Commun.* **1994**, 881–882. (b) Bazzicalupi, C.; Bencini, A.; Bianchi, A.; Fusi, V.; Mazzanti, L.; Paoletti, P.; Valtancoli, B. *Inorg. Chem.* **1995**, *34*, 3003–3010.

(28) Murthy, N. N.; Karlin, K. D. *J. Chem. Soc., Chem. Commun.* **1993**, 1236–1238.

The coordination geometry of the metal ion results in an almost regular square pyramid, with the basal plane described by the N1, N2, N3 secondary nitrogen atoms and N5 (max deviation from the mean plane 0.006(6) Å for N5), while the apical position is occupied by N4 belonging to the remaining thiocyanate (see Figure 2a). The metal is shifted toward the apical position, 0.2517(8) Å apart from the basal plane, and the Cu–N4 apical bond forms an angle of 2.7(2)° with the normal to the basal plane. To our knowledge, only a few cases of Cu–isothiocyanate bond are reported in the literature.<sup>29,30,31</sup> In addition, the Cu(II)–isothiocyanate bond is preferentially found in bipyramidal environments.<sup>30</sup>

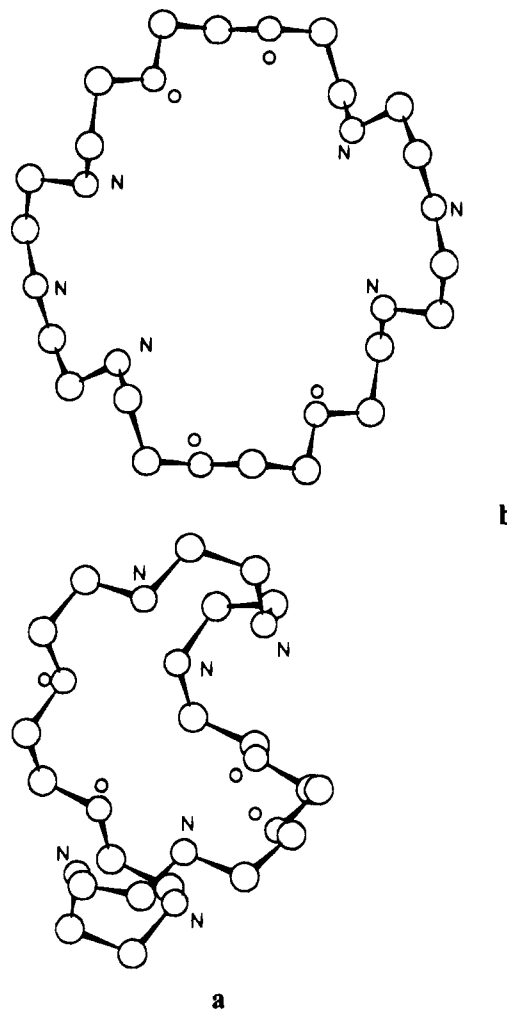
Close comparisons can be found in the binuclear copper(II) azido complex of bisdien (Chart 1)<sup>32</sup> where the Cu(N<sub>3</sub>)<sub>2</sub> units replace Cu(NCS)<sub>2</sub> in the [Cu<sub>2</sub>L1(NCS)<sub>4</sub>] complex. In both complexes the ligands assume an overall chair-type conformation and the crystal packing results from a very similar H-bond network (Figure 2b). In compound **b** the H-bond arrangement involves the N2 secondary nitrogen of the ligand and the N4 atom belonging to the SCN<sup>−</sup> ion lying on the apical position of the symmetry related complex molecule (N2···N4 distance 3.124(7) Å). It is also of interest that in [Cu<sub>2</sub>L1(NCS)<sub>4</sub>] the Cu···Cu intramolecular distance is longer than that found in [Cu<sub>2</sub>(bisdien)(N<sub>3</sub>)<sub>4</sub>] (6.182(2) Å vs 5.973 Å). This is due to the presence in bisdien of shorter ethereal chains linking the two triaza units which force the two metal ions at closer distance.

Furthermore, in compound **b** the intermolecular Cu···Cu' distance (5.954(2) Å) is shorter than the intramolecular one. The crystal packing gives rise to almost linear chains of Cu(II) ions, as shown in Figure 2b.

In the two molecular structures of **a** and **b**, the macrocycle L1 assumes different conformations (see Figure 3).<sup>33</sup> In **a** the bridging hydroxide forces the two zinc ions at close distance, leading to a screw-shaped conformation of the macrocycle. This arrangement defines a tridimensional internal cavity of approximate dimensions 3 × 4 × 6 Å<sup>3</sup>, while in **b** the macrocyclic framework is chair-shaped and more elongated and approximately defines an internal surface of dimensions 9 × 10 Å<sup>2</sup>. These remarkably different conformations reveal a significant flexibility of the macrocycle in metal ion binding.

[Cu<sub>2</sub>L1(NCS)<sub>4</sub>]<sub>2</sub>Na<sub>2</sub>S<sub>2</sub> (**c**). The crystal consists of a tridimensional polymer formed by [Cu<sub>2</sub>L1(NCS)<sub>4</sub>] binuclear complex molecules, Na<sup>+</sup> ions and disulfur anions linked together by metal–donor atom interactions. Figures 4 and 5 show ORTEP<sup>26</sup> drawings of the polymeric structure and of the [Cu<sub>2</sub>L1(NCS)<sub>4</sub>] complex, respectively. Both the [Cu<sub>2</sub>L1(NCS)<sub>4</sub>] complex and the S<sub>2</sub><sup>2−</sup> ions lie around crystallographic inversion centers. Selected bond lengths and angles for the coordination environment of the copper and of the sodium atoms are reported in Table 7.

The coordination geometry of the copper atom is square pyramidal, very similar to that found in compound **b**. The basal plane is determined by the three adjacent nitrogen belonging to the ligand and by N2 of a SCN<sup>−</sup> ion. The deviations from the mean plane are in the range 0.02(2)–0.03(2) Å, while the copper



**Figure 3.** Drawings showing the different conformations of the macrocycle L1 in [Zn<sub>2</sub>L1(μ-OH)]<sup>3+</sup> (**a**) and in [Cu<sub>2</sub>L1(NCS)<sub>4</sub>] (**b**) (obtained by using the Insight Discover program with input coordinates from X-ray data).<sup>30</sup>

atom is 0.288(3) Å apart from this plane, shifted toward the apical position occupied by the N1 nitrogen atom of the second thiocyanate. The Cu–N1 bond forms with the basal plane an angle of 3.2(6)°. The coordination bond distances and angles are equal, within the standard deviations, to those found for the copper ion in compound **b**. The Cu···Cu intramolecular distance is 6.367(4) Å. The shortest Cu···Cu intermolecular distance is 7.206(4) Å.

As shown in Figure 4 the Na<sup>+</sup> and S<sub>2</sub><sup>2−</sup> ions give rise to the polymeric linkage between the dicopper complex molecules. Each Na<sup>+</sup> is tricoordinated by the S3 atom of the disulfide ion and by the S1 and S1'' symmetry related sulfur atoms belonging to the SCN<sup>−</sup> ions which lie on the apical position of the square pyramidal arrangement around the Cu(II) ion. Each S–Na–S angular value is almost 120° (max dev. = 6.3° for S1–Na–S1''), while the Na–S3–S3'''–Na''' moiety is almost linear. The shortest copper–sodium distances are 5.689(8) Å (Cu···Na'') and 5.706(8) Å (Cu···Na).

**Solution Studies. Basicity.** Table 8 collects the basicity constants of L1 and L2 potentiometrically determined in 0.15 mol dm<sup>−3</sup> NaCl aqueous solution at 298.1 K. As far L1 is concerned, the first four basicity constants range between 9.66 and 7.40 log units, while the fifth and the sixth ones are less than 4 log units. This grouping can be rationalized considering the minimization of electrostatic repulsion between positive

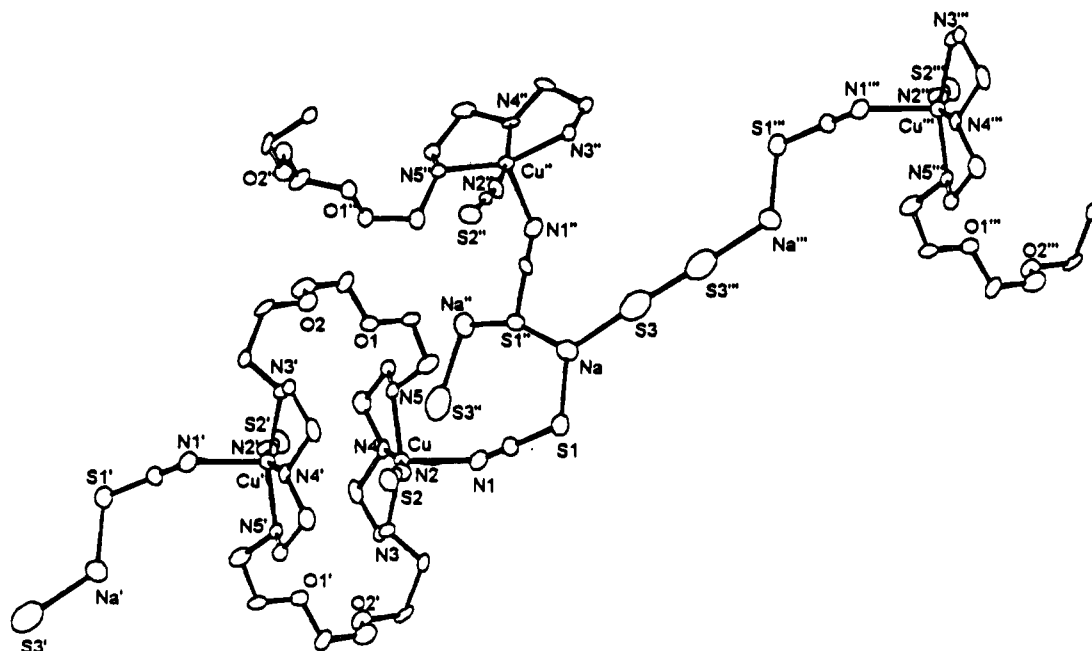
(29) Cannas, M.; Carta, G.; Marongiu, G. *J. Chem. Soc., Dalton Trans.* **1974**, 553–555.

(30) Cannas, M.; Carta, G.; Marongiu, G. *J. Chem. Soc., Dalton Trans.* **1974**, 550–553 and references therein.

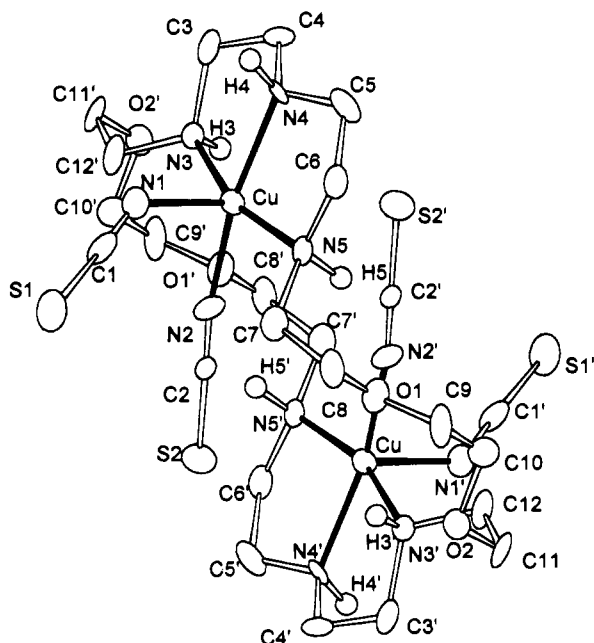
(31) Drew, M. G. B.; Yates, P. C.; Esho, F. S.; Trocha-Grimshaw, J.; Lavery, A.; McKillop, K. P.; Nelson, S. M.; Nelson, J. *J. Chem. Soc., Dalton Trans.* **1988**, 2995–3003.

(32) Comarmond, J.; Plumeré, P.; Lehn, J. M.; Agnus, Y.; Louis, R.; Weiss, R.; Kahn, O.; Morgenster-Badarau, I. *J. Am. Chem. Soc.* **1982**, *104*, 6330–6340.

(33) Insight Discover, Biosym Technologies Inc., 9685 Scranton Road, San Diego, CA, 92121-2777.



**Figure 4.** ORTEP drawing showing the polymeric structure of  $[\text{Cu}_2\text{L1}(\text{NCS})_4]\cdot\text{Na}_2\text{S}_2$  (symmetry transformations: single prime,  $1-x, -y, 1-z$ ; double prime,  $0.5+x, -0.5-y, z$ ; triple prime,  $1-x, -1-y, -z$ ).



**Figure 5.** ORTEP drawing of the  $[\text{Cu}_2\text{L1}(\text{NCS})_4]$  complex in  $[\text{Cu}_2\text{L1}(\text{NCS})_4]\cdot\text{Na}_2\text{S}_2$ .

charges in protonated species of polyaza macrocycles.<sup>34</sup> In other words, the first four protons can occupy alternate positions in the macrocycle, separated by unprotonated nitrogens or by the polyoxa chains; the much lower affinity of the ligand for the fifth and the sixth protons is due to the fact that these protonation reactions occur at the central nitrogens at each end of the macrocycle. Consequently, in the penta- and in the hexaprotonated receptor, three protonated nitrogen atoms are necessarily contiguous, leading, of course, to increased coulombic repulsion between protonated amine groups. A similar behavior is found for the L2 ligand (see Table 8).

**Cu(II) and Zn(II) Complexation.** The coordination characteristics of L1 and L2 toward  $\text{Zn}^{2+}$  and  $\text{Cu}^{2+}$  have been

**Table 7.** Selected Bond Lengths (Å) and Angles (deg) for  $[\text{Cu}_2\text{L1}(\text{NCS})_4]\cdot\text{Na}_2\text{S}_2$  (c)<sup>a</sup>

Cu-N2	1.97(2)	Na-S1''	2.41(1)
Cu-N4	2.00(2)	Na-S1	2.42(1)
Cu-N5	2.04(2)	Na-S3	2.43(2)
Cu-N3	2.06(2)		
Cu-N1	2.24(2)		
N2-Cu-N4	164.8(8)	N4-Cu-N1	94.4(7)
N2-Cu-N5	93.6(7)	N5-Cu-N1	98.7(8)
N4-Cu-N5	85.0(7)	N3-Cu-N1	98.3(8)
N2-Cu-N3	92.0(7)	S1''-Na-S1	126.3(3)
N4-Cu-N3	84.9(7)	S1''-Na-S3	119.0(4)
N5-Cu-N3	160.8(7)	S1-Na-S3	114.6(5)
N2-Cu-N1	100.8(8)		

<sup>a</sup> Symmetry transformation used to generate equivalent position:  $0.5+x, -0.5-y, z$ .

**Table 8.** Protonation Constants of L1 and L2 in Aqueous Solution (298.1 K, NaCl 0.15 mol dm<sup>-3</sup>)

reaction	log K	
	L1	L2
$\text{L} + \text{H}^+ = [\text{HL}]^+$	9.66(1)	9.69(2)
$[\text{HL}]^+ + \text{H}^+ = [\text{H}_2\text{L}]^{2+}$	8.78(1)	8.98(1)
$[\text{H}_2\text{L}]^{2+} + \text{H}^+ = [\text{H}_3\text{L}]^{3+}$	8.23(1)	8.43(2)
$[\text{H}_3\text{L}]^{3+} + \text{H}^+ = [\text{H}_4\text{L}]^{4+}$	7.40(1)	7.81(1)
$[\text{H}_4\text{L}]^{4+} + \text{H}^+ = [\text{H}_5\text{L}]^{5+}$	3.99(1)	6.13(2)
$[\text{H}_5\text{L}]^{5+} + \text{H}^+ = [\text{H}_6\text{L}]^{6+}$	3.18(1)	3.99(2)
$[\text{H}_6\text{L}]^{6+} + \text{H}^+ = [\text{H}_7\text{L}]^{7+}$		2.81(2)

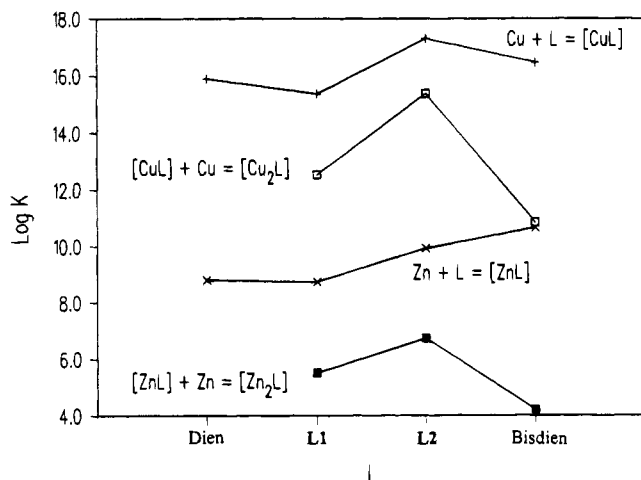
studied in 0.15 mol dm<sup>-3</sup> NaCl aqueous solutions at 298.1 K and the stability constants of their complexes are reported in Table 9. Both ligands form mononuclear and binuclear complexes with the investigated metal ions. A plot of the constants (log K) for the equilibria  $\text{M}^{2+} + \text{L} = [\text{ML}]^{2+}$  and  $[\text{ML}]^{2+} + \text{M}^{2+} = [\text{M}_2\text{L}]^{4+}$  (where L = L1, L2, bisdien,<sup>13a</sup> and dien (diethylenetriamine)<sup>35</sup> and M = Cu and Zn) is reported in Figure 6.

**Mononuclear Complexes.** As far the stability of the  $[\text{ML1}]^{2+}$  (M =  $\text{Zn}^{2+}$  or  $\text{Cu}^{2+}$ ) is concerned, some general features can be outlined. First of all it is to be noted that the

(34) (a) Bianchi, A.; Micheloni, M.; Paoletti, P. *Coord. Chem. Rev.* **1991**, *110*, 17-113. (b) Bencini, A.; Bianchi, A.; Paoletti, P.; Paoli P. *Pure Appl. Chem.* **1993**, *65*, 381-386.

(35) Smith, R. M.; Martell, A. E. *Critical Stability Constants*; Plenum Press: New York: 1975, Vol 2; 1982, 1st supplement.





**Figure 6.** Plots of the constants for the equilibria  $M^{2+} + L = [ML]^{2+}$  and  $[ML]^{2+} + M = [M_2L]^{4+}$  ( $M = Zn, Cu$ ) for dien, **L1**, **L2**, and bisdien. Charges are omitted for clarity.

**Table 9.** Logarithms of the Equilibrium Constants Determined in 0.15 mol dm<sup>-3</sup> NaCl at 298.1 K for the Complexation Reactions of Cu<sup>2+</sup> and Zn<sup>2+</sup> with **L1** and **L2**

reaction	log <i>K</i>	
	<b>L1</b>	<b>L2</b>
Cu <sup>2+</sup> + <b>L</b> = CuL <sup>2+</sup>	15.36(4)	17.29(4)
CuL <sup>2+</sup> + H <sup>+</sup> = CuLH <sup>3+</sup>	8.35(8)	8.83(5)
CuLH <sup>3+</sup> + H <sup>+</sup> = CuLH <sub>2</sub> <sup>4+</sup>	7.50(7)	8.51(5)
CuLH <sub>2</sub> <sup>4+</sup> + H <sup>+</sup> = CuLH <sub>3</sub> <sup>5+</sup>	3.52(4)	4.87(6)
CuLH <sub>3</sub> <sup>5+</sup> + H <sup>+</sup> = CuLH <sub>4</sub> <sup>6+</sup>		3.56(7)
CuL <sup>2+</sup> + OH <sup>-</sup> = CuLOH <sup>+</sup>	3.93(7)	
CuL <sup>2+</sup> + Cu <sup>2+</sup> = Cu <sub>2</sub> L <sup>4+</sup>	12.52(5)	15.37(8)
Cu <sub>2</sub> L <sup>4+</sup> + H <sup>+</sup> = Cu <sub>2</sub> LH <sup>5+</sup>		3.15(8)
Cu <sub>2</sub> L <sup>4+</sup> + OH <sup>-</sup> = Cu <sub>2</sub> LOH <sup>3+</sup>	5.79(4)	4.1(1)
Cu <sub>2</sub> LOH <sup>3+</sup> + OH <sup>-</sup> = Cu <sub>2</sub> L(OH) <sub>2</sub> <sup>2+</sup>	3.55(6)	
Zn <sup>2+</sup> + <b>L</b> = ZnL <sup>2+</sup>	8.73(6)	9.92(6)
ZnL <sup>2+</sup> + H <sup>+</sup> = ZnLH <sup>3+</sup>	8.4(1)	8.81(4)
ZnLH <sup>3+</sup> + H <sup>+</sup> = ZnLH <sub>2</sub> <sup>4+</sup>	7.17(9)	8.31(7)
ZnLH <sub>2</sub> <sup>4+</sup> + H <sup>+</sup> = ZnLH <sub>3</sub> <sup>5+</sup>	6.0(2)	5.38(8)
ZnL <sup>2+</sup> + OH <sup>-</sup> = ZnLOH <sup>+</sup>	4.5(1)	4.1(1)
ZnLOH <sup>+</sup> + OH <sup>-</sup> = ZnL(OH) <sub>2</sub>	2.7(1)	
ZnL <sup>2+</sup> + Zn <sup>2+</sup> = Zn <sub>2</sub> L <sup>4+</sup>	5.51(5)	6.73(7)
Zn <sub>2</sub> L <sup>4+</sup> + OH <sup>-</sup> = Zn <sub>2</sub> LOH <sup>3+</sup>	6.13(9)	5.5(1)
Zn <sub>2</sub> LOH <sup>3+</sup> + OH <sup>-</sup> = Zn <sub>2</sub> L(OH) <sub>2</sub> <sup>2+</sup>	4.5(1)	5.0(1)

stability of these species is markedly lower than those presented by the analogous complexes of aza macrocyclic ligands containing six nitrogen donors. In particular, Figure 6 evidences that the  $[ML]^{2+}$  complexes are characterized by stability constants lower than those reported for the corresponding complexes of bisdien (Chart 1). Martell proposed that bisdien may use both dien units for the coordination of a single metal ion, forming four coordinate bonds to Cu<sup>2+</sup> and a larger number of coordinate bonds to Zn<sup>2+</sup>.<sup>13a</sup> On the other hand, as shown in Figure 6, the formation constants of the  $[ML]^{2+}$  complexes are very similar to those of dien.<sup>35</sup> In the case of the Zn<sup>2+</sup> complexes, the constants are equal within the experimental error.

Furthermore, the  $[ML]^{2+}$  complexes present a high tendency to bear protonation, the two first protonation constants being only 1.2–1.3 log units lower than the corresponding basicity constants of the **L1** free amine. The rather high values of the equilibrium constants for the protonation of the  $[ML]^{2+}$  species can be reasonably ascribed to the protonation of nitrogen atoms not bound to the metal cation.

These observations point out that the metal ion is coordinated by one of the two triamine moieties, while the other one does not participate in the coordination. Since the ethereal oxygens in aqueous solution have weak coordinative ability toward Cu<sup>2+</sup>

and Zn<sup>2+</sup>, we may suppose a little contribution of the polyoxa chains to the stabilization of the  $[ML]^{2+}$  species.

Furthermore, the  $[ML]^{2+}$  complexes form stable hydroxo species. In the mononuclear complexes only three nitrogen donor atoms bind to the metal ions and facile deprotonation of coordinated water molecules produces a monohydroxylated species of the  $[CuL]^{2+}$  complex and mono- and dihydroxylated species of the  $[ZnL]^{2+}$  complex.

The features of the  $[ML]^{2+}$  complexes are similar to those of the complexes formed by **L1**. The most relevant difference is the larger stability presented by the  $[CuL_2]^{2+}$  and  $[ZnL_2]^{2+}$  species with respect to the analogous **L1** complexes (see Figure 6). This finding can be explained by considering that the tetraaza moiety of **L2** is the preferential binding site for these metal ions.

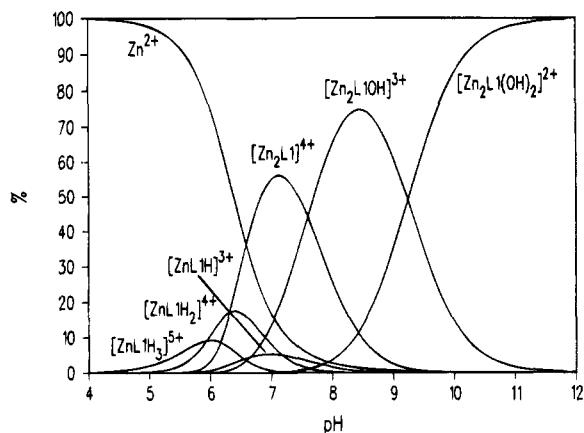
In conclusion, **L1** and **L2** show different ligational properties in their 1:1 metal chelates with respect to bisdien. While bisdien may use both triamine units in the coordination of a single metal ion, in  $[ML]^{2+}$  and  $[ML_2]^{2+}$  only one of the two binding units seems to be used in the complexation of Cu<sup>2+</sup> and Zn<sup>2+</sup>.

**Binuclear Complexes.** Figure 6 shows that the constants for the addition of a second metal ion to the  $[ML]^{2+}$  (**L** = **L1** or **L2**) complexes, *i.e.* for the equilibrium  $[ML]^{2+} + M^{2+} = [M_2L]^{4+}$ , are remarkably higher than those found for the analogous equilibria of bisdien.<sup>13a</sup> Two main factors can explain these thermodynamics observations: (i) the formation by bisdien of binuclear chelates involves the detachment of some coordinated nitrogen donors, and (ii) the presence in **L1** and **L2** of longer polyoxa chains leads to a larger molecular flexibility and allows the two coordinated metal ions to be localized far apart, in order to achieve a better minimization of electrostatic repulsion. Furthermore, the constants for the equilibria  $[ML]^{2+} + M^{2+} = [M_2L]^{4+}$  are remarkably lower than those found for the formation of the  $[ML]^{2+}$  species (see Figure 6). This can be ascribed mainly to coulombic repulsion between the two metal centers, and, to a lesser extent, to statistical effects. A similar behavior is observed for **L2**. In the case of the Zn(II) complexes of **L2**, the difference between the equilibrium constants for the addition of the first and the second metal ion ( $\Delta \log K = 3.19$ ) is equal, within the experimental error, to the analogous difference ( $\Delta \log K = 3.22$ ) found for the Zn(II)/**L1** system. This indicates that, also with **L2**, the second metal is coordinated by a triamine moiety not involved in the binding of the first one.

It is worth noting that both  $[M_2L_1]^{4+}$  and  $[M_2L_2]^{4+}$  complexes show a marked tendency to form mono- and dihydroxo species in aqueous solution. In the case of the  $[Cu_2L_2]^{4+}$  complex only a monohydroxo species is present in solution. However, in all the systems with metal to ligand 2:1 molar ratio, such species are largely present in aqueous solution even at neutral or slight alkaline pH's, as shown in Figure 7 for the system **L1**/Zn(II).

The behavior of the dinuclear Cu<sup>2+</sup> and Zn<sup>2+</sup> complexes in alkaline solution is interesting in that they can give structural information on their hydroxo species. Particularly, the constants for the addition of the first OH<sup>-</sup> to the  $[M_2L_1]^{4+}$  or  $[M_2L_2]^{4+}$  complexes are rather high (they range between 6.13 and 4.1 logarithmic units) in comparison with the analogous constants for the addition of hydroxo groups to the corresponding mononuclear complexes. This indication of a strong binding of the hydroxide ion leads to suppose that this group is bridged between the two metal centers, as actually observed in the crystal structure of the  $[Zn_2L_1(\mu-OH)]^{3+}$  cation.

From the equilibrium constants reported in Table 9, we calculate the p*K*<sub>a</sub> of the water-bound molecule in the



**Figure 7.** Distribution diagram of the species for the system L1/Zn(II) as a function of pH (NaCl, 0.15 mol dm<sup>-3</sup>, 298.1 K, [L1] = 1 × 10<sup>-3</sup>, [Zn<sup>2+</sup>] = 2 × 10<sup>-3</sup> mol dm<sup>-3</sup>).

[Zn<sub>2</sub>L(H<sub>2</sub>O)]<sup>4+</sup> complex (pK<sub>a</sub> = 7.60 and 8.2 for L = L1 and L2, respectively). These pK<sub>a</sub> values are very close, especially for L1 to the pK<sub>a</sub> values reported for other Zn(II) macrocyclic complexes active in the hydrolysis of phosphoesters.<sup>6</sup> It is to be noted that the pK<sub>a</sub> value for [Zn<sub>2</sub>L1(H<sub>2</sub>O)]<sup>4+</sup> is somewhat higher than the analogous L2 complex. This difference can be ascribed to a lower tendency of the Zn(II) ion coordinated by the tetraaza moiety of L2 to bind further species from the medium.

The binuclear [Cu<sub>2</sub>L1(H<sub>2</sub>O)]<sup>4+</sup> and [Cu<sub>2</sub>L2(H<sub>2</sub>O)]<sup>4+</sup> complexes show a similar behavior (pK<sub>a</sub> = 7.94 and 9.6 in the case of L1 and L2, respectively), thus suggesting also in this case a bridging coordination of an OH<sup>-</sup> ion.

**Concluding Remarks.** Thermodynamic and structural data indicate that in the [M<sub>2</sub>(OH)L1]<sup>3+</sup> and [M<sub>2</sub>(OH)L2]<sup>3+</sup> species the OH<sup>-</sup> ion bridges the two metal centers. The distance between the two Zn(II) ions (3.5 Å) in the [Zn<sub>2</sub>L1(μ-OH)]<sup>3+</sup> complex cation is very close to that found in the phospholipase C (3.3 Å), for which a bridging hydroxide group has been observed. Furthermore, The Zn···Zn distance in the [Zn<sub>2</sub>L1(μ-OH)]<sup>3+</sup> ion is considerably shorter than the Cu···Cu distance in the [Cu<sub>2</sub>L1(NCS)<sub>4</sub>] complex (6.18 Å). This reveals a marked flexibility of the macrocycle, which allows the two metal ions to approach each other producing cooperativity in the binding of substrate molecules. Considering (i) the presence of two cooperating metal centers and (ii) the high pK<sub>a</sub> values of the coordinated water molecule, these complexes seem to be promising synthetic models for binuclear Zn(II) enzymes responsible for binding of phosphate esters and subsequent hydrolysis of the phosphate ester bond.

Further studies on binding and hydrolysis of phosphoesters are in progress.

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**Supporting Information Available:** Tables of crystallographic data, hydrogen atom positional parameters, isotropic and anisotropic thermal factors, and bond distances and angles (21 pages). Ordering information is given on any current masthead page.

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