176 Inorg. Chem. 1988, 27, 176-180

Contribution from the Department of Chemistry, University of Florence, I-50144 Firenze, Italy,
Facultad de Ciencias Quimicas, University of Valencia, Valencia, Spain, and ISSECC (CNR), I-50121 Firenze, Italy

Synthesis and Ligational Properties of the Two Very Large Polyazacycloalkanes $[33]aneN_{11}$ and $[36]aneN_{12}$ Forming Trinuclear Copper(II) Complexes

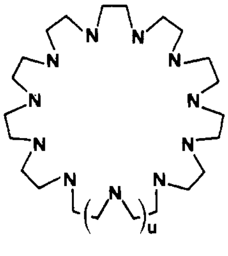
Andrea Bencini,[1a] Antonio Bianchi,[1b] Enrique Garcia-España,[1c] Mauro Micheloni,*[1a]
and Piero Paoletti*[1a]

Received February 17, 1987

The synthesis and characterization of the two new large polyazacycloalkanes 1,4,7,10,13,16,19,22,25,28,31-undecaazacyclotritriacontane, $[33]aneN_{11}$ (L1), and 1,4,7,10,13,16,19,22,25,28,31,34-dodecaazacyclohexatriacontane, $[36]aneN_{12}$ (L2), are described. The protonation constants and the stability constants of the copper(II) complexes of both macrocycles were determined by potentiometry at 25 °C in 0.15 mol dm^{-3} $NaClO_4$. Both macrocycles form very stable trinuclear species $[Cu_3L]^{6+}$; log K = 48.03 for L = L1 and log K = 51.43 for L = L2. The values of the constants as well as the electronic spectra of the $[Cu_3L]^{6+}$ (L = L1, L2) species are consistent with the hypothesis that all nitrogen atoms are coordinated to the copper(II) ions. Possible structures of the trinuclear species in solution are presented and discussed. Many other species are formed at the equilibrium: $[Cu_2L]^{4+}$, $[Cu_2LH]^{5+}$, $[Cu_2LH_2]^{6+}$, $[Cu_2LH_3]^{7+}$, $[Cu_3LOH]^{5+}$, and $[Cu_3L(OH)_2]^{4+}$ (with L = L1 and L = L2), $[Cu_2(L2)H_4]^{8+}$, $[Cu_2(L1)OH]^{3+}$, and $[Cu_3(L2)H]^{7+}$. The relative equilibrium constants have been determined.

Introduction

Some interesting complexation features, e.g. "anion coordination" and polynuclear complex formation, are displayed by large polyazacycloalkanes.[2-4] The adjective "large" has been used[5] to describe polyazacycloalkanes having more than six nitrogen donor atoms. In recent papers[5-8] we have studied four polyazacycloalkanes having the general formula $[3k]aneN_k$ (with k = 7-10) and able to form polynuclear metal complexes. In order to better understand the influence of the cyclic topology on the binding properties of these synthetic macrocyclic compounds, we have reported in the present publication the synthesis and the characterization as well as the ligational behavior toward hydrogen (basicity) and copper(II) ion of two very large polyazacycloalkanes: 1,4,7,10,13,16,19,22,25,28,31-undecaazacyclotritriacontane ($[33]aneN_{11}$, abbreviated as L1), and 1,4,7,10,13,16,19,22,25,28,31,34-dodecaazacyclohexatriacontane ($[36]aneN_{12}$, abbreviated as L2), k = 11 and k = 12 in the $[3k]aneN_k$ series.



u=1; L1

u=2; L2

Experimental Section

Synthesis of the Macrocycles. The overall synthetic path followed to obtain both macrocyclic ligands is reported in Figure 1. The synthetic procedure described in Figure 1 was modeled on the general procedure described by Atkins et al.[9] for smaller polyazamacrocycles. Some of the synthetic steps have been already reported in our recent publications;[7,8] however, for the purpose of clarity, each step is fully described. All chemicals were reagent grade and were utilized without further purification.

1,4,7,10,13-Pentakis(*p*-tolylsulfonyl)-1,4,7,10,13-pentaazatridecane (3). The starting material was obtained from the commercial 1,4,7,10,13-pentaazatridecane (**1**, Fluka product) by double distillation under reduced pressure. The fraction collected was that one between 265 and 270 °C at 0.1 Torr. A solution of **1** (19.9 g, 0.105 mol) in 100 cm^3 of pyridine was added to a solution of *p*-toluenesulfonyl chloride (100 g, 0.53 mol) in 300 cm^3 of pyridine placed in a 1-dm^3 four-necked round-bottom flask equipped with a mechanical stirrer. The addition of the pentaamine **1** solution was carried out in such a way that the reaction temperature was kept at 40-50 °C. After the addition the reaction mixture was maintained at 50 °C for 2 h. Then it was allowed to cool at room temperature and added to a vigorously stirred mixture of water and ice (2.5 dm^3) containing the amount of HCl necessary to neutralize the pyridine. The product obtained was filtered off, washed with water and ethanol, and dissolved in 300 cm^3 of chloroform. The resulting solution was washed three times with 0.1 mol dm^{-3} HCl and three times with water and then dried over Na_2SO_4. To the filtered warm solution was added 1 dm^3 of hot ethanol. When this mixture was cooled, a white product separated. The product was filtered off, washed with ethanol and diethyl ether, recrystallized from a chloroform/ethanol mixture (1:4), and then dried under vacuum at 50 °C: yield 40.7 g (40.5%); mp 173-175 °C; TLC,[10] one product with R_f 0.31. Anal. Calcd for $C_{43}H_{53}N_5S_5O_{10}$: C, 53.76; H, 5.77; N, 7.30; S, 16.70. Found: C, 53.6; H, 5.6; N, 7.2; S, 16.5.

3,6,9,12,15-Pentakis(*p*-tolylsulfonyl)-3,6,9,12,15-pentaazaheptadecane-1,17-diol (5). A finely powdered mixture of **3** (50 g, 0.052 mol), ethylene carbonate (10.6 g, 0.12 mol), and KOH (0.5 g) was placed in a 1-dm^3 three-necked round-bottom flask equipped with a mechanical stirrer, condenser, and thermometer. The stirred mixture was heated on an oil bath until it melted and then kept at 170 °C for 4 h. The mixture was allowed to cool at 110 °C, and then 500 dm^3 of methanol was rapidly added. The solution was refluxed for 1 h and then cooled at room temperature with stirring overnight. The white crude product obtained was filtered, washed with methanol, and recrystallized from an ethanol/methylene chloride mixture (4:1): yield 52.85 g (82.4%); mp 194-196 °C; TLC,[10] one product with R_f 0.21. Anal. Calcd for $C_{47}H_{61}N_5S_5O_{12}$: C, 53.85; H, 5.86; N, 6.68. Found: C, 53.7; H, 5.8; N, 6.6.

***O,O'*-Bis(methylsulfonyl)-3,6,9,12,15-pentakis(*p*-tolylsulfonyl)-3,6,9,12,15-pentaazaheptadecane-1,17-diol (7).** A solution of **5** (42 g, 0.04 mol) and 12.2 g of triethylamine in 500 cm^3 of anhydrous methylene chloride was cooled to -10 °C under nitrogen in a 1-dm^3 four-necked round-bottom flask equipped with mechanical stirrer. A 10.1-g (0.088-mol) portion of methanesulfonyl chloride in 50 cm^3 of dry methylene chloride was added dropwise over a period of 20 min, with stirring. The

---

[1] (a) University of Florence. (b) ISSECC (CNR). (c) University of Valencia.

[2] Graf, E.; Lehn, J. M. *J. Am. Chem. Soc.* **1976**, *98*, 6403. Dietrich, B.; Hosseini, M. W.; Lehn, J. M.; Session, R. B. *Ibid.* **1981**, *103*, 1282. Kimura, E.; Sakonaka, A.; Yatsunami, T.; Kodama, M. *Ibid.* **1981**, *103*, 3041.

[3] Peter, F.; Gross, M.; Hosseini, M. W.; Lehn, J. M. *J. Electroanal. Chem.* **1983**, *144*, 279. Manfrin, M. F.; Sabbatini, N.; Moggi, L.; Balzani, V.; Hosseini, M. W.; Lehn, J. M. *J. Chem. Soc., Chem. Commun.* **1984**, 555. Garcia-España, E.; Micheloni, M.; Paoletti, P.; Bianchi, A. *Inorg. Chim. Acta* **1985**, *102*, 9.

[4] Comarmond, J.; Dietrich, B.; Lehn, J. M.; Louis, R. *J. Chem. Soc., Chem. Commun.* **1985**, 75.

[5] Bianchi, A.; Mangani, S.; Micheloni, M.; Nanini, V.; Orioli, P.; Paoletti, P.; Seghi, B. *Inorg. Chem.* **1985**, *24*, 1182.

[6] Micheloni, M.; Paoletti, P.; Bianchi, A. *Inorg. Chem.* **1985**, *24*, 3702.

[7] Bencini, A.; Bianchi, A.; Garcia-España, E.; Giusti, M.; Micheloni, M.; Paoletti, P. *Inorg. Chem.* **1987**, *26*, 681.

[8] Bencini, A.; Bianchi, A.; Garcia-España, E.; Giusti, M.; Mangani, S.; Micheloni, M.; Orioli, P.; Paoletti, P. *Inorg. Chem.* **1987**, *26*, 1243.

[9] Atkins, T. J.; Richman, J. E.; Dettle, W. F. *Org. Synth.* **1978**, *58*, 86.

[10] TLC measurements were carried out on precoated silica gel 60 F-254 (Merck) TLC plates with a chloroform/acetone (50:1) mixture as eluent. In the case of products **5** and **6** (see Figure 1) the mixture was 10:1 in the same components.

0020-1669/88/1327-0176$01.50/0 © 1988 American Chemical Society

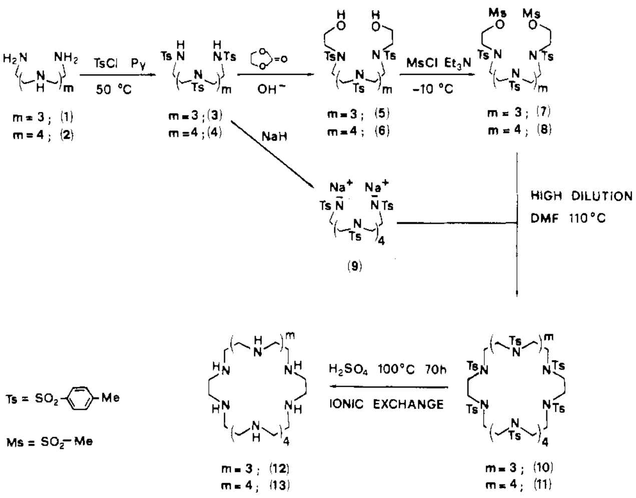


Figure 1. Reaction sequence for the synthesis of macrocycles L1 and L2.

reaction mixture was kept at −10 °C for 30 min, then allowed to warm up to room temperature, and added to a vigorously stirred mixture of water and ice containing 50 cm^3 of concentrated HCl. The organic phase was separated, washed three times with water, and dried over anhydrous Na_2SO_4. The dry solution was reduced to 100 cm^3, and 500 cm^3 of hot methanol was added. By slow cooling a white powder separated. The crude product was filtered off, washed with methanol, and recrystallized from a hot methylene chloride/methanol (1:4) mixture: yield 41 g of **7** (85%); mp 191–194 °C; TLC,[10] one product with R_f 0.33. IR spectra demonstrated that mesylation had occurred since no bands in the O–H region (3300–3500 cm^{-1}) were observed. Anal. Calcd for $C_{49}H_{65}N_5S_7O_{16}$: C, 48.86; H, 5.44; N, 5.81; S, 18.63. Found: C, 48.9; H, 5.4; N, 5.7; S, 18.6.

1,4,7,10,13,16-Hexakis(*p*-tolylsulfonyl)-1,4,7,10,13,16-hexaazahexadecane (4). The starting material, commercial 1,4,7,10,13,16-hexaazadecane (PENTEN, Fluka product, 80%) was purified by double distillation under reduced pressure. The fraction collected was that one between 280 and 285 °C at 0.1 Torr. A solution of **2** (50.0 g, 0.215 mol) in 200 cm^3 of pyridine was added dropwise to a solution of *p*-toluenesulfonyl chloride (246.2 g, 1.29 mol) in 700 cm^3 of pyridine placed in a 1 dm^3 four-necked round-bottom flask equipped with a mechanical stirrer. The addition of the hexaamine **2** solution was carried out in such a way that the reaction temperature was kept at 40–50 °C. After the addition the reaction mixture was maintained at 50 °C for 2 h; then it was allowed to cool at room temperature and added to a vigorously stirred mixture of water and ice (2.5 dm^3) containing the amount of HCl necessary to neutralize the pyridine. The product obtained was filtered off, washed with water and ethanol, and dissolved in 300 cm^3 of chloroform. The resulting solution was washed three times with 0.1 mol dm^{-3} HCl and three times with water and then dried over Na_2SO_4. To the filtered warm solution was added 1 dm^3 of hot ethanol. The product obtained was filtered off, washed with water, ethanol, and diethyl ether, and then dried in an oven at 110 °C. The resulting product was recrystallized twice from a DMF/water mixture (3:2), then washed with water, ethanol, and diethyl ether, and dried in an oven at 110 °C: yield 98.0 g (39.4%); mp 260–265 °C; TLC,[10] one product with R_f 0.27. Anal. Calcd for $C_{52}H_{64}N_6S_6O_{12}$: C, 53.95; H, 5.57; N, 7.26. Found: C, 53.6; H, 5.5; N, 7.2.

3,6,9,12,15,18-Hexakis(*p*-tolylsulfonyl)-3,6,9,12,15,18-hexaazaeicosane-1,20-diol (6). A finely powdered mixture of **4** (50 g, 0.043 mol), ethylene carbonate (9.13 g, 0.104 mol), and KOH (0.5 g) was placed in a 1-dm^3 three-necked round-bottom flask equipped with a mechanical stirer, condenser, and thermometer. The stirrer mixture was heated on an oil bath until it melted and then kept at 200 °C for 4 h. The mixture was allowed to cool at 110 °C, and then 500 cm^3 of methanol was rapidly added. The solution was refluxed for 1 h and then cooled at room temperature with stirring overnight. The crude product obtained was filtered, washed with methanol, dissolved in 300 cm^3 of methylene chloride, and boiled with a small amount of active carbon. To the filtered solution was added 600 cm^3 of hot ethanol; the white solid that separated on cooling was filtered, washed with ethanol, and dried in an oven at 110 °C. A total of 39 g of this product was obtained; TLC[10] analysis showed that the product was a mixture of three different substances. The separation into the single components of the mixture was achieved as follows: portions of 10 g of the starting material were chromatographed over a silica gel (230–400 mesh) column (200 g, 7 cm in diameter) with chloroform. A total 38 fractions were collected for each portion; all fractions were analyzed by TLC,[10] and only those containing the product at R_f 0.18 were collected together and concentrated at 50 cm^3. The white product that separated on addition of 400 cm^3 of ethanol was filtered, washed with ethanol, and dried in an oven at 110 °C: yield 16.8 g (40%); mp 222–225 °C; TLC,[10] one product with R_f 0.18. Anal. Calcd for $C_{56}H_{72}N_6S_6O_{14}$: C, 54.00; H, 5.83; N, 6.75. Found: C, 53.9; H, 5.9; N, 6.7.

***O,O′*-Bis(methylsulfonyl)-3,6,9,12,15,18-hexakis(*p*-tolylsulfonyl)-3,6,9,12,15,18-hexaazaeicosane-1,17-diol (8).** A solution of **6** (16.8 g, 0.0135 mol) and 4.11 g of triethylamine in 300 cm^3 of anhydrous methylene chloride was cooled to −10 °C under nitrogen in a 1-dm^3 four-necked round-bottom flask equipped with a mechanical stirrer. A solution of 3.56 g (0.031 mol) of methanesulfonyl chloride in 30 cm^3 of dry methylene chloride was added dropwise over a period of 30 min, with stirring. The reaction mixture was kept at −10 °C for 30 min, then allowed to warm up at room temperature, and added to a vigorously stirred mixture of water and ice containing 50 cm^3 of concentrated HCl. The organic phase was separated, washed three times with water, and dried over anhydrous Na_2SO_4. The dry solution was reduced to 50 cm^3, and 300 cm^3 of hot methanol was added. By slow cooling a white powder separated. The crude product was filtered off, washed with methanol, and recrystallized from a hot methylene chloride/methanol (1:4) mixture: yield 14 g of **8** (74%); mp 201–205 °C; TLC,[10] one product with R_f 0.33. IR spectra demonstrated that mesylation had occurred since no bands in the O–H region (3300–3500 cm^{-1}) were observed. Anal. Calcd for $C_{58}H_{76}N_6S_8O_{18}$: C, 49.70; H, 5.46; N, 5.99. Found: C, 49.7; H, 5.5; N, 5.9.

1,4,7,10,13,16,19,22,25,28,31-Undecakis(*p*-tolylsulfonyl)-1,4,7,10,13,16,19,22,25,28,31-undecaazacyclotritriacontane (10). A solution of **4** (23.15 g, 0.02 mol) in 1 dm^3 of anhydrous DMF was treated with sodium hydride (12 g) in small portions under nitrogen. When the hydrogen evolution had ceased, the solution of **9** (see Figure 1) was filtered in one of the two additional funnels of a 3-dm^3 four-necked flask, equipped also with a mechanical stirrer and condenser. In the second funnel a solution of **7** (24.1 g, 0.02 mol) in 1 dm^3 of anhydrous DMF was placed. The two solutions were added simultaneously at a constant rate to 0.5 dm^3 of anhydrous DMF vigorously stirred and heated at 110 °C in the flask. The addition was carried out over 4 h and then the temperature maintained at 110 °C for an additional 1 h. The resulting solution was then reduced at 300 cm^3 and added to a stirred mixture of water and ice (2.5 dm^3). The crude product obtained was filtered off, washed with water and ethanol, and dried under vacuum at 50 °C. The product was dissolved in chloroform and rapidly eluted with chloroform through a thick silica gel layer in order to remove products with R_f 0. The eluted solution is very concentrated; the white precipitate obtained on adding hot ethanol was filtered, washed with methanol, and dried in an oven at 110 °C. A total of 35 g of product was obtained. Portions of 12 g of this product were chromatographed over a silica gel (230–400 mesh) column (200 g, 7 cm in diameter) with chloroform. Many fractions were collected for each portion; all fractions were analyzed by TLC,[10] and only those containing the product at R_f 0.69 were collected together. To the final concentrated (50 cm^3) eluted solution was added 300 cm^3 of ethanol. The white product that separated was filtered, washed with ethanol, and dried at 50 °C under vacuum: yield 8.1 g of **10** (18.7%); mp 233–236 °C; TLC,[10] one product with R_f 0.69. IR spectra demonstrated that cyclization had occurred since no bands in the N–H region (3300–3500 cm^{-1}) were observed. Anal. Calcd for $C_{99}H_{121}N_{11}S_{11}O_{22}$: C, 54.80; H, 5.62; N, 7.10. Found: C, 54.6; H, 5.5; N, 7.0.

1,4,7,10,13,16,19,22,25,28,31,34-Dodecakis(*p*-tolylsulfonyl)-1,4,7,10,13,16,19,22,25,28,31,34-dodecaazacyclohexatriacontane (11). A solution of **4** (11.52 g, 0.099 mol) in 700 cm^3 of anhydrous DMF was treated with sodium hydride (6 g) in small portions under nitrogen. When the hydrogen evolution had ceased, the solution of **9** (see Figure 1) was filtered in one of the two additional funnels mounted on a 3-dm^3 four-necked flask, equipped also with a mechanical stirrer and condenser. In the second funnel was placed a solution of **8** (13.95 g, 0.099 mol) in 700 cm^3 of anhydrous DMF. The two solutions were added simultaneously at a constant rate to 0.5 dm^3 of anhydrous DMF vigorously stirred and heated at 110 °C in the flask. The addition was carried out over 4 h and then the temperature maintained at 110 °C for 1 h more. The resulting solution was then reduced at 300 cm^3 and added to a stirred mixture of water and ice (2.5 dm^3). The crude product obtained was filtered off, washed with water and ethanol, and dried under vacuum at 50 °C. Portions of this product were chromatographed over a silica gel (230–400 mesh) column (200 g, 7 cm in diameter) with chloroform. Many fractions were collected for each portion; all fractions were analyzed by TLC,[10] and only those containing the product at R_f 0.67 were collected together. To the final concentrated (50 cm^3) eluted solution was added 300 cm^3 of methanol. The white product that separated was

Table I. Experimental Details of the Emf Measurements

curve	ligand	init concns, mmol Cu(II)	 ligand	 HCl	pH range	no. of data points
1	L1		0.1033	1.6843	2.1–11.0	133
2	L1		0.0466	0.9685	2.4–10.4	81
3	L2		0.0534	1.3745	2.2–10.6	39
4	L2		0.0395	0.6823	2.5–10.5	64
5	L1	0.1881	0.0688	0.7568	2.4–11.0	99
6	L1	0.1361	0.0685	0.7534	2.4–10.9	50
7	L1	0.1610	0.0822	0.9039	2.3–11.1	81
8	L2	0.1609	0.0574	0.8874	2.2–11.0	124
9	L2	0.1302	0.0632	1.1193	2.3–11.0	77

Table II. Basicity Constants for the Large Macrocycles L1 and L2 in Aqueous Solution (25 °C in 0.15 mol dm^{-3} $NaClO_4$)

reacn	log *K* L = L1	 L = L2
$H^a + L = HL$	9.79 (3)^b	9.75 (5)
$H + HL = H_2L$	9.48 (3)	9.65 (5)
$H + H_2L = H_3L$	9.02 (3)	8.88 (5)
$H + H_3L = H_4L$	8.64 (3)	8.96 (5)
$H + H_4L = H_5L$	8.06 (3)	8.12 (5)
$H + H_5L = H_6L$	6.44 (3)	7.82 (5)
$H + H_6L = H_7L$	4.49 (3)	5.66 (5)
$H + H_7L = H_8L$	3.58 (2)	4.27 (4)
$H + H_8L = H_9L$	2.76 (2)	3.58 (4)
$H + H_9L = H_{10}L$	2.26 (2)	2.62 (4)
$H + H_{10}L = H_{11}L$	1.7 (1)	2.3 (1)
$H + H_{11}L = H_{12}L$		1.0^c

[a] Charges omitted for clarity. [b] Values in parentheses are standard deviations in the last significant figure. [c] Estimated.

filtered, washed with methanol, and dried at 50 °C under vacuum: yield 3.5 g of **11** (18.5%); mp >300 °C; TLC,[10] one product with R_f 0.67. IR spectra demonstrated that cyclization had occurred since no bands in the N–H region (3300–3500 cm^{-1}) were observed. Anal. Calcd for $C_{108}H_{132}N_{12}S_{12}O_{24}$: C, 54.80; H, 5.62; N, 7.10. Found: C, 54.6; H, 5.6; N, 7.0.

1,4,7,10,13,16,19,22,25,28,31-Undecaazacyclotritriacontane (L1). The removal of tosyl groups from **10** was performed with concentrated H_2SO_4, by following the procedure already described for other similar compounds. A 3.5-g portion of **10** (1.61 mmol) yielded 1.2 g (81.7%) of $L1 \cdot 11HCl \cdot 2H_2O$. Anal. Calcd for $C_{22}H_{70}N_{11}Cl_{11}O_2$: C, 29.01; H, 7.75; N, 16.92; Cl, 42.81. Found: C, 29.0; H, 7.9; N, 17.0; Cl, 42.78. The ^{13}C NMR spectrum of $L1 \cdot 11HCl$ (water with 15% D_2O, 20 MHz) consists of only one signal at δ 44.5 ($-CH_2-$).

1,4,7,10,13,16,19,22,25,28,31,34-Dodecaazacyclohexatriacontane (L2). The removal of tosyl groups from **11** was performed by the procedure previously described for L1. A 2.0-g portion of **11** (0.85 mmol) yielded 0.66 g (76%) of $L2 \cdot 12HCl \cdot 4H_2O$. Anal. Calcd for $C_{24}H_{80}N_{12}Cl_{12}O_4$: C, 28.10; H, 7.86; N, 16.37; Cl, 41.45. Found: C, 28.2; H, 7.9; N, 16.6; Cl, 41.40. The ^{13}C NMR spectrum of $L2 \cdot 12HCl$ (water with 15% D_2O, 20 MHz) consists of only one signal to δ 44.6 ($-CH_2-$).

$L1 \cdot 9HClO_4$ and $L2 \cdot 10HClO_4$. The hydrogen perchlorate salts of L1 and L2 were obtained by treating ethanolic solutions of the free amines with concentrate $HClO_4$. The products were filtered off, washed with ethanol, and dried in a desiccator. Anal. Calcd for $C_{22}H_{64}N_{11}Cl_9O_{36}$: C, 19.18; H, 4.68; N, 11.18. Found: C, 19.1; H, 4.7; N, 11.2. Calcd for $C_{24}H_{70}N_{12}Cl_{10}O_{40}$: C, 18.95; H, 4.64; N, 11.05. Found: C, 19.0; H, 4.6; N, 11.1.

Copper Complexes: $Cu_3(L1)(ClO_4)_6 \cdot 2H_2O$ and $Cu_3(L2)(ClO_4)_6 \cdot 3H_2O$. A solution of the appropriate free macrocyclic amine (1 mmol) in ethanol (15 cm^3) was added to a solution of $Cu(ClO_4)_2 \cdot 6H_2O$ in hot ethanol (10 cm^3). After cooling, the solid compound was filtered off, washed with ethanol, and dried in a desiccator. (*Caution*! Perchlorate salts can be explosive and must be handled with care. Compounds should not be heated as solids.) Anal. Calcd for $C_{22}H_{59}N_{11}O_{26}Cu_3Cl_6$: C, 20.37; H, 4.58; N, 11.88; Cu, 14.70. Found: C, 20.2; H, 4.6; N, 12.0; Cu, 14.7. Calcd for $C_{24}H_{66}N_{12}O_{27}Cu_3Cl_6$: C, 21.22 H, 4.90; N, 12.38; Cu, 14.04. Found: C, 21.4; H, 4.9; N, 12.5; Cu, 13.9.

Materials. All potentiometric measurements were carried out in 0.15 mol dm^{-3} $NaClO_4$ (C. Erba ACS grade) purified according to the procedure already described.[11] Standardized CO_2-free solutions of NaOH, used in the potentiometric titrations, were prepared by following the procedure described in ref 12.

Emf Measurements. The potentiometric titrations were carried out by using equipment (potentiometer, buret, stirrer, cell, microcomputer, etc.) that has been fully described.[13] The standard potential of the cell, $E°$, was calculated by applying the Gran method.[14] The initial concentrations of the reagents and the pH range explored for each titration curve are shown in Table I. For each system the titration curves were treated either as a single set or as separate entities without significant variation on the values of the equilibrium constants. Furthermore, in the case of the stepwise protonation constants of L1 and L2, the titrations were carried out by using both the hydrochloride and hydrogen perchlorate salts of the two macrocycles as starting material. Excess HCl or $HClO_4$ was respectively added to adjust the initial pH. Both separate and simultaneous treatment of the resulting potentiometric data showed that the amounts of chloride ion present in the potentiometric solution did not affect the values of the basicity constants. The computer program SUPERQUAD[15] was used to process data and calculate both basicity and stability constants.

Spectroscopy. Proton-decoupled ^{13}C NMR spectra were recorded with a Varian FT-80A spectrometer operating at 20.0 MHz using water with 15% (w/w) D_2O as solvent; chemical shifts are reported in ppm from $SiMe_4$ with dioxane as secondary reference standard [$\delta(\text{dioxane}) = \delta(SiMe_4) + 67.4$]. The electronic spectra were recorded on a Perkin-Elmer Lambda 9 spectrophotometer.

Results and Discussion

Protonation. The observed basicity constants for macrocycles L1 and L2 are reported in Table II. The macrocycles studied can be considered as belonging to a series with the general formula $[3k]aneN_k$ with $k = 11$ for L1 and $k = 12$ for L2. The adjective large is used when k is greater than 6.[5] As far as we know, these are the largest macrocycles of the above series that have been so far synthesized. In the case of L2 the last protonation constant (log k_{12}, see Table II) has been only estimated and kept constant during the refinement cycles of the calculation. The behavior of polyazacycloalkanes toward hydrogen ion addition (basicity) is well-studied.[16] Indeed, as expected, the results reported in Table II show that both macrocycles L1 and L2 behave as fairly strong bases in the first protonation steps and as much weaker bases in the last protonation steps. Charge-repulsion effects and hydrogen-bonding formation have been invoked to explain this grouping of the basicity constants, typical of all polyaza macrocycles.[16] The prevalent electrostatic nature of the basicity constants grouping phenomenon is demonstrated by the fact that the difference between the two groups of basicity constants becomes bigger as the macrocyclic size is reduced. For large macrocycles, the positive charges that accumulate in the cyclic framework as the degree of protonation increases experience weaker repulsions than those that accumulate on smaller macrocycles. The above considerations on the electrostatic repulsions of polycharged macrocycles of different sizes raise an important question: is the cyclic molecular topology for large polyaza macrocycles still important? In other words, are L1 and L2 too large to retain ligational properties due to the cyclic topology? The answer is that both L1 and L2 ligational properties (protonation and metal complex formation) are still very much influenced by the cyclic topology of the molecules. In the case of protonation L1 and L2 form highly charged protonated species in the neutral pH range. The cyclic topology of these polycharged cations increases the electric field and makes these species strongly interacting with anions. In our recent crystallographic studies the crystal structure of a

---

(11) Micheloni, M.; May, P. M.; Williams, D. R. *J. Inorg. Nucl. Chem.* **1978**, *40*, 1209.

(12) Micheloni, M.; Sabatini, A.; Vacca, A. *Inorg. Chim. Acta* **1977**, *25*, 41.

(13) Bianchi, A.; Bolongi, L.; Dapporto, P.; Micheloni, M.; Paoletti, P. *Inorg. Chem.* **1984**, *23*, 1201.

(14) Gran, G. *Analyst* (*London*) **1952**, *77*, 661. Rossotti, F. J. C.; Rossotti, H. *J. Chem. Educ.* **1965**, *42*, 375.

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

(16) Micheloni, M.; Paoletti, P.; Vacca, A. *J. Chem. Soc., Perkin Trans. 2* **1978**, 945. Micheloni, M.; Paoletti, P.; Sabatini, A. *Ibid.* **1978**, 828. Bartolini, M.; Bianchi, A.; Micheloni, M.; Paoletti, P. *Ibid.* **1982**, 1345. Leugger, A. P.; Hertli, L.; Kaden, T. A. *Helv. Chim. Acta* **1978**, *61*, 2296.

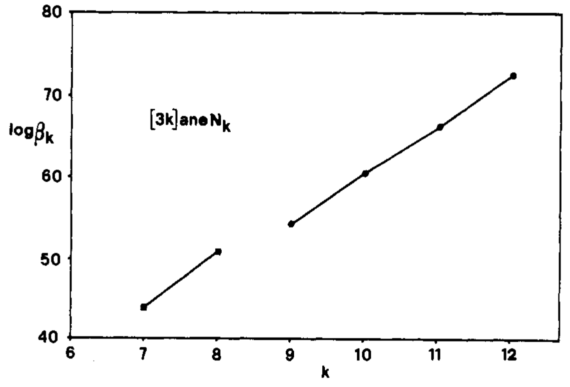


Figure 2. Overall protonation constants for large polyazacycloalkanes of general formula [3k]aneN$_k$ as a function of k. Values (■) were obtained at 25 °C and I = 0.5 mol dm^{-3}.

"supercomplex" containing the octaprotonated derivative of the large macrocycle [30]aneN$_{10}$ (k = 10 in the general formula [3k]aneN$_k$) has been determined.[17] The structure shows that the charged macrocycle adopts a very stiff configuration, elliptical in shape, imposed by the electrostatic repulsions. Since the conformation is due to electrostatic repulsions, it is reasonable to assume that it is preserved in solution and adopted also by the highly protonated species of L1 and L2. In Figure 2 the overall basicity constants for the [3k]aneN$_k$ series as a function of k have been plotted. There is a very constant increase of the overall basicity as the size of the macrocycle is increased by a $-CH_2-CH_2-NH-$ group. The two macrocycles L1 and L2 are both well-aligned with the expected basicity increment. In the drawing of Figure 2, the values of the overall basicity constants for the macrocycles [21]aneN$_7$[6] and [24]aneN$_8$[5] are slightly higher because the basicity constants have been determined at higher ionic strength (I = 0.5 mol dm^{-3}) than that of the other macrocycles (I = 0.15 mol dm^{-3}).

Complex Formation. The copper(II) complexes formed with L1 and L2 and their stability constants are reported in Table III. Owing to the great number of nitrogen atoms present in the macrocycles L1 and L2, many species are formed in a narrow pH range at the equilibrium and great care has to be taken in the selection process for the equilibrium model.[18] The most important binding characteristic of L1 and L2 is the ability to form very stable trinuclear copper(II) complexes: log K_{Cu_3L} = 48.03 and 51.43 for L1 and L2, respectively (see Table III). It is interesting to note that in the series [3k]aneN$_k$ the macrocycle with k = 7 forms both mono- and binuclear copper(II) complexes[6] while macrocycles with $7 < k \leq 10$ form only binuclear species.[5,7-9] Following this trend, we expected that further increase of the size and of the number of donor atoms would lead to macrocycles able to bind more than two copper(II) ions. In the series [3k]aneN$_k$ L1 and L2 are the first to form trinuclear species. The electronic spectra of the aqueous solution of the species $[Cu_3L]^{6+}$ show a wide absorption band at 16 430 cm^{-1} (ϵ = 730 dm^3 mol^{-1} cm^{-1}) for L1 and at 16 630 cm^{-1} (ϵ = 800 dm^3 mol^{-1} cm^{-1}) for L2. In the case of L2 there are 12 nitrogen donor atoms. The high value of the formation constant of the trinuclear species and the low value of the equilibrium constant relative to the addition of one hydrogen ion to the trinuclear species $[Cu_3L2]^{6+}$ to form $[Cu_3L2H]^{7+}$ indicates that all donor atoms are involved in the complex formation. As expected, for the process M-N + H$^+$ = M + N-H$^+$ the equilibrium constant is much smaller (log K = 4.0) than the protonation constant of the first nitrogen atom in the free L2 (log k = 9.75, see Table II) and even smaller than that relative to the proton addition to the equally charged H_6L2^{6+} (log K = 5.66, see Table II). Furthermore, the equilibrium constant for the reaction $3Cu^{2+} + HL2^{+} = [Cu_3L2H]^{7+}$ (log K = 45.6, see Table III) is similar to that of the reaction $3Cu^{2+} + L1 = [CuL1]^{6+}$ (log K = 48.03, see Table III). In both cases 11 donor atoms are available for 3 copper(II) ions. The slight difference between the two equilibrium constants is further reduced

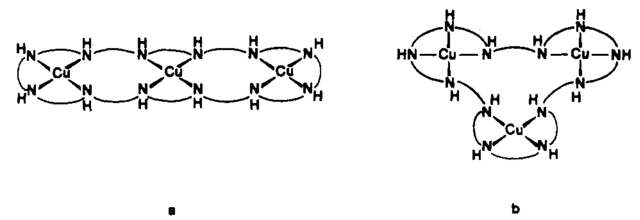


Figure 3. Schematic representation of the arrangement of Cu(II) ions in two possible structures of the trinuclear species $[Cu_3L2]^{6+}$ in solution: (a) "linear"; (b) "triangular".

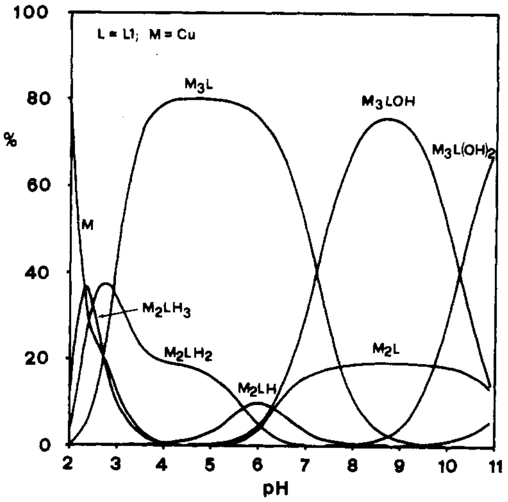


Figure 4. Distribution diagram for the system Cu(II)/L1 (charges omitted).

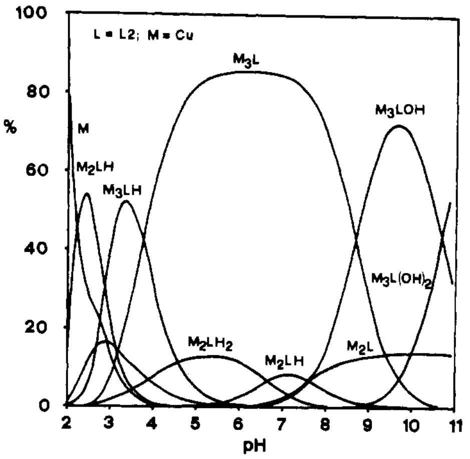


Figure 5. Distribution diagram for the system Cu(II)/L2 (charges omitted).

---

[17] Bianchi, A.; Garcia-España, E.; Mangani, S.; Micheloni, M.; Orioli, P.; Paoletti, P. *J. Chem. Soc., Chem. Commun.* **1987**, 729.

[18] On the basis of a critical evaluation of the least-squares results and of the statistical analysis of the weighted residuals supplied by the SUPERQUAD[15] program we have considered acceptable only those models for which the value of the variance of the residuals σ^2 is not greater than 9 (estimated errors of 0.3 mV on the emf readings and 0.003 cm^3 on the titrant volume). Different equilibrium models for the complex formation have been produced by eliminating or introducing species in the selected model. The σ^2 values obtained were used to perform an F test.[19] None of these σ^2 values were acceptable at the chosen significance level, and therefore the correspondent models were rejected. To further control the consistency of the experimental data, the protonation and complex formation curves, for each macrocycle, were collected together in a unique set of data and all the equilibrium constants simultaneously refined. The equilibrium constants obtained were equal, within the standard deviations, to those obtained (reported in Tables II and III) by treating protonation data and complex formation data as separate sets of data.

[19] Freund, J. E. *Mathematical Statistics*; Prentice Hall: New York, 1962; p 199.

Table III. Formation Constants of Copper(II) Complexes for the Large Macrocycles L1 and L2 in Aqueous Solution (25 °C in 0.15 mol dm^{-3} $NaClO_4$)

reacn	log *K*	
	L = L1	L = L2
$2Cu^a + L = Cu_2L$	38.77 (6)[b]	39.25 (7)
$2Cu + L + H = Cu_2LH$	45.28 (6)	47.09 (7)
$2Cu + L + 2H = Cu_2LH_2$	51.18 (5)	53.96 (8)
$2Cu + L + 3H = Cu_2LH_3$	53.86 (6)	58.07 (8)
$2Cu + L + 4H = Cu_2LH_4$		61.42 (8)
$2Cu + L + H_2O = Cu_2LOH + H$	27.29 (9)	
$3Cu + L = Cu_3L$	48.03 (6)	51.43 (7)
$3Cu + L + H = Cu_3LH$		55.38 (7)
$3Cu + L + H_2O = Cu_3LOH + H$	40.62 (9)	42.53 (9)
$3Cu + L + 2H_2O = Cu_3L(OH)_2 + 2H$	30.2 (1)	31.62 (9)
$Cu_2L + Cu = Cu_3L$	9.3	12.2
$Cu_2L + H = Cu_2LH$	6.5	7.8
$Cu_2LH + H = Cu_2LH_2$	5.9	6.9
$Cu_2LH_2 + H = Cu_2LH_3$	2.7	4.1
$Cu_2LH_3 + H = Cu_2LH_4$		3.4
$Cu_3L + H = Cu_3LH$		4.0
$3Cu + HL = Cu_3LH$		45.6
$Cu_2L + OH = Cu_2LOH$	2.3	
$Cu_3L + OH = Cu_3LOH$	6.3	4.8
$Cu_3LOH + OH = Cu_3L(OH)_2$	3.3	2.9

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

if we take into account the electrostatic charge repulsion contribution, which is more unfavorable for the first equilibrium, where the reacting species $HL2^+$ is charged, while L1 is not. These experimental evidences are consistent with the fact that one M–N bond is broken on addition of one proton to the trinuclear species $[Cu_3L]^{6+}$. A further evidence of the full coordination of L2 in the trinuclear species can be obtained from the stepwise equilibrium $[Cu_2L]^{4+} + Cu^{2+} \rightleftarrows [Cu_3L]^{6+}$; log *K* = 12.2 for L = L2 (see Table III) is significantly higher than log K = 9.3 found for L = L1, where only 11 donor atoms are involved in the formation of the trinuclear species. The difference 12.2 − 9.3 = 2.9 is comparable with the value of 4.3 logarithm units, which is the average contribution, for each donor atom $^1/_2(\log k_{Cu_3L1}/11) + {}^1/_2(\log k_{Cu_3L2}/12)$, to the overall stability of the trinuclear species found for L1 and L2. From the previously experimental evidences, when the molecular topology is taken into account, a possible structure of the $[Cu_3L2]^{6+}$ in solution can be hypothesized (see Figure 3).

For both macrocycles many other species are present at the equilibrium (see Table III). In Figures 4 and 5 the species distribution diagrams for the systems Cu(II)/L1 and Cu(II)/L2 have been reported. At a glance it is evident that, in the pH range investigated, the most important species are those containing three copper(II) ions and in particular the $[Cu_3L]^{6+}$ species. Only in the case of L2 is the monoprotonated, trinuclear species $[Cu_3L2H]^{7+}$ formed. This species does not add any protons because this would reduce the available ten donor atoms for three copper(II) ions. For the same reason no proton can be added to the $[Cu_3L1]^{6+}$ species. The stable trinuclear hydroxo species $[Cu_3LOH]^{5+}$ and $[Cu_3L(OH)_2]^{4+}$ are formed by both ligands. It is worth noting that, for both macrocycles L1 and L2, the well-characterized solid trinuclear complexes $Cu_3L1(ClO_4)_6 \cdot 2H_2O$ and $Cu_3L2(ClO_4)_6 \cdot 3H_2O$ were isolated. Besides the trinuclear species many other, less important, species are present in the equilibria investigated. The larger L2 forms a slightly more stable $[Cu_2L]^{4+}$ species (log *K* = 39.25) than L1 (log *K* = 38.77). In the $[3k]aneN_k$ series there is a small but clear increase in the stability of the binuclear species $[Cu_2L]^{4+}$ as the macrocycle becomes larger. The diminution of the electrostatic repulsions between the two positive metal ions as the macrocyclic size increases would be a simple, rational explanation of the above trend. When only two copper(II) ions are bound to the macrocycle, many nitrogen atoms can easily add hydrogen ions to form binuclear, protonated species. The species $[Cu_2L2]^{4+}$ can take up four hydrogen ions in a stepwise manner to form $[Cu_2L2H]^{5+}$, $[Cu_2L2H_2]^{6+}$, $[Cu_2L2H_3]^{7+}$, and $[Cu_2L2H_4]^{8+}$, respectively. For the last tetraprotonated species it is likely that, in order to minimize the electrostatic repulsions, the two copper(II) ions are bound at the largest possible distance while the four protons are bound to the intermediate nitrogen atoms. With reference to Figure 3a, the protons would replace the central copper(II) ion. In the case of L1, as expected, the maximum number of hydrogen ions that can be added to the $[Cu_2L1]^{4+}$ species is only three to form $[Cu_2L1H]^{5+}$, $[Cu_2L1H_2]^{6+}$, and $[Cu_2L1H_3]^{7+}$, respectively.

Acknowledgment. We thank Dr. S. Seniori Costantini for microanalyses and Dr. M. Giusti for technical help. We also thank a reviewer for helpful suggestions regarding the equilibrium studies.

Registry No. **1**, 112-57-2; **2**, 4067-16-7; **3**, 99142-42-4; **4**, 111060-05-0; **5**, 107010-90-2; **6**, 111085-42-8; **7**, 107035-78-9; **8**, 111060-06-1; **10**, 111060-08-3; **11**, 111060-09-4; L1, 60464-68-8; L1·11HCl, 111060-07-2; L1·9$HClO_4$, 111060-11-8; L2, 24904-24-3; L2·12HCl, 111060-10-7; L2·10$HClO_4$, 111060-12-9; TsCl, 98-59-9; MsCl, 124-63-0; $Cu_3(L1)(ClO_4)_6$, 111060-14-1; $Cu_3(L2)(ClO_4)_6$, 111060-16-3; ethylene carbonate, 96-49-1.

Supplementary Material Available: Table of the initial conditions of the potentiometric measurements and computer output of the program SUPERQUAD giving individual data points for emf measurements (101 pages). Ordering information is given on any current masthead page.