Synthesis and Selectivity in Metal Ion Coordination of the New Ligands 1,4,7-Trimethyl-1,7-bis(4-carboxybenzyl)-1,4,7-triazaheptane (L) and 1,4,7,16,19,22-Hexamethyl-1,4,7,16,19,22-hexaaza[9.9]paracyclophane (L1). Crystal Structures of $[PdLH_2Cl]NO_3 \cdot 2.6H_2O$ and $[Cu_2L1Cl_2](BPh_4)(ClO_4) \cdot CH_3CN$

Carla Bazzicalupi, Andrea Bencini,* Antonio Bianchi,* Vieri Fusi, Claudia Giorgi, Piero Paoletti,* Annalisa Stefani, and Barbara Valtancoli

Department of Chemistry, University of Florence, Via Maragliano 75/77, 50144 Florence, Italy

Received August 10, 1994[⊗]

The synthesis of 1,4,7-trimethyl-1,7-bis(4-carboxybenzyl)-1,4,7-triazaheptane (LH_2) and 1,4,7,16,19,22-hexamethyl-1,4,7,16,19,22-hexaaza[9.9]paracyclophane (**L1**) is described. The interaction of both ligands with Cu^{2+}, Zn^{2+}, Cd^{2+}, and Pd^{2+} ions has been studied by potentiometric titrations and microcalorimetry (LH_2/Cu^{2+},Cd^{2+}) in 0.15 mol dm^{-3} NaCl solution at 298.10.1 K. The stability of LH_2 complexes with these cations is rather low. Thermodynamic data suggest the N_3 moiety is the binding site for Cu^{2+} and Pd^{2+}, while in the case of Zn^{2+} and Cd^{2+} the carboxylate groups seem to be preferred. X-ray data confirm the coordination site for Pd^{2+}. Crystals of $[PdLH_2Cl](NO_3) \cdot 2.6H_2O$ are triclinic, space group $P\bar{1}$ ($Z = 2$), with $a = 8.472(3)$ Å, $b = 12.178(2)$ Å, $c = 14.498(4)$ Å, $\alpha = 78.26(2)°$, $\beta = 87.20(3)°$, $\gamma = 77.72(2)°$, $R = 0.0727$, and $wR_2 = 0.2294$. The Pd^{2+} ion is coordinated by the three amino groups of LH_2 and a Cl^- anion in a square coordination environment; the two protons are located on the carboxylic groups. **L1** forms both mono- and binuclear complexes with Cu^{2+} in aqueous solution but does not interact with Zn^{2+} and Cd^{2+}. Pd^{2+} complexes are also formed. Crystals of $[Cu_2L1Cl_2](ClO_4)(BPh_4) \cdot CH_3CN$ are monoclinic, space group $P2_1/m$ ($Z = 2$), with $a = 11.526(2)$ Å, $b = 13.552(2)$ Å, $c = 18.078(6)$ Å, $\beta = 96.47(2)°$, $R = 0.0823$, and $wR_2 = 0.2366$. The two Cu^{2+} ions are coordinated by three nitrogen atoms of **L1** and a Cl^- anion in a square coordination environment, the ligand behaving as a ditopic receptor. Selectivity in metal ion binding is discussed.

Introduction

The development of highly preorganized macrocyclic and macropolycyclic ligands has enhanced the success in molecular recognition promoting selective binding, transformation, and transfer of large varieties of substrates.[1] Particularly, azamacrocyclic receptors able to bind different kinds of substrates, such as inorganic or organic cations,[2−6] anionic species,[7] and neutral molecules[8] have been studied to elaborate their use as selective recognizers, molecular carriers, and catalysts.

Structural factors have been shown to play significant roles to determine the strength of the interactions between the polyaza receptor and the guest molecule.[9-11] In this context, to introduce into the molecular framework structural features that impart high selectivity in the recognition of different guests is one of the goals in design of synthetic receptors.

Aromatic subunits are often introduced as integral parts of the host molecules. Cyclic ligands containing aromatic rings in their backbone, cyclophanes, have received much attention for the recognition of lipophilic species.[12−16] More recently, polyazacyclophanes have been also synthesized and employed

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1994.

(1) (a) Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. J.; Sen, D. *Chem. Rev.* **1985,** *85,* 271. (b) Krakowiak., K. E.; Bradshaw, J. S.; Zamecka-Krakowiak, D. J. *Chem. Rev.* **1989,** *89,* 929. (c) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1991,** *91,* 1721. (d) Bradshaw, J. S.; Krakowiak., K. E.; Izatt, R. M. *Tetrahedron* **1992,** *48,* 4475. (e) Lehn, J. M. *Angew. Chem., Int. Ed. Engl.* **1988,** *27,* 89. (f) Christensen, J. J.; Izatt R. M., Eds. *Synthesis of Macrocycles, the Design of Selective Complexing Agents*; Wiley: New York, 1987. (g) Mertes, K. B.; Lehn, J. M. Multidentate Macrocyclic and Macropolycyclic Ligands. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Ed.; Pergamon Press: Oxford, U.K., 1987, 915. (h) Gokel, G. W. *Crown Ethers and Cryptands;* Monographs in Supramolecular Chemistry; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, U.K. 1992.

(2) (a) Lindoy L. F., Ed., *The Chemistry of Macrocyclic Ligand Complexes*; Cambridge Univ. Press: Cambridge, U.K. 1989. (b) Dobler, M. *Ionophores and their Structure;* Wiley Interscience Publication: New York, 1981.

(3) (a) Pascard, C.; Riche, C.; Cesario, M.; Kotzyba-Hibert, F.; Lehn, J. M. *J. Chem. Soc., Chem. Commun.* **1982,** 557. (b) Kumar, A.; Mageswaran, S.; Sutherland, I. O. *Tetrahedron* **1986,** *42,* 3291. (c) Pratt, A.; Sutherland, I. O.; Newton, R. F. *J. Chem. Soc., Perkin Trans. 1* **1988,** 13. (d) Sutherland, I. O. *Chem. Soc. Rev.* **1986,** *15,* 63. (e) Sutherland, I. O. *Pure Appl. Chem.* **1989,** *61,* 1547.

(4) Graf, E.; Kintzinger, J. P.; Lehn, J. M.; LeMoigne, J. *J. Am. Chem. Soc.* **1982,** *104,* 1672.

(5) Metz, B.; Rosalky, J. M.; Weiss, R. *J. Chem. Soc., Chem. Commun.* **1976,** 533.

(6) (a) Lehn, J. M. *Acc. Chem. Res.* **1978,** 49. (b) Lehn, J. M. *Pure Appl. Chem.* **1978,** *50,* 871.

(7) (a) Diederich, B.; Hosseini, M. W.; Lehn, J. M.; Session R. B. *J. Am. Chem. Soc.* **1981,** *103,* 1282. (b) Hosseini, M. W.; Lehn, J. M.; Mertes, M. P. *Helv. Chim. Acta* **1983,** *66,* 2454. (c) Hosseini, M. W.; Lehn, J. M.; Maggiora, L.; Mertes, M. P.; Mertes, K. B. *J. Am. Chem. Soc.* **1985,** *107,* 909. (d) Hosseini, M. W.; Lehn, J. M.; Maggiora, L.; Mertes, M. P.; Mertes, K. B. *J. Am. Chem. Soc.* **1987,** *109,* 537. (e) Hosseini, M. W.; Lehn, J. M.; *Helv. Chim. Acta* **1988,** *71,* 749. (e) Mertes, M. P.; Mertes, K. B. *Acc. Chem. Res.* **1990,** *23,* 413 and references therein.

(8) (a) Vögtle, F.; Sieger, H.; Müller, W. *Top. Curr. Chem.* **1981,** *98,* 107. (b) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L.; Tarbet, B. J. *Chem. Rev.* **1992,** *92,* 1261.

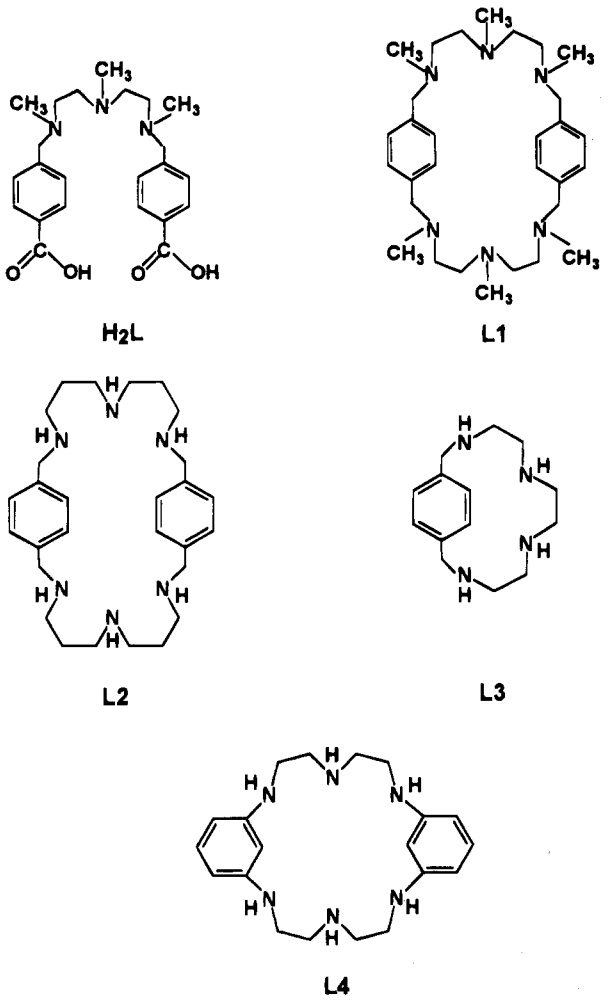
(9) (a) Hosseini, M. W.; Blacker, A. J.; Lehn, J. M. *J. Am. Chem. Soc.* **1990,** *112,* 3896. (b) Claude, S.; Lehn, J. M.; Schmidt, F.; Vigneron, J. P. *J. Chem. Soc., Chem. Commun.* **1991,** 1182

(10) Kimura, E.; Kuramoto, Y.; Koike, T.; Kodama, M. *J. Org. Chem.* **1990,** *55,* 42 .

(11) (a) Bencini, A.; Bianchi, A.; Burguette, M. I.; Garcia-España, E.; Luis, S. V.; Ramirez, J. A. *J. Am. Chem. Soc.* **1992,** *114,* 1919. (b) Bencini, A.; Bianchi, A.; Dapporto, P.; Garcia-España, E.; Micheloni, M.; Ramirez, J. A.; Paoletti, P.; Paoli, P. *Inorg. Chem.* **1992,** *31,* 1902. (c) Bencini, A.; Bianchi, A.; Burguette, M. I.; Dapporto, P.; Domenech, A.; Garcia-España, E.; Luis, S. V.; Paoli, P.; Ramirez, J. A. *J. Chem. Soc., Perkin Trans. 2* **1994,** 569.

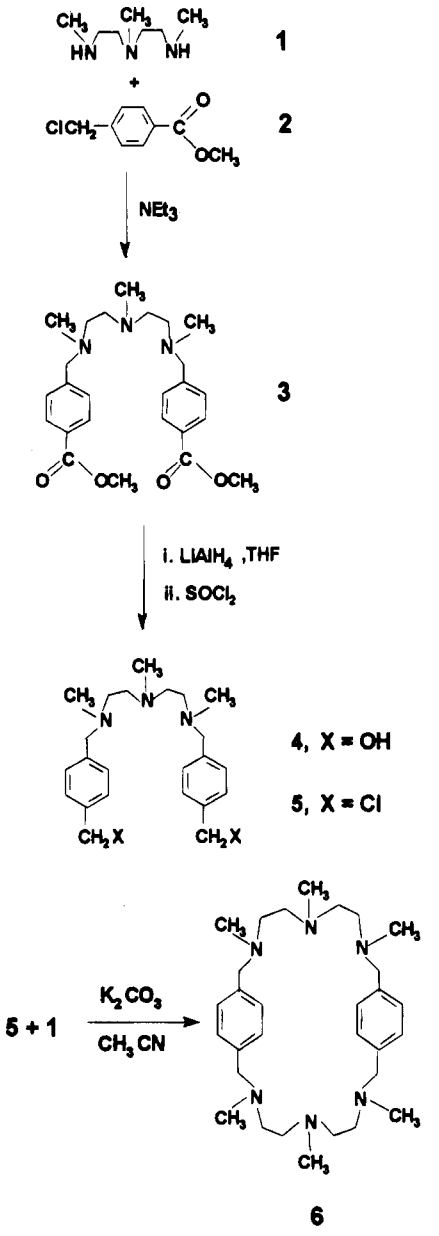
0020-1669/95/1334-0552$09.00/0

Chart 1



in metal ion complexation studies. The presence of rigid aromatic systems gives particular ligational properties to the ligands defining distinct preorganized binding lodgings for the metal ions within the ligand itself. For example the ligand 1,5,9,17,21,25-hexaaza[11.11]paracyclophane (**L2**; Chart 1) presents two almost independent N_3 binding sets where two metal ions can be accommodated.[17] On the other hand, the presence of a rigid aromatic spacer in 2,5,8,11-tetraaza[12]-paracyclophane (**L3**; Chart 1) also allows this small macrocycle to accommodate two Cu^{2+} ions behaving as a bis-bidentate receptor.[18a]

Scheme 1



In this paper we report on the synthesis and coordination properties of the title ligand **L1** and of its modified open-chain precursor LH_2 (Chart 1). The presence in **L1** of *p*-xylene spacers, the short ethylenic chains connecting the amino groups, and nitrogen methylation contribute to the molecular crowding and stiffening making **L1** a promising candidate for selective metal ion recognition among parent ligands (Chart 1).

Experimental Section

The 200.0 MHz ^1H NMR and 50.32 MHz ^{13}C spectra were recorded at 298 K in a Bruker AC-200 spectrometer.

CF-FAB mass spectra were performed with a VG-7070EQ mass spectrometer.

Synthesis of the Compounds. The macrocycle 1,4,7,16,19,22-hexamethyl-1,4,7,16,19,22-hexaaza[9.9]paracyclophane (**L1**) was obtained by following the synthetic procedure depicted in Scheme 1. 1,4,7-Trimethyl-1,4,7-triazaheptane (**1**) was synthesized as reported in ref 19.

(12) Diederich, F. *Cyclophanes;* Monographs in Supramolecular Chemistry; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, U.K., 1992.
(13) (a) Dietrich, B.; Fyles, T. M.; Lehn, J. M.; Pease, L. G.; Fyles, D. L. *J. Chem. Soc., Chem. Commun.* **1978**, 934. (b) Jazwinski, J.; Lehn, J. M.; Meric, M.; Vigneron, J-P.; Cesario, M.; Guilhem, J.; Pascard, C. *Tetrahedron Lett.* **1987**, *42*, 3489.
(14) (a) Vögtle, F.; Muller, W. M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 712. (b) Vögtle, F.; Muller, W. M.; Werner, V.; Losensky, H. W. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 901.
(15) Murakami, Y.; KiKuchi, J.; Ohno, T.; Hirayama, T.; Hisaeda, Y.; Nishimura, Y.; Snyder, J. P.; Steliou, K. *J. Am. Chem. Soc.* **1991**, *113*, 8229.
(16) Pietraszkiewicz, M.; Gasiorowki, R. *Chem. Ber.* **1990**, *123*, 405.
(17) McKenzie, C. J.; Toflund, H.; Pietraszkiewicz, M.; Stoiek, Zb.; Slowinski, K. *Inorg. Chim. Acta* **1993**, *210*, 143.
(18) (a) Andrés, A.; Bazzicalupi, C.; Bianchi, A.; Doménech, A.; Garcia-España, E.; Luis, S. V.; Miravet, J. F. *J. Chem. Soc., Dalton Trans.* in press. (b) Andrés, A.; Burguete, M. I.; Garcia-España, E.; Luis, S. V.; Miravet, J. F.; Soriano, C. *J. Chem. Soc., Perkin Trans. 2* **1993**, 749
(19) Bencini, A.; Bianchi A.; Dapporto P.; Fusi, V.; Garcia-España, E.; Micheloni, M.; Paoletti, P.; Paoli, P.; Rodriguez, A.; Valtancoli, B. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1059.

Methyl *p*-(α-chloromethyl)benzoate (2). This compound was prepared by following the procedure reported by Codington et al. for the analogous bromo derivative.[20] A methanol solution of 4-(chloromethyl)benzoic acid (Aldrich Chemical Co.) (25 g, 0.15 mol) and 98% H_2SO_4 (10 cm^3) was refluxed with stirring for 75 min and then concentrated to 50 cm^3. After cooling of the solution to room temperature, water was added to precipitate a white solid which was filtered off, recrystallized from a 1:2 methanol:water mixture, and dried in vacuum. Yield: 21.6 g (80%). Anal. Calcd for $C_9H_9O_2Cl$: C, 58.55; H, 4.91. Found: C, 58.4; H, 4.9.

1,4,7-Trimethyl-1,7-bis(4-(methylcarbonyl)benzyl)-1,4,7-triazaheptane (3). A solution of **2** (48 g, 0.26 mol) in anhydrous NEt_3 (200 cm^3) was added dropwise to a boiling solution of **1** (18.9 g, 0.13 mol) in anhydrous NEt_3 (300 cm^3) over a period of 1 h. After the addition was completed, the solution was heated at reflux for a further 7 h. The resulting suspension was filtered and the solution was evaporated to dryness to give a yellowish oil, which was dissolved in the minimum quantity of chloroform and chromatographed on neutral alumina (70−230 mesh, activity I), eluting with chloroform. The eluted fractions were collected and evaporated to dryness to give a colorless oil. Yield: 31 g (54%). Anal. Calcd for $C_{25}H_{35}N_3O_4$: C, 68.00; H, 8.00; N, 9.52. Found: C, 67.8; H, 8.1; N, 9.4. ^{13}C NMR ($CDCl_3$): δ 42.5, 42.8, 51.8, 55.1, 55.8, 62.3, 126.3, 128.7, 129.4, 144.5, 166.7 ppm.

1,4,7-Trimethyl-1,7-bis(4-(α-hydroxymethyl)benzyl)-1,4,7-triazaheptane (4). A solution of **3** (11.8 g, 0.027 mol) in dry THF (100 cm^3) was added to a suspension of $LiAlH_4$ (6 g, 0.16 mol) in dry THF (100 cm^3), cooled to 0 °C over a period of 1 h. After the addition was completed, the suspension was heated at reflux for 12 h. After cooling of the suspension to room temperature, water (15 cm^3) and then 15% NaOH aqueous solution (30 cm^3) were added dropwise. The resulting suspension was filtered, and the filtrate was evaporated to give compound **4** as a yellowish oil. Yield: 9.7 g (93%). Anal. Calcd for $C_{23}H_{37}N_3O_2$: C, 71.28; H, 9.62; N, 10.84. Found: C, 71.3; H, 9.3; N, 10.7. ^{13}C NMR ($CDCl_3$): δ 41.1, 41.8, 50.7, 52.2, 61.9, 64.5,128.8, 129.4, 132.7, 144.1 ppm.

This compound can be purified as its trihydrochloride salt **4**·3HCl, which was obtained in almost quantitative yield by adding 37% HCl to an ethanolic solution of **4**. Anal. Calcd for $C_{23}H_{40}N_3O_2Cl_3$: C, 55.59; H, 8.14; N, 8.46. Found: C, 55.8; H, 7.8; N, 8.4.

1,4,7-Trimethyl-1,7-bis(*p*-(α-chloromethyl)benzyl)-1,4,7-triazaheptane (5). $SOCl_2$ (70 cm^3) was added dropwise to a suspension of **4**·3HCl (12.3 g, 0.025 mol) in $CHCl_3$ (150 cm^3) over a period of 1 h. After the addition was completed, the suspension was heated at reflux for 3 h. The suspension was then evaporated to 50 cm^3 and filtered, to give compound **5**·3HCl as a white solid. Yield: 13.2 g (98%). Anal. Calcd for $C_{25}H_{36}N_3Cl_5$: C, 51.90; H, 6.82; N, 7.90. Found: C, 51.6; H, 6.8; N, 7.8. ^{13}C NMR (CD_3CN): δ 34.1, 41.4, 41.6, 51.6, 52.2, 61.5,129.4, 129.8, 132.6, 132.9 ppm.

1,4,7,16,19,22-Hexamethyl-1,4,7,16,19,22-hexaaza[9.9]paracyclophane (L1). Compound **1** (3.8 g, 0.026 mol) and K_2CO_3 (36.1 g, 0.26 mol) were suspended in refluxing CH_3CN (300 cm^3). To this mixture, a suspension of **5** (13.9 g, 0.026 mol) in CH_3CN (250 cm^3) was added dropwise over a period of 7 h. After the addition was completed, the suspension was refluxed for 8 h and then filtered. The filtrate was vacuum evaporated to yield the crude product which was chromatographed on neutral alumina (70−230 mesh, activity I) eluting with a 100:1.5 $CHCl_3$/MeOH mixture. The eluted fractions were collected and evaporated to dryness to afford pure **L1** as a white solid. Yield: 4.5 g (35%). ^1H NMR ($CDCl_3$): δ 2.16 (s, 12 H), 2.22 (s, 6 H), 2.41 (m, 16 H), 3.30 (s, 8 H), 7.25 (s, 8 H). ^{13}C NMR ($CDCl_3$): δ 42.8, 43.7, 52.4, 52.7, 61.5, 130.9, 137.4 ppm. MS (FAB): *m/e* 496 ($M + H^+$). Anal. Calcd for $C_{30}H_{50}N_6$: C, 72.83; H, 10.18; N, 16.99. Found: C, 72.5; H, 10.3; N, 16.7.

L1·6HCl·1.5H₂O. This compound was obtained in almost quantitative yield by adding 37% HCl to an ethanolic solution of **L1**. Anal. Calcd for $C_{30}H_{59}N_6O_{1.5}Cl_6$: C, 48.70; H, 8.03; N, 11.30. Found: C, 48.8; H, 8.0; N, 11.3.

1,4,7-trimethyl-1,7-bis(4-carboxybenzyl)-1,4,7-triazaheptane (LH_2). A solution of **3** (1 g, 2.2 mmol) in ethanol (40 cm^3) was added to a solution of NaOH (3 g, 0.075 mol) in water (25 cm^3). The resulting solution was heated to reflux with stirring over a period of 6 h and then evaporated to dryness. The resulting white solid was dissolved in the minimum amount of water. A 65% aqueous solution of $HClO_4$ was added to the solution until the precipitation of a white solid occurred. The precipitate (LH_2·3$HClO_4$) was recrystallized from water. Yield: 0.93 g (53%). ^1H NMR (D_2O, pH 3): δ 2.32 (s, 3 H), 2.91 (s, 6 H), 3.12 (t, 4 H), 3.41 (t, 4 H), 4.44 (s, 4 H), 7.60 (d, 4 H), 7.97 ppm (d, 4H. ^{13}C NMR (D_2O, pH 3): δ 41.3, 41.7, 52.3, 52.5, 61.1, 131.7, 132.6, 133.3, 134.8, 171.2 ppm. Anal. Calcd for $C_{23}H_{34}N_3Cl_3O_{16}$: C, 38.63; H, 4.80; N, 5.87. Found: C, 38.7; H, 5.0; N, 5.8.

[Cu₂L1Cl₂](BPh₄)(ClO₄)·CH₃CN. A solution of $Cu(ClO_4)_2$·6H_2O (75 mg, 0.2 mmol) in MeOH (10 cm^3) was added to a solution of **L1** in MeOH. To the resulting blue solution, NaCl (10 mg, 0.4 mmol) and $NaBPh_4$ (35 mg, 0.1 mmol) in CH_3CN (20 cm^3) were added. Crystals of the complex, suitable for X-ray crystallography, were obtained by slow evaporation of this solution at room temperature. *Caution! Although no difficulties were encountered, perchlorate salts of metal complexes with organic ligands are potentially explosive and must be handled with extreme care.* Anal. Calcd for $C_{56}H_{73}N_7BCl_3O_4Cu_2$: C, 58.36; H, 6.38; N, 8.50. Found: C, 58.4; H, 6.4; N, 8.4.

[PdLH₂Cl]NO₃·3H₂O. To a solution of LH_2·3$HClO_4$ (125 mg, 0.16 mmol) in water, $Pd(NO_3)_2$ (37 mg, 0.16 mmol) and NaCl (30 mg) were added at room temperature. The resulting solution was neutralized by adding small amounts of 0.1 mol dm^{-3} NaOH. Crystals of the complex were obtained by slow evaporation of this solution at room temperature Anal. Calcd for $C_{23}H_{37}N_4Cl_3O_{10}Pd$: C, 41.14; H, 5.55; N, 8.34. Found: C, 41.1; H, 5.6; N, 8.3. X-ray analysis revealed that the water content of this compound is actually 2.6 molecules.

X-ray Structure Analysis. Analyses on single crystals of [PdLH₂Cl](NO_3)·2.6H_2O and [Cu₂L1Cl₂]$(ClO_4)(BPh_4)$·CH_3CN were carried out with an Enraf-Nonius CAD4 X-ray diffractometer that uses an equatorial geometry; a summary of the crystal data is reported in Table 1.

A prismatic yellow crystal of [PdLH₂Cl](NO_3)·2.6H_2O (approximate dimensions 0.4 × 0.5 × 0.5 mm) and a prismatic blue crystal of [Cu₂L1Cl₂]$(ClO_4)(BPh_4)$·CH_3CN (approximate dimensions 0.3 × 0.6 × 0.4 mm) were mounted on the diffractometer and used for data collections at room temperature with graphite-monochromated Mo Kα radiation. Cell parameters for both compounds were determined by least-squares refinement of diffractometer setting angles for 25 carefully centered reflections ($14 \le 2\theta \le 24°$). The intensity of two standard reflections per compound were monitored periodically during data collections: no loss of intensity was recognized.

A total of 4992 ($2\theta_{max} = 50°$) and 2326 ($2\theta_{max} = 40°$) reflections for [PdLH₂Cl](NO_3)·2.6H_2O and [Cu₂L1Cl₂]$(ClO_4)(BPh_4)$·CH_3CN, respectively, were collected. Intensity data for both collections were

Table 1. Crystal Data and Structure Refinement for [PdLH₂Cl](NO_3)·2.6H_2O (**1**) and [Cu₂L1Cl₂]$(ClO_4)(BPh_4)$·CH_3CN (**2**)

	(1)	(2)
empirical formula	$C_{23}H_{36.2}ClN_4O_{9.6}Pd$	$C_{56}H_{73}BCl_3Cu_2N_7O_4$
fw	664.21	1152.46
temp, K	298	298
radiation	Mo Kα, graphite monochromated	
wavelength, Å	0.71069	0.71069
space group	$P\bar{1}$	$P2_1/m$
a, Å	8.472(3)	11.526(2)
b, Å	12.178(2)	13.552(2)
c, Å	14.498(4)	18.078(6)
α, deg	78.26(2)	90
β, deg	87.20(3)	96.47(2)
γ, deg	77.72(2)	90
V, $Å^3$	1431.0(7)	2806(1)
Z	2	2
D_c, g/cm^3	1.542	1.364
μ, mm^{-1}	0.799	0.952
crystal size, mm	0.4 × 0.5 × 0.5	0.3 × 0.6 x 0.4
R^a [I > 2σ(I)]	0.0727	0.0823
w$R2^b$	0.2294	0.2366

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

(20) Codington, J. F.; Mosettig, E. *J. Org. Chem.* **1952**, *17*, 1034.

corrected for Lorentz and polarization effects; absorption corrections were applied by the Walker and Stuart method,[21] once the structures were solved.

The structures were solved by the Patterson method which showed the palladium and the copper atoms for $[PdLH_2Cl](NO_3)\cdot 2.6H_2O$ and $[Cu_2L1Cl_2](ClO_4)(BPh_4)\cdot CH_3CN$, respectively. Subsequent Fourier maps showed all non-hydrogen atoms in both structures. Refinements were performed by means of the full-matrix least-squares method. In both cases the function minimized was $\Sigma w(F_o^2 - F_c^2)^2$ with $w = 1/[\sigma^2(F_o^2) + (0.1543P)^2 + 2.92P]$ for $[PdLH_2Cl](NO_3)\cdot 2.6H_2O$ and $w = 1/[\sigma^2(F_o^2) + (0.1570P)^2 + 1.62P]$ for $[Cu_2L1Cl_2](ClO_4)(BPh_4)\cdot CH_3CN$ ($P = (\max(F_o^2,0) + 2F_c^2)/3$).

All calculations, carried out on a DEX 486-DX computer, were performed with the SHELX-76[22] and the SHELX-93[22] programs which use the analytical approximation for the atomic scattering factors and anomalous dispersion corrections for all the atoms from ref 23.

$[PdLH_2Cl](NO_3)\cdot 2.6H_2O$. The compound crystallizes in the triclinic family, space group $P\bar{1}$ ($Z = 2$). All non-hydrogen atoms were anisotropically refined while an isotropic, fixed temperature factor ($U = 0.052$ Å^2) was used for the hydrogen atoms, which have been introduced in calculated positions, and their coordinates wer refined according to those of the linked carbon atoms. The O7 oxygen atom of a disordered water molecule has been refined with population parameter 0.6. The ΔF map, carried out in the last refinement step, did not allow the location of the two acidic protons and the hydrogen atoms of the solvent molecules. The final agreement factors for 356 refined parameters, corresponding to the atomic coordinates listed in Table 2, were $R = 0.073$ (for 4297 unique observed reflections with $I > 2.0\sigma(I)$) and $wR^2 = 0.2294$.

$[Cu_2L1Cl_2](ClO_4)(BPh_4)\cdot CH_3CN$. Crystals of the compound belong to the monoclinic space group $P2_1/m$. The $[Cu_2L1Cl_2]^{2+}$ cation possesses a symmetry plane, and only half the molecular formula is contained in the asymmetric unit ($Z = 2$). Anisotropic thermal parameters have been used for the copper, chlorine, oxygen, nitrogen, and boron atoms; the hydrogen atoms of the ligand molecule were introduced in calculated positions and refined in agreement with the linked carbon atoms with an overall, fixed temperature factor $U = 0.068$ Å^2. Two peaks linked to each other have been found in the difference Fourier map, one of them lying on the symmetry plane, and have been assigned to a disordered CH_3CN solvent molecule and consequently refined. The final agreement factors for 216 refined parameters, corresponding to the atomic coordinates listed in Table 3, were $R = 0.082$ (for 1559 unique observed reflections with $I > 2.0\sigma(I)$) and $wR^2 = 0.2366$.

Potentiometric Measurements. Equilibrium constants for complexation reactions with LH_2 and **L1** were determined by pH-metric measurements ($pH = -\log [H^+]$) in 0.15 mol dm^{-3} NaCl at 298.10.1 K, by using the potentiometric equipment that has been already described.[24] 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 CO_2-free NaOH solutions and determining the equivalent point by Gran's method,[25] which allows the determination of the standard potential E°, and the ionic product of water ($pK_w = 13.73(1)$ at 298.1 K in 0.15 mol dm^{-3} NaCl). Concentrations of 1×10^{-3}–2×10^{-3} mol dm^{-3} of ligand and metal ion were employed in the potentiometric measurements by performing three titration experiments (about 100 data points each) in the pH ranges 2.5–10.5 (Cu^{2+}), 2.5–7.5 (Zn^{2+}), 2.5–8.5 (Cd^{2+}), and 3.5–10.5 (Pd^{2+}). The computer program SUPERQUAD[26] was used to calculate equilibrium constants from emf data. Ligands protonation constants were from ref 27. All titrations were treated either as single sets or as separated entities, for each system, without significant variation in the values of the determined constants.

Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters (Å$^2 \times 10^3$) for $[PdLH_2Cl](NO_3)\cdot 2.6H_2O$

	x/a	y/b	z/c	U(eq)
Pd	3108(1)	1552(1)	3124(1)	44(1)
Cl	5850(2)	1311(2)	3220(2)	59(1)
O(1)	1324(9)	250(7)	−1687(5)	87(2)
O(2)	1756(11)	1916(7)	−1512(5)	98(3)
C(1)	1781(9)	813(8)	−1215(5)	59(2)
C(2)	2389(8)	372(7)	−242(5)	49(2)
C(3)	2247(10)	−716(7)	257(6)	60(2)
C(4)	2787(10)	−1109(7)	1126(6)	58(2)
C(5)	3574(9)	−446(7)	1583(5)	54(2)
C(6)	3772(9)	594(6)	1094(5)	53(2)
C(7)	3192(10)	1015(6)	207(5)	53(2)
C(8)	4163(10)	−860(7)	2582(5)	59(2)
N(1)	3130(7)	−239(5)	3271(4)	46(1)
C(9)	3764(11)	−770(7)	4249(5)	60(2)
C(10)	1389(9)	−331(6)	3235(5)	49(2)
C(11)	325(9)	653(6)	3578(5)	48(2)
N(2)	679(6)	1763(4)	3052(4)	35(1)
C(12)	49(9)	2018(6)	2076(5)	48(2)
C(13)	30(9)	2718(6)	3540(5)	47(2)
C(14)	898(8)	3696(5)	3166(5)	45(2)
N(3)	2658(7)	3297(5)	3270(3)	40(1)
C(15)	3133(11)	3239(7)	4264(5)	55(2)
C(16)	3547(9)	4103(6)	2661(5)	48(2)
C(17)	3384(8)	4186(6)	1609(4)	42(1)
C(18)	4485(8)	3506(6)	1145(5)	44(2)
C(19)	4426(8)	3588(5)	172(5)	41(1)
C(20)	3194(8)	4408(6)	−325(4)	43(1)
C(21)	2091(9)	5115(6)	128(5)	54(2)
C(22)	2178(10)	5027(7)	1082(6)	56(2)
C(23)	3078(10)	4550(7)	−1394(5)	53(2)
O(3)	4213(7)	3858(5)	−1756(3)	58(1)
O(4)	2090(9)	5263(6)	−1841(4)	82(2)
N(4)	7692(8)	3697(5)	−4448(5)	53(2)
O(41)	8893(10)	4024(8)	−4774(7)	108(3)
O(42)	6518(10)	3827(7)	−4919(7)	100(2)
O(43)	7636(12)	3294(7)	−3623(7)	108(3)
O(5)	3818(8)	4147(6)	−3642(4)	73(2)
O(6)	1357(12)	2867(9)	−3316(6)	117(3)
O(7)	1902(18)	1158(12)	−4199(11)	104(4)

Microcalorimetric Measurements. The enthalpies of complexation of Cu^{2+} and Cd^{2+} with L^{2-} have been determined in 0.15 mol dm^{-3} NaCl at 298.1 K by means of an automated system composed of a Thermometric AB thermal activity monitor (Model 2277) equipped with a perfusion/titration device and a Hamilton pump (Model Microlab M) coupled with a 0.250 cm^3 gastight Hamilton syringe (Model 1750 LT). The microcalorimeter was checked by determining the enthalpy of reaction of strong acid (HCl) with strong base (NaOH). The value obtained, −13.55(5) kcal mol^{-1}, was in agreement with literature values.[28] Further checks were performed by determining the enthalpies of protonation of ethylenediamine. Typically 1.5 cm^3 of 5×10^{-3} mol dm^{-3} acidic ligand solution containing the metal ion (3×10^{-3} mol dm^{-3}) in 0.15 mol dm^{-3} NaCl was charged into the calorimetric ampule. After thermal equilibration, 0.015 cm^3 portions of 0.15 mol dm^{-3} NaOH standard solution were delivered. Under the reaction conditions and with employment of the determined equilibrium constants, the concentrations of the species present in solution before and after addition were calculated and the corresponding enthalpies of reaction were determined from the calorimetric data by means of the KK88 program.[29] The enthalpies of protonation were from ref 27. At least three titrations (about 30 points each) were performed for each system. The titration

(21) Walker, N.; Stuart, D. D. *Acta Crystallogr., Sect. A* **1983**, *39*, 158.
(22) (a) Sheldrick, G. M. *SHELX-76, Program for Crystal Structure Determination*; University of Cambridge: Cambridge, England, 1976. (b) Sheldrick, G. M. *SHELXL-93*; University of Göttingen: Göttingen, Germany, 1993.
(23) *International Tables for X-ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. IV.
(24) Bianchi, A.; Bologni, L.; Dapporto, P.; Micheloni, M.; Paoletti, P. *Inorg. Chem.* **1984**, *23*, 1201.
(25) (a) Gran, G. *Analyst (London)* **1952**, *77*, 661. (b) Rossotti, F. J.; Rossotti, H. *J. Chem. Educ.* **1965**, *42*, 375.
(26) Gans, P.; Sabatini, A.; Vacca, A. *J. Chem. Soc., Dalton Trans.* **1985**, 1195.
(27) Bazzicalupi, C.; Bencini, A.; Bianchi A.; Fusi, V.; Paoletti, P.; Valtancoli, B. *J. Chem. Soc., Perkin Trans. 2*, in press.
(28) Hall, J. P.; Izzat, R. M.; Christensen, J. J. *J. Phys. Chem.* **1963**, *67*, 2605.
(29) Micheloni, M. KK88 computer program (Fortran); last version of the KK77 computer program, written by A. Vacca.

Table 3. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for $[Cu_2L1Cl_2](ClO_4)(BPh_4)\cdot CH_3CN$

	x/a	*y/b*	*z/c*	*U*(eq)
Cu(1)	7513(2)	2500	5222(1)	39(1)
Cu(2)	12347(2)	2500	7889(1)	41(1)
Cl(1)	8427(5)	2500	4211(3)	64(2)
Cl(2)	13748(4)	2500	7156(3)	72(2)
N(1)	6724(11)	2500	6147(7)	37(4)
C(1)	7574(16)	2500	6810(10)	46(5)
C(2)	6009(11)	1572(10)	6108(7)	50(4)
C(3)	6716(11)	739(11)	5911(7)	53(4)
N(2)	7269(8)	993(8)	5235(5)	43(3)
C(4)	6417(12)	817(13)	4578(8)	76(5)
C(5)	8300(11)	369(11)	5143(7)	48(4)
C(6)	9268(9)	440(9)	5781(6)	33(3)
C(7)	9393(12)	−292(11)	6335(7)	59(4)
C(8)	10363(11)	−241(12)	6855(8)	60(4)
C(9)	11233(10)	436(10)	6857(6)	39(3)
C(10)	11077(10)	1151(10)	6301(6)	37(3)
C(11)	10132(9)	1164(10)	5784(6)	35(3)
C(12)	12319(12)	357(12)	7393(8)	62(4)
N(3)	12385(8)	983(9)	8063(5)	50(3)
C(13)	13540(13)	813(14)	8496(9)	88(6)
C(14)	11441(13)	741(12)	8528(8)	69(5)
C(15)	11230(13)	1603(11)	9012(8)	60(4)
N(4)	11074(11)	2500	8552(8)	52(5)
C(16)	9907(17)	2500	8105(11)	58(6)
B	7284(17)	2500	9892(10)	31(5)
C(17)	8146(13)	2500	10686(9)	29(4)
C(18)	9369(15)	2500	10688(10)	41(5)
C(19)	10124(15)	2500	11338(9)	42(5)
C(20)	9686(16)	2500	11989(10)	45(5)
C(21)	8500(16)	2500	12013(11)	49(5)
C(22)	7777(16)	2500	11373(9)	42(5)
C(23)	7526(9)	1497(9)	9391(6)	31(3)
C(24)	8352(10)	791(10)	9613(7)	39(3)
C(25)	8542(11)	−29(11)	9172(7)	51(4)
C(26)	7925(11)	−135(12)	8501(7)	59(4)
C(27)	7040(13)	506(12)	8273(9)	71(5)
C(28)	6841(11)	1296(11)	8718(7)	54(4)
C(29)	5932(14)	2500	10089(9)	34(5)
C(30)	5341(10)	1640(11)	10222(7)	50(4)
C(31)	4239(12)	1631(13)	10487(7)	66(4)
C(32)	3722(19)	2500	10604(11)	67(6)
Cl(3)	3059(5)	2500	4466(4)	63(2)
O(1)	2155(21)	2500	4883(16)	161(10)
O(2)	3675(14)	1705(12)	4597(14)	217(10)
O(3)	2587(25)	2500	3775(14)	235(17)
C(33)	4934(30)	2500	2649(19)	142(12)
C(34)	4943(27)	1244(27)	2785(17)	203(12)

curves for each system were treated either as a single set or as separated entities without significant variation in the values of the enthalpy changes.

Results and Discussion

Synthesis. Methyl p-(α-chloromethyl)benzoate (**2**; Scheme 1) was prepared by following the procedure reported by Codington et al. for the analogous bromo derivative.[20]

Reactions of **1**[19] with methyl *p*-(α-chloromethyl)benzoate (**2**) carried out under the usual mild conditions (CH_3CN in the presence of a base) led to the diester **3** in very poor yields. Better yields (70%) are obtained by using more drastic conditions (NEt_3, 100 °C). LH_2 can be simply obtained by hydrolysis of the diester **3**.

The bis(chloromethyl) derivative **5** is synthesized from **3** by standard methods. Reduction of the diester **3** with $LiAlH_4$ in THF (at reflux, 15 h) yields the corresponding dialcohol **4** (90%), which can be purified as its hydrochloride salt. Compound **5** is obtained by treating the above dialcohol with $SOCl_2$ in $CHCl_3$ (60 °C, 4 h) and isolated as its trihydrochloride salt (93%). Reaction of **5** with compound **1** in CH_3CN in the presence of K_2CO_3, a modification of the method of Richman and Atkins,[30] affords the macrocycle **L1**.

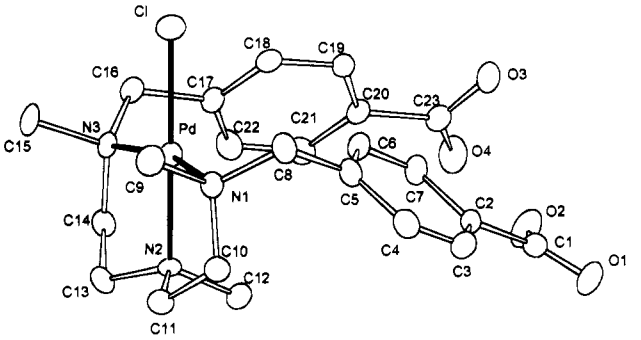


Figure 1. ORTEP drawing of the $[PdLH_2Cl]^+$ cation. Ellipses are at the 30% probability level.

Table 4. Selected Bond Lengths (Å) and Angles (deg) for $[PdLH_2Cl](NO_3)\cdot 2.6H_2O$

Pd−N(2)	2.024(5)	Pd-N(1)	2.143(6)
Pd−N(3)	2.130(5)	Pd-Cl	2.286(2)
N(2)−Pd−N(3)	85.9(2)	N(2)−Pd−Cl	179.5(2)
N(2)−Pd−N(1)	85.1(2)	N(3)−Pd−Cl	94.0(2)
N(3)−Pd−N(1)	165.3(2)	N(1)−Pd−Cl	94.9(2)

Compound **4** is a versatile building block for the assembly of macrocyclic or macropolycyclic structures. The same synthetic procedure can produce other *p*-cyclophane receptors by substitution of **1** with other reagents in the cyclization reaction, originating macrocyclic molecules characterized by two 1,4-benzo units that link two different binding moieties.[31]

Description of the Structures. $[PdLH_2Cl]NO_3\cdot 2.6H_2O$. The crystal structure consists of $[PdLH_2Cl]^+$ complex cations, nitrate anions, and lattice water molecules. Figure 1 shows an ORTEP[32] drawing of the $[PdLH_2Cl]^+$ cation with atom labeling. A selected list of bond lengths and angles for the metal coordination environment is reported in Table 4.

The palladium atom is coordinated to the three nitrogen atoms of the ligand molecule (the Pd−N bond distances fall in the range 2.024(5)−2.143(6) Å) and a chloride ion (Pd−Cl = 2.286(2) Å), in a resulting square planar coordination geometry. The four donor atoms are almost coplanar (maximum deviation 0.137(6) Å for N1), and the metal ion is displaced 0.0894(6) Å from this plane, shifted toward the aromatic rings. Both N−Pd−N angles are less than 90° because of the short ethylenic chains. The planes defined by the two aromatic rings C2−C3−C4−C5−C6−C7 and C17−C18−C19−C20−C21−C22 form a dihedral angle of 71.4(6)° and give rise respectively to angles of 112.2(5) and 99.9(7)°, with respect to the planes formed by the donor atoms. The pairs of atoms C6, C7 and C18, C19 are separated by a mean distance of 3.74 Å from each other; the shortest distance is 3.50(1) Å for C7···C19. As a consequence of this arrangement, molecular strain is shown by the N1−C8−C5 and N3−C16−C17 angles, whose values are 113.0(6) and 115.1(5)°, respectively, instead of the sp^3 theoretical one. Both carboxylic groups are almost coplanar with respect to the linked aromatic rings (the dihedral angles are 12.3(7)° for C1, O1, O2 and 5(1)° in the case of C23, O3, O4). The two C−O bond distances of each carboxylic groups are significantly different (C1−O1 = 1.19(1) Å, C1−O2 =

(30) Richman, J. E.; Atkins, T. J. *J. Am. Chem. Soc.* **1974**, *96*, 2268.
(31) Bazzicalupi, C.; Bencini, A.; Bianchi A.; Fusi, V.; Giorgi, C.; Micheloni, M.; Paoletti, P.; Valtancoli, B. *Tetrahedron Lett.* **1994**, *35*, 8469.
(32) Johnson, C. K. *ORTEP*; Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1971.

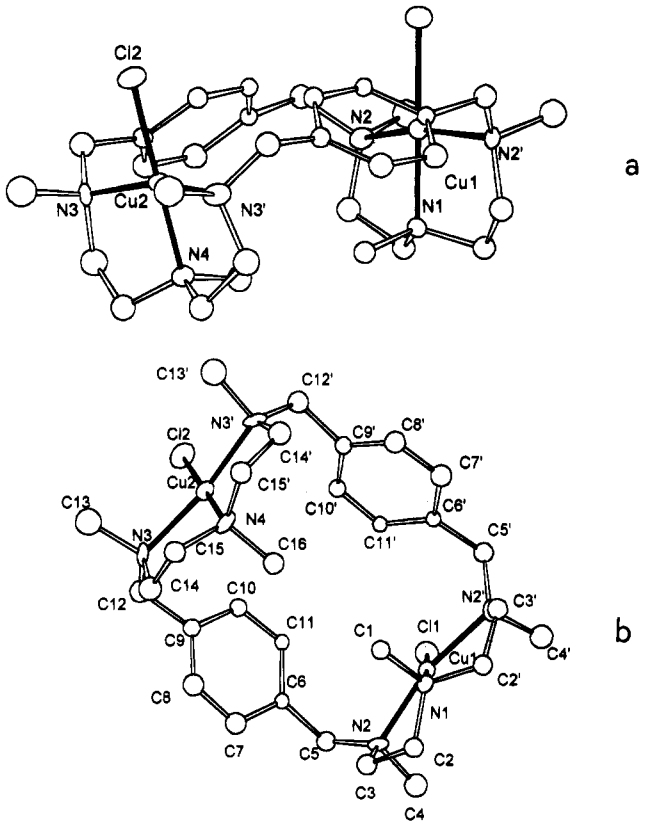


Figure 2. ORTEP drawings of the $[Cu_2L1Cl_2]^{2+}$ cation: (a) Lateral view; (b) top view. Ellipses are at the 30% probability level.

Table 5. Selected Bond Lengths (Å) and Angles (deg) for $[Cu_2L1Cl_2](ClO_4)(BPh_4)\cdot CH_3CN$[a]

Cu(1)−N(1)	1.992(13)	Cu(2)−N(4)	1.996(14)
Cu(1)−N(2)	2.062(11)	Cu(2)−N(3)	2.079(11)
Cu(1)−Cl(1)	2.210(6)	Cu(2)−Cl(2)	2.201(5)
N(1)−Cu(1)−N(2)	85.1(3)	N(4)−Cu(2)−N(3)	85.0(3)
N(1)−Cu(1)−N(2)[1]	85.1(3)	N(4)−Cu(2)−N(3)[1]	85.0(3)
N(2)−Cu(1)−N(2)[1]	164.1(5)	N(3)−Cu(2)−N(3)[1]	162.7(6)
N(1)−Cu(1)−Cl(1)	178.7(4)	N(4)−Cu(2)−Cl(2)	179.9(4)
N(2)−Cu(1)−Cl(1)	95.1(3)	N(3)−Cu(2)−Cl(2)	95.0(3)
N(2)[1]−Cu(1)−Cl(1)	95.1(3)	N(3)1−Cu(2)−Cl(2)	95.0(3)

[a] Superscript 1 indicates equivalent atom generated by the following symmetry transformation: x, $0.5 - y$, z.

1.32(1) Å; C23−O3 = 1.30(1) Å, C23−O4 = 1.179(9) Å). This feature led us to suppose that the acidic protons are localized on O2 and O3. The short interatomic distances, due to H-bond interactions, between O2, O3 and the O6 and O5 oxygen atoms of two water molecules (O2···O6 = 2.64(1) Å and O3···O5 = 2.727(8) Å) support this hypothesis.

The oxygen atoms of the lattice water molecules are also involved in a hydrogen bond network connecting each of them and the O41 and O42 oxygen atoms of the nitrate anion (O5···O6 = 2.83(1) Å, O6···O7 = 2.61(2) Å, O42···O5 = 2.87(1) Å, O41···O6′ = 2.96(1) Å, O42···O5′ = 2.85(1) Å; the primed atoms are symmetry related).

$[Cu_2L1Cl_2](ClO_4)(BPh_4)\cdot CH_3CN$. The crystal structure consists of $[Cu_2L1Cl_2]^{2+}$ complex cations, perchlorate and tetraphenylborate anions, and disordered CH_3CN molecules. Figure 2 shows an ORTEP[32] drawing of the $[Cu_2L1Cl_2]^{2+}$ cation with atom labeling. A selected list of bond lengths and angles for the metal coordination environment is reported in Table 5. The complex possesses a crystallographic symmetry plane defined by the metal centers, the chloride ions, the N1 and N4 donor atoms, and the C1 and C16 methyl groups.

Each copper atom is localized in an N_3 subunit, 6.945(3) Å apart from each other. Both metal ions are coordinated by three nitrogens and a chloride anion, in a square planar arrangement. Considering the mean plane determined by the N1, N2, N2′, and Cl1 (maximum deviation 0.23(1) Å for N1), Cu1 is 0.109(2) Å shifted toward the other metal cation. In the coordination environment of Cu2, the N3, N3′, and N4 nitrogens, together with Cl2, give rise to a mean plane (maximum deviation 0.24(1) Å for N4), Cu2 being shifted 0.139(2) Å toward the other Cu(II) ion. Similarly to what is observed for $[PdLH_2Cl]^+$, the N−Cu−N angles are less than 90° because of the ethylenic chains.

The coordination planes of the two metals are almost parallel, forming a dihedral angle of 13.6(2)°. The macrocycle adopts a boat conformation with the chloride ions located on the same side. The two aromatic rings are rather close to each other, the shortest distance being 3.62(2) Å for C11···C11′, and define two planes forming a dihedral angle of 69(1)°, which is equal, within the experimental error, to the analogous angle found in the $[PdLH_2Cl]^+$ cation. In addition, these two planes are almost perpendicular to the coordination planes of the metal ions (the dihedral angles are 83.5(8) and 85.3(7)° with respect to the coordination planes of Cu1 and Cu2). As a consequence, the complex gives rise to a nearly parallelepipedic internal cavity of approximate dimensions 4 × 6 × 7 Å. The N2−C5−C6 and N3−C12−C9 angles show molecular strain, their values being 114(1) and 117(1)°, respectively.

It is worth noting that the macrocycle **L1** is highly rigid. Actually, the overall conformation of the molecule in the present structure does not show any remarkable differences from that found in the $[L1H_4](ClO_4)_4$ salt.[27] In both compounds the ligand is boat-shaped with all the nitrogen atoms in *endo* conformations. The methyl groups bound to the benzylic nitrogens point outside the cavity, while the remaining two (C1, C16) point inside. As a consequence, the macrocyclic cavity is hindered by the aromatic rings and the C1, C16 methyl groups.

To our knowledge, few structures of Cu^{2+} complexes with polyazaparacyclophane ligands have been reported.[17,18] The closest comparisons are in the binuclear complex of the **L2** ligand, $[Cu_2L2(CH_3CO_2)_2](ClO_4)_2\cdot 5H_2O$,[17] where each Cu^{2+} ion is coordinated by three nitrogen atoms of the macrocycle and one bidentate acetate anion. However, the absence of methyl groups and the presence of propylenic chains give rise to an increased flexibility of this macrocycle with respect to **L1**, leading to a longer Cu−Cu distance (8.40 Å).

Solution Equilibria. The protonation behaviors of L^{2-} and **L1** in aqueous solution were analyzed by potentiometry, microcalorimetry, and ^1H and ^{13}C NMR studies, and the results are presented elsewhere.[27]

Complexation Equilibria by LH_2. It has been shown[27] that the LH_2 species has an ionic structure in which the two protons are located on the benzylic nitrogens. The main species is found in the 4−6.5 pH range, while in more acidic solutions first the carboxylate groups and then the central amino group undergo protonation. Depending on pH, both the triamine moiety and the carboxylate groups are available for metal complexation. The ligational ability of this ligand has been tested toward Cu^{2+}, Zn^{2+}, Cd^{2+}, and Pd^{2+}, and the equilibrium constants determined in 0.15 mol dm^{-3} NaCl solutions at 298.1 K are collected in Tables 6 (Cu^{2+}, Zn^{2+}, Cd^{2+}) and 7 (Pd^{2+}). In the case of Pd^{2+} the formation of chloro complexes was also considered. Treatment of emf data by means of the computer program SUPERQUAD[26] revealed one Cl^- is always involved in Pd^{2+} complexation equilibria (Table 7).

Table 6. Logarithms of the Equilibrium Constants Determined in 0.15 mol dm^{-3} NaCl Aqueous Solution at 298.1 K for the Complexation Reactions of Cu^{2+}, Zn^{2+}, and Cd^{2+} with L^{2-}

reacn	log K		
	Cu^{2+}	Zn^{2+}	Cd^{2+}
$L^{2-} + M^{2+} = ML$	9.29(1)[a]	3.49(2)	4.84(5)
$L^{2-} + M^{2+} + H^+ = MLH^+$			12.18(8)
$L^{2-} + M^{2+} + 2H^+ = MLH_2^{2+}$			18.30(3)
$L^{2-} + M^{2+} + H_2O = MLOH^- + H^+$	1.11(1)		−3.22(6)
$L^{2-} + M^{2+} + 2H_2O = ML(OH)_2^{2-} + 2H^+$	−9.24(5)		
$ML + H^+ = MLH^+$			7.3(1)
$MLH^+ + H^+ = MLH_2^{2+}$			6.1(1)
$ML + OH^- = MLOH^-$	5.55(4)		5.7(1)
$MLOH^- + OH^- = ML(OH)2^{2-}$	3.38(7)		

[a] Values in parentheses are standard deviations on the last significant figure.

Table 7. Logarithms of the Equilibrium Constants Determined in 0.15 mol dm^{-3} NaCl Aqueous Solution at 298.1 K for the Complexation Reactions of Pd^{2+} with L^{2-}

reacn	log K
$Pd^{2+} + L^{2-} + Cl^- = PdLCl^-$	19.10(2)[a]
$Pd^{2+} + L^{2-} + Cl^- + H^+ = PdLHCl$	23.15(2)
$PdLCl^- + H^+ = PdLHCl$	4.05(4)

[a] Values in parentheses are standard deviations on the last significant figure.

As can be deduced from Table 6, the stability of the Zn^{2+} and Cd^{2+} complexes is rather low, especially for Zn^{2+}. For this reason the potentiometric measurements involving these metal ions were limited to acidic−neutral media (pH < 7.5) for Zn^{2+} or slightly alkaline (pH < 8.5) for Cd^{2+} in order to avoid the formation of insoluble metal hydroxides. Under these conditions Zn^{2+} forms the unique **ZnL** species, while also mono-, and diprotonated and monohydroxylated complexes are formed by **CdL**. On the other hand, the Cu^{2+} complexes are more stable allowing the solution study to be performed also in alkaline solution (pH 10.5), where mono- and dihydroxylated species are produced. Although the **CdL** complex presents a significantly lower stability than **CuL**, Cd^{2+} complexation takes place in more acidic solution than for Cu^{2+}, due to the tendency of the former metal ion to form protonated species (Figure S1, supplementary material). The equilibrium constants for the successive addition of two protons to **CdL** (log K = 7.3(1) and 6.1(1), Table 6) are very high, if compared with the protonation constants of the free ligand, and their magnitude could justify protonation of two uncoordinated amino groups. This means that at least two nitrogen donors are excluded from coordination in the Cd^{2+} complex and the carboxylate groups play an important role in the binding of the metal ion. To confirm this rather surprising behavior we performed microcalorimetric measurements to determine the enthalpic and entropic contributions to the formation of the Cd^{2+} complexes reported in Table 8. Complexation of Cd^{2+} by L^{2-} to produce **CdL** is almost athermic and promoted by a favorable entropic contribution as generally observed, and expected, for Cd^{2+} carboxylate complexes.[33] Otherwise, the stability of the Cd^{2+} complexes with polyamine ligands is mainly enthalpic in nature. Furthermore, as far as the protonation of **CdL** is considered (Table 8), the enthalpic terms for the reactions $CdL + H^+ = CdLH^+$ ($-\Delta H^\circ$ = 6.0(2) kcal mol^{-1}) and $CdLH^+ + H^+ = CdLH_2^{2+}$ ($-\Delta H^\circ$ = 7.2(1) kcal mol^{-1}) are very similar to the enthalpy changes for the first two protonation steps of L^{2-} (5.76 and 8.68 kcal mol^{-1}, respectively)[27] involving the two benzylic amino groups.

(33) Smith, R. L.; Martell, A. E. *Critical Stabuility Constants*; Plenum: New York, 1975.

Table 8. Thermodynamic Parameters Determined in 0.15 mol dm^{-3} NaCl at 298.1 K for the Complexation Reactions of Cu^{2+} and Cd^{2+} with L^{2-}

reacn	$-\Delta G^\circ$, kcal mol^{-1}	$-\Delta H^\circ$, kcal mol^{-1}	$T\Delta S^\circ$, kcal mol^{-1}
$Cu^{2+} + L^{2-} = CuL$	12.7(1)[a]	12.9(2)	−0.2(2)
$Cd^{2+} + L^{2-} = CdL$	6.60(7)	1.1(2)	5.5(2)
$Cd^{2+} + L^{2-} + H^+ = CdLH^+$	16.6(1)	7.1(1)	9.5(2)
$Cd^{2+} + L^{2-} + 2H^+ = CdLH_2^{2+}$	24.96(4)	14.3(1)	10.7(1)
$CdL + H^+ = CdLH^+$	10.0(1)	6.0(2)	4.0(3)
$CdLH^+ + H^+ = CdLH_2^{2+}$	8.3(1)	7.2(1)	1.1(2)

[a] Values in parentheses are standard deviations on the last significant figure.

Considering that proton transfer processes involving carboxylate groups are almost athermic, these results clearly evidence that protonation of **CdL** occurs on nitrogen atoms and, consequently, the carboxylate groups are the principal coordination sites for the metal ion.

In agreement with these observations, the equilibrium constant for the protonation of the $PdLCl^-$ complex (log K = 4.05(4)), taking place on the carboxylate groups, as demonstrated by the crystal structure of $(PdLH_2Cl)NO_3 \cdot 2.6H_2O$, is lower by more than 2 orders of magnitude than the protonation constants of the **CdL** complex.

A different behavior is observed for the **CuL** complex. First of all the thermodynamic data for the formation of **CuL** are in agreement with the values observed for many other copper(II) complexes with polyamine ligands.[33] The stability of the complex is almost entirely due to the enthalpic contribution (Table 8). In addition **CuL** does not present any tendency toward protonation. The electronic spectrum of an aqueous solution of **CuL** is characterized by a main absorption at 651 nm (400 dm^3 mol^{-1} cm^{-1}) typical of distorted octahedral coordination environments in copper(II) complexes with polyamines. These are evidence of Cu^{2+} complexation by the N_3 moiety of the ligand.

Pd^{2+} forms with LH_2 the sparingly soluble complex $(PdLH_2Cl)Cl$ which crystallized in the potentiometric cell during emf data acquisition for complexation study. For this reason the pH-metric titrations in the presence of Pd^{2+} were performed from alkaline (pH 10.5) toward acidic (pH 3.5) solutions until formation of the solid was observed. In this pH range Pd^{2+} forms the complexed species $PdLCl^-$ and PdLHCl (Table 7). Also in the case of Pd^{2+} the stability of the complexes formed by **L** is low in comparison with other palladium(II) complexes with polyamines.

Complexation Equilibria by L1. As far as the macrocyclic ligand **L1** is concerned, it is to be noted that its ligational properties are strictly related to its ditopic nature. In fact **L1** presents a marked tendency to form both mononuclear and binuclear copper(II) complexed species (Table 9); the equilibrium constant for the binding of Cu^{2+} by $CuL1^{2+}$ (log K = 8.32(4), Table 9) is similar to that determined for the formation of $CuL1^{2+}$ (log K = 10.03(3), Table 9). This behavior is clearly depicted by the distribution diagrams of the species formed as a function of pH in the system Cu^{2+}/**L1** reported in Figure S2 (supplementary material). Both mononuclear and binuclear complexed species abound in solutions containing the ligand and the metal ion in equimolecular quantities (Figure S2a) over the entire pH range. On the other hand, for 2:1 Cu^{2+}:**L1** molar ratios, the formation of monometallic complexes is depressed and only the species $CuL1H_2^{4+}$ is formed in acidic media (Figure S2b). The complex $CuL1^{2+}$ presents a marked tendency toward protonation (Table 9) forming mono- and diprotonated species. The equilibrium constants for the successive proto-

Table 9. Logarithms of the Equilibrium Constants Determined in 0.15 mol dm^{-3} NaCl at 298.1 K for the Complexation Reactions of Cu^{2+} with **L1**

reacn	log K
$Cu^{2+} + L1 = CuL1^{2+}$	10.03(3)[a]
$Cu^{2+} + L1 + H^+ = CuL1H^{3+}$	17.96(2)
$Cu^{2+} + L1 + 2H^+ = CuL1H^{4+}$	24.73(1)
$Cu^{2+} + L1 + H_2O = CuL1OH^+ + H^+$	1.34(4)
$Cu^{2+} + L1 + 2H_2O = CuL1(OH) + 2H^+$	−9.78(5)
$2Cu^{2+} + L1 = Cu_2L1^{4+}$	18.35(1)
$2Cu^{2+} + L1 + H_2O = Cu_2L1OH^{3+} + H^+$	10.43(3)
$2Cu^{2+} + L1 + 2H_2O = Cu_2L1(OH)_2^{2+} + 2H^+$	2.39(2)
$CuL1^{2+} + H^+ = CuL1H^{3+}$	7.93(4)
$CuL1H^{3+} + H^+ = CuL1H_2^{4+}$	6.77(3)
$CuL1^{2+} + OH^- = CuL1OH^+$	5.04(5)
$CuL1OH^+ + OH^- = CuL1(OH)_2$	2.6(1)
$CuL1^{2+} + Cu^{2+} = Cu_2L1^{4+}$	8.32(4)
$Cu_2L1^{4+} + OH^- = Cu_2L1OH^{3+}$	5.81(5)
$Cu_2L1OH^{3+} + OH^- = Cu_2L1(OH)^{2+}$	5.69(5)

[a] Values in parentheses are standard deviations on the last significant figure.

nation of this complex are high indicating that protonation occurs on the uncoordinated N_3 donor set.

All these observations agree with the involvement of two identical moieties of the ligand in the coordination to both first and second Cu^{2+} ions, as observed in the molecular structure of the $(Cu_2L1Cl_2)^{2+}$ complex (Figure 2). In other words, the presence of the rigid spacers between the two triamine chains prevents the metal ion from binding to both N_3 donor sets. Consequently, only three nitrogen donor atoms bind the metal ions and facile deprotonation of the coordinated water molecules produces mono- and dihydroxylated species of both mono- and bimetallic complexes. The equilibrium constants for the addition of the first and the second OH^- anions to Cu_2L1^{4+} are almost equal within experimental errors (log K = 5.81(5) and 5.69(5), respectively) and very close to the equilibrium constant (log K = 5.04(5)) for the binding of the first OH^- to the monometallic $CuL1^{2+}$ complex, suggesting the hydroxide anions in $Cu_2L1(OH)_2^{2+}$ are located on two separated metal centers. Presumably, $Cu_2L1(OH)_2^{2+}$ has an array similar to $Cu_2L1Cl_2^{2+}$ in the observed structure (Figure 2).

It is worth noting that **L1** exhibits a poor coordination tendency toward Cu^{2+} in comparison with the analogous metacyclophane **L4** (Chart 1) ($L4 + Cu^{2+} = CuL4^{2+}$, log K = 13.79; $CuL4^{2+} + Cu^{2+} = Cu_2L4^{4+}$, log K = 9.68).[34] It is well-known that methyls have electron σ-donating properties. On the other hand, nitrogen methylation prevents the formation of H-bonds between water and amino groups, which contribute, *via* the H_2O- - -HN interaction, to the σ-donating ability of amino groups in aqueous solution.[35] Furthermore, the presence of methyl groups and two 1,4-benzo subunits, together with the short ethylenic chains, leads to a molecular crowding and stiffening of the receptor. Both these electronic and steric factors explain the low binding ability toward metal cations exhibited by **L1**.

Such a rigidity and molecular crowding could also justify the rather unusual planar array of the four donors found in the $[Cu_2L1Cl_2]^{2+}$ complex cation. As reported above, the conformation of the ligand in the $[Cu_2L1Cl_2]^{2+}$ complex does not differ markedly from that found for the $[H_4L1]^{4+}$ cation,[27] confirming the high rigidity shown by the present molecule. Finally, the ligand **L2** (Chart 1) gives rise to a bimetallic Cu^{2+} complex, with each metal ion pentacoordinated by three nitrogens and a bidentate carboxylate anion. The more flexible structure of **L2** can be invoked to explain this relevant difference from the present case.

The electronic spectrum of the solid compound $[Cu_2L1Cl_2](ClO_4)(BPh_4)\cdot CH_3CN$ is very similar to that obtained for aqueous solutions containing Cu_2L1^{4+}, which presents two absorptions at 628 nm (ϵ 351 dm^3 mol^{-1} cm^{-1}) and 509 nm (ϵ 263 dm^3 mol^{-1} cm^{-1}), suggesting a planar coordination of Cu^{2+} also in aqueous solution.

It is of interest that the [CuL] and the $[CuL1]^{2+}$ complexes show similar stability constants, while, as observed by potentiometric studies, **L1** does not form detectable amounts of Zn^{2+} and Cd^{2+} complexes in aqueous solution. On the other hand, **L1** binds two Pd^{2+} ions forming the bimetallic complexed cation $Pd_2L1Cl_2^{2+}$ which has been isolated as its diperchlorate salt. These results give credence to the idea that the carboxylate groups of L^{2-} are the sites of coordination for both Cd^{2+} and Zn^{2+}. The N_3 binding subunits of L^{2-} and **L1**, constrained within these ligands, have poor coordinative ability so that metal ions which normally produce very stable complexes with polyamines, such as Cu^{2+} and Pd^{2+}, form complexes of lower stability with L^{2-} and **L1**, while Zn^{2+} and Cd^{2+} prefer the carboxylate groups of L^{2-} and do not interact appreciably with **L1**.

The high selectivity in metal cations complexation achieved by cyclization of the open ligand LH_2 is a stimulating result. In fact, the lipophilic character of the polyaza-*p*-cyclophane **L1** can be modulated by appropriate substitution on the aromatic spacers producing a new group of ditopic receptors for metal ion recognition, separation, and selective transport.

Acknowledgment. Financial support by the Italian Ministero dell'Università e della Ricerca Scientifica e Tecnologica (quota 60%) and the Progetto Finalizzato di Chimica Fine of the Italian Research Council (CNR) is gratefully acknowledged.

Supplementary Material Available: Tables S1−S10, listing crystallographic data, hydrogen positional parameters, isotropic and anisotropic thermal factors, bond distances and angles, and least-square planes, and plots of distribution diagrams for the complexes formed in the systems Cu^{2+}/**L** and Cd^{2+}/**L** (Figure S1) and Cu^{2+}/**L1** (Figure S2) (17 pages). Ordering information is given on any current masthead page.

IC9409468

(34) Menif, R.; Martell, A. E.; Squattrito, P. J.; Clearfield, A. *Inorg. Chem.* **1990**, *29*, 4723.
(35) Golub, G.; Cohen, H.; Meyerstein, D. *J. Chem. Soc., Chem. Commun.* **1992**, 397.