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Interaction of "Long" Open-Chain Polyazaalkanes with Hydrogen and Copper(II) Ions

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The series of polyazaalkanes 1,16-dimethyl-1,4,7,10,13,16-hexaazahexadecane (Me_2pentaen), 1,19-dimethyl-1,4,7,10,13,16,19-heptaazanonadecane (Me_2hexaen), 1,22-dimethyl-1,4,7,10,13,16,19,22-octaazadocosane (Me_2heptaen), 1,25-dimethyl-1,4,7,10,13,16,19,22,25-nonaazapentacosane (Me_2octaen), and 1,28-dimethyl-1,4,7,10,13,16,19,22,25,28-decaazaoctacosane (Me_2nonaen) have been synthesized and characterized. Their protonation behavior has been studied potentiometrically at 298.15 K in 0.15 mol dm^{-3} $NaClO_4$ as well as by ^{13}C NMR spectroscopy. A protonation pattern that minimizes electrostatic repulsions between polyammonium sites has been found. The interaction of these polyamines with copper(II) has been studied by potentiometric measurements under the same experimental conditions. All these ligands form both mono- and binuclear copper(II) complexes. While the stability of the mononuclear complexes remains almost unaffected along the series, that of the binuclear complexes increases from $\log K = 28.031$ (7) for $[Cu_2(Me_2pentaen)]^{4+}$ to $\log K = 41.17$ (3) for $[Cu_2(Me_2nonaen)^{4+}$. The formation enthalpies of the $[CuL]^{2+}$ species determined by direct microcalorimetry present an almost constant value of about −25.0 kcal mol^{-1} for all the terms of the series.

Introduction

One of the main characteristics of the coordination chemistry of macrocyclic ligands is their ability to impose on the coordinated metal ion a preferred geometry because of the preorganized arrangement of their binding sites. This fact is closely related to the origin of the so-called "macrocyclic effect".[2-10]

However, as the size of the macrocycles increases, their flexibility grows to such an extent that the coordination geometry of their metal complexes largely depends on the metal ion. Large macrocycles can rearrange themselves in order to satisfy the stereochemical requirements of the coordinated metal ions. As a matter of fact, the molecular structures we have obtained for the binuclear complexes of the ligand 1,4,7,10,13,16,19,22,25,28-decaazacyclotriacontane, [30]aneN_{10}, clearly support the above considerations.[11-14] In these structures it can be seen, as the conformation of the macrocycle and the coordination geometry strongly vary for the different metal ions. These considerations put forward the following question: *What would happen for open-chain polyamines of similar length and set of nitrogen donors*? To answer the question, we have accomplished the synthesis of the series of terminally methylated azaalkanes containing six to ten nitrogen atoms, 1,16-dimethyl-1,4,7,10,13,16-hexaazahexadecane, 1,19-dimethyl-1,4,7,10,13,16,19-heptaazanonadecane, 1,22-dimethyl-1,4,7,10,13,16,19,22-octaazadocosane, 1,25-dimethyl-1,4,7,10,13,16,19,22,25-nonaazapentacosane, and 1,28-dimethyl-1,4,7,10,13,16,19,22,25,28-decaazaoctacosane hereafter abbreviated as Me_2pentaen, Me_2hexaen, Me_2heptaen, Me_2octaen,

$$CH_3\text{-}NH\text{-}CH_2\text{-}CH_2\text{-}NH\left[CH_2\text{-}CH_2\text{-}NH\right]_n CH_2\text{-}CH_2\text{-}NH\text{-}CH_2\text{-}CH_2\text{-}NH\text{-}CH_3$$

n=2 Me_2pentaen
n=3 Me_2hexaen
n=4 Me_2heptaen
n=5 Me_2octaen
n=6 Me_2nonaen

and Me_2nonaen, respectively, and studied their protonation and coordination behavior toward copper(II) ions. In the same way we have denominated $[3k]aneN_k$ macrocycles with more than six nitrogen atoms as "large",[15] we may name their open-chain counterparts as "long". Methylation on the terminal nitrogens has been performed in order to allow for an appropriate comparison with the cyclic counterparts $[3k]aneN_k$. The important point is to produce ligands with the same set and type of nitrogen donors that form complexes of similar sizes in order to have similar hydration energies.[16]

Experimental Section

Synthesis of the Compounds. All chemicals were reagent grade and were used without further purification.

***O*,*O'*-Bis(methylsulfonyl)-3,6,9-tris(*p*-tolylsulfonyl)-3,6,9-triazaundecane-1,11-diol (1), *O*,*O'*-bis(methylsulfonyl)-3,6,9,12-tetrakis(*p*-tolylsulfonyl)-3,6,9,12-tetraazatetradecane-1,14-diol (2), *O*,*O'*-bis(methylsulfonyl)-3,6,9,12,15-pentakis(*p*-tolylsulfonyl)-3,6,9,12,15-pentaazaheptadecane-1,17-diol (3), and *O*,*O'*-bis(methylsulfonyl)-3,6,9,12,15,18-hexakis(*p*-tolylsulfonyl)-3,6,9,12,15,18-hexaazaicosane-1,20-diol (4)** have been synthesized as previously reported.[11,17-19]

1,16-Dimethyl-1,4,7,10,13,16-hexakis(*p*-tolylsulfonyl)-1,4,7,10,13,16-hexaazahexadecane (5). A solution of *N*-methyl-*p*-toluenesulfonamide (8.9 g, 0.048 mol) in 30 cm^3 of dry ethanol was added to a solution of sodium ethanolate (0.052 mol) in dry ethanol under an inert atmosphere. The resulting suspension was refluxed for 20 min; then the solvent was removed by distillation at reduced pressure and the product dried in vacuo at 80 °C in a oil bath. The sodium salt was redissolved, under an

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inert atmosphere, in 100 cm^3 of dry DMF and the solution warmed at 110 °C. To this solution was added dropwise, under stirring, 24 g of **2** (0.024 mol) in 200 cm^3 of dry DMF over 2 h, and the reaction mixture was kept at 110 °C for a further 2 h. The solution was cooled at room temperature, and 1 dm^3 of water was added to separate the crude product. This was filtered out, washed with water and then with ethanol and diethyl ether, and recrystallized from an ethanol/chloroform mixture; yield 25.7 g (88.8%); mp 257–260 °C. Anal. Calcd for $C_{54}H_{68}N_6O_{12}S_6$: C, 54.71; H, 5.78; N, 7.09. Found: C, 54.5; H, 5.8; N, 7.2.

1,16-Dimethyl-1,4,7,10,13,16-hexaazahexadecane (6). A 10-g amount of **5** (0.0084 mol) was dissolved in 20 cm^3 of 98% H_2SO_4 and the solution kept at 100 °C for 72 h. The solution was then cooled at room temperature and added dropwise to 300 cm^3 of stirred diethyl ether. The white solid that separated was filtered out, washed with diethyl ether, and dried in vacuo. The product was dissolved in 100 cm^3 of water, and 1 mol dm^{-3} NaOH solution was added to separate the free amine. The yellowish solid amine was filtered out, washed with cold water, and dried in vacuo. The product was then dissolved in 200 cm^3 of dry ethanol, and the mixture was boiled 10 min in the presence of activated carbon, filtered, and cooled at room temperature. **6**$\cdot$6HCl$\cdot{}^1/_2H_2O$ separated as a crystalline white powder by addition of an excess of 37% HCl. The compound was filtered out, washed with ethanol and then with diethyl ether, and dried in vacuo at 80 °C: yield 3.3 g (80%). Anal. Calcd for $C_{12}H_{32}Cl_6N_6O_{0.5}$: C, 29.52; H, 6.81; N, 17.22. Found: C, 29.5; H, 6.8; N, 17.1.

1-Methyl-1,4-bis(*p*-tolylsulfonyl)-1,4-diazabutane (7). A solution of *N*-methyl-ethylenediamine (2.2 g, 0.025 mol) in 30 cm^3 of benzene was added, at room temperature over about 20 min, to a stirred solution of 11.4 g of *p*-toluenesulfonyl chloride (0.06 mol) in 100 cm^3 of dry benzene containing 6.1 g of triethylamine (0.06 mol). A slightly exothermic reaction started with the addition, and the formation of some white solid compound was observed. The reaction mixture was maintained under stirring for a further 1.5 h at room temperature. Then H_2O (80 cm^3) was added to redissolve the precipitate, and the organic phase was washed twice with 40 cm^3 of water, dried over Na_2SO_4, and evaporated to dryness. The yellowish solid residue was washed with diethyl ether and then recrystallized from toluene (100 cm^3): yield 7.3 g (76%); mp 102–104 °C. Anal. Calcd for $C_{17}H_{22}O_4N_2S_2$: C, 53.38; H, 5.80; N, 7.37. Found: C, 53.3; H, 5.8; N, 7.2.

1,19-Dimethyl-1,4,7,10,13,16,19-heptakis(*p*-tolylsulfonyl)-1,4,7,10,13,16,19-heptaazanonadecane (8). A 0.6-g amount of Na (0.026 mol) was dissolved in 30 cm^3 of dry ethanol, under a nitrogen atmosphere, and the resulting solution was added to a solution of **7** (10 g, 0.026 mol) in 50 cm^3 of dry ethanol. The suspension obtained was refluxed 30 min. The solvent was distilled off, and the solid residue was dried in vacuo at 80 °C in a oil bath. The sodium salt of **7** was dissolved in 200 cm^3 of dry DMF, under a nitrogen atmosphere, and the solution warmed at 110 °C. A 7.8-g amount of **1** (0.01 mol) in 250 cm^3 of dry DMF was added, dropwise under stirring, to the above solution. The reacting mixture was kept at 110 °C for a further 2 h and then cooled at room temperature. A 1.5-dm^3 volume of water was added dropwise to separate the crude product **8**. This compound was filtered out washed with water, ethanol, and diethyl ether, and recrystallized from a methylene chloride/ethanol mixture: yield 7.1 g (51.4%); mp 232–234 °C. Anal. Calcd for $C_{63}H_{79}N_7O_{14}S_7$: C, 54.72; H, 5.76; N, 7.09. Found: C, 54.6; H, 5.7; N, 7.1.

1,19-Dimethyl-1,4,7,10,13,16,19-heptaazanonadecane (9). The hydrolysis of compound **8** to obtain the amine **9** has been performed by following the procedure reported for **6**. **9** was purified as the heptahydrochloride: yield 80.5%. Anal. Calcd for $C_{14}H_{37}Cl_7N_7$: C, 30.10; H, 6.68; N, 17.55. Found: C, 30.0; H, 6.6; N, 17.5.

1,22-Dimethyl-1,4,7,10,13,16,19,22-octakis(*p*-tolylsulfonyl)-1,4,7,10,13,16,19,22-octaazadocosane (10). This compound was synthesized from **2** (0.01 mol) and **7** (0.026 mol) by following the procedure reported for **8**: yield 6.8 g (43.0%); mp 272–275 °C. Anal. Calcd for $C_{72}H_{90}N_8O_{16}S_8$: C, 54.73; H, 5.74; N, 7.09. Found: C, 54.3; H, 5.7; N, 7.0.

1,22-Dimethyl-1,4,7,10,13,16,19,22-octaazadocosane (11). The acidic hydrolysis of compound **10** was performed as described for the previous compounds **5** and **8**. **11** was purified as the octahydrochloride dihydrated salt **11**$\cdot$8HCl$\cdot$2H_2O. Anal. Calcd for $C_{16}H_{46}Cl_8N_8O_2$: C, 28.50; H, 6.88; N, 16.62. Found: C, 28.3; H, 6.9; N, 16.5.

1,25-Dimethyl-1,4,7,10,13,16,19,22,25-nonakis(*p*-tolylsulfonyl)-1,4,7,10,13,16,19,22,25-nonaazapentacosane (12). This compound was synthesized from **3** (0.01 mol) and **7** (0.026 mol) by following the procedure reported for **8**: yield 7.5 g (42.2%); mp 252–255 °C. Anal. Calcd for $C_{81}H_{101}N_9O_{18}S_9$: C, 54.74; H, 5.73; N, 7.09. Found: C, 54.3; H, 5.7; N, 7.0.

1,25-Dimethyl-1,4,7,10,13,16,19,22,25-nonaazapentacosane (13). The acidic hydrolysis of compound **12** was performed as described for the previous compounds **5** and **8**. **13** was purified as the nonahydrochloride salt **13**$\cdot$9HCl. Anal. Calcd for $C_{16}H_{46}Cl_8N_8O_2$: C, 30.12; H, 6.60; N, 17.56. Found: C, 30.1; H, 6.5; N, 17.5.

1,28-Dimethyl-1,4,7,10,13,16,19,22,25,28-decakis(*p*-tolylsulfonyl)-1,4,7,10,13,16,19,22,25,28-decaazaoctacosane (14). This compound was synthesized from **4** (0.01 mol) and **7** (0.026 mol) by following the procedure reported for **8**: yield 6.2 g (31.5%); mp 225–227 °C. Anal. Calcd for $C_{90}H_{112}N_{10}O_{20}S_{10}$: C, 54.74; H, 5.72; N, 7.09. Found: C, 54.1; H, 5.8; N, 6.9.

1,28-Dimethyl-1,4,7,10,13,16,19,22,25,28-decaazaoctacosane (15). The acidic hydrolysis of compound **14** was performed as described for the previous compounds **5** and **8**. **15** was purified as the decahydrochloride salt **15**$\cdot$10HCl. Anal. Calcd for $C_{20}H_{52}Cl_{10}N_{10}$: C, 30.13; H, 6.57; N, 17.57. Found: C, 30.0; H, 6.5; N, 17.5.

Emf Measurements. The potentiometric titrations were carried out, in 0.15 mol dm^{-3} $NaClO_4$ solutions at 298.15 K, by using the equipment (potentiometer, cell, buret, stirrer, microcomputer, etc.) that has been fully described.[20] The acquisition of the emf data was performed with the computer program PASAT.[21] The reference electrode was an Ag/AgCl electrode in saturated KCl solution. The glass electrode was calibrated as a hydrogen concentration probe by titration of well-known amounts of HCl with CO_2-free NaOH solutions and determining the equivalent point by Gran's method,[22] which gives the standard potential, $E°$, and the ionic product of water. The computer program SUPERQUAD[23] was used to calculate the protonation and stability constants. The concentrations of the copper(II) solutions were determined gravimetrically by standard methods. The titration curves for each system were treated either as a single set or as separated curves without significant variations in the values of the stability constants. Furthermore, the sets of data were merged together and treated simultaneously to give the final stability constants.

Microcalorimetry. The enthalpy changes have been determined by means of a fully automatized equipment having a Thermal Activity Monitor Model 2277 (Thermometric AB) microcalorimeter as a calorimetric unit. Solutions of the metal ions (0.01 mol dm^{-3}, addition volumes ranging from 20 to 40 μL) were added to 2.5 cm^3 solutions of the free ligand (0.001 mol dm^{-3}). Corrections for the heats of dilution of the reacting solutions were applied.

Spectroscopy. The 200.0-MHz ^{1}H and 50.32-MHz ^{13}C NMR spectra were recorded at room temperature with a Varian Gemini spectrometer in D_2O solutions with dioxane as a reference standard ($\delta = 67.4$ ppm). The UV–vis spectra were recorded with a Perkin-Elmer Lambda 9 spectrophotometer.

Results and Discussion

Synthetic Procedure. In order to obtain appropriate open-chain counterparts of large macrocyclic [3*k*]aneN$_k$ ligands, linear polyamines containing only secondary nitrogen donor atoms, connected by ethylenic chains, have been prepared. Terminally methylated polyamines of this type, containing up to 10 nitrogens, can be obtained from commercially available products by following the two synthetic pathways reported in Scheme I. Accordingly with these procedures, linear polyamines containing n nitrogen atoms can be converted into the longer ligands with $n + 2$ (pathway 1) or $n + 4$ (pathway 2) nitrogen donor atoms, respectively.

Protonation of the Ligands. The observed basicity constants for the ligands Me$_2$pentaen, Me$_2$hexaen, Me$_2$heptaen, Me$_2$octaen, and Me$_2$nonaen are presented in Table I. If the overall basicities for both cyclic and open-chain amines are reported versus the number of nitrogens in each ligand, two almost parallel straight lines are obtained. The overall basicities of the open-chain polyamines are always greater than those of their cyclic counterparts. Cyclization produces less basic character due to the greater concentration of charge density in these molecules. Nevertheless, the parallelism found between both straight lines suggests similar protonation patterns. Protons bind the polyamines

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Scheme I

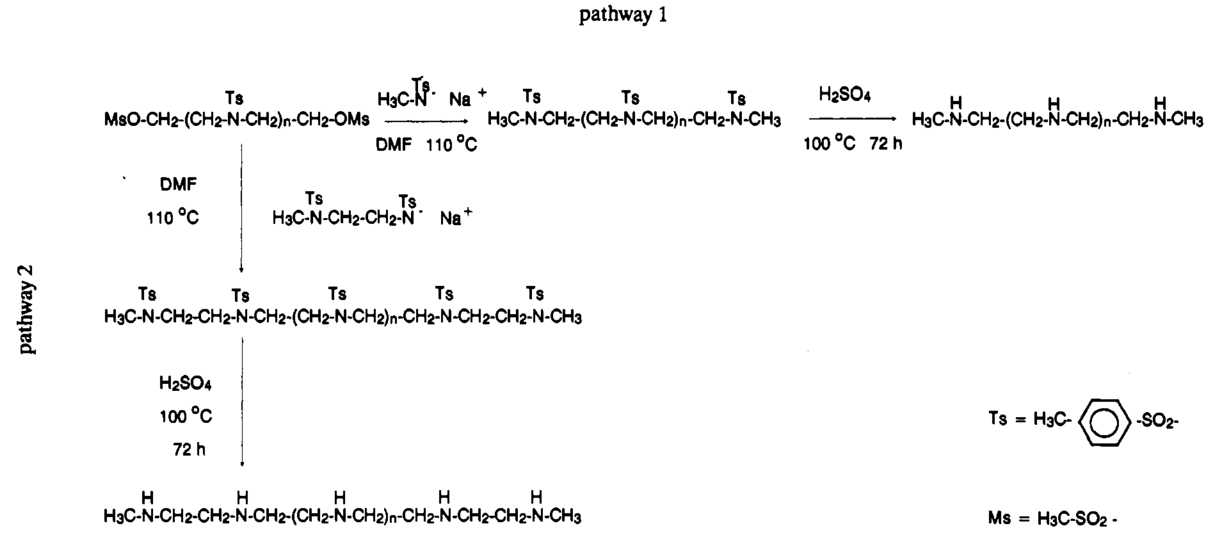


Table I. Protonation Constants of the Long Polyazacycloalkanes Me_2pentaen, Me_2hexaen, Me_2heptaen, Me_2octaen, and Me_2nonaen in Aqueous Solution at 298.15 K in 0.15 mol dm^{-3} $NaClO_4$

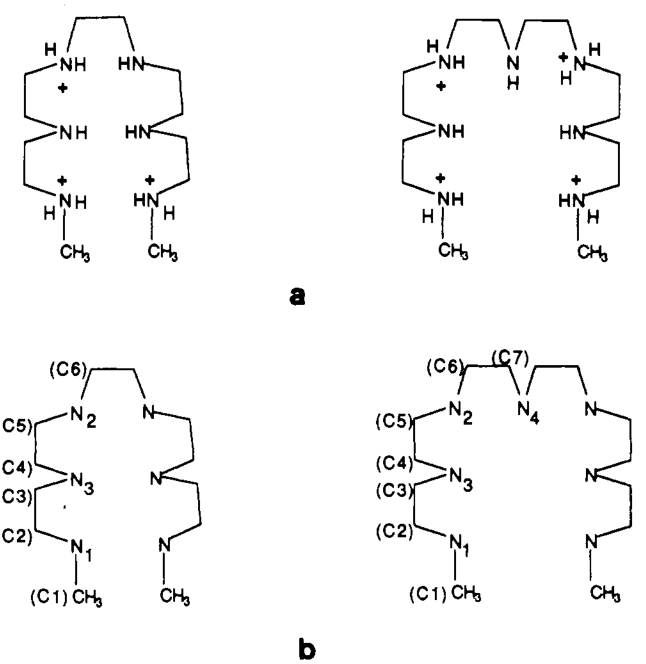
	log *K*				
reacn[a]	Me_2pentaen	Me_2hexaen	Me_2heptaen	Me_2octaen	Me_2nonaen
L + H	10.279 (6)[b]	10.220 (8)	10.391 (7)	10.58 (1)	10.27 (2)
L + 2H	19.799 (5)	19.816 (4)	20.160 (6)	20.296 (9)	19.99 (2)
L + 3H	28.640 (6)	28.751 (6)	29.444 (7)	29.65 (1)	29.26 (2)
L + 4H	35.182 (9)	36.797 (5)	38.050 (6)	38.35 (1)	37.98 (2)
L + 5H	38.99 (1)	41.548 (6)	44.73 (1)	46.28 (1)	46.22 (2)
L + 6H	41.50 (1)	44.921 (7)	49.17 (1)	51.38 (1)	52.80 (2)
L + 7H		47.37 (1)	52.48 (1)	55.26 (1)	57.34 (2)
L + 8H			55.41 (1)	58.20 (1)	60.84 (2)
L + 9H				60.94 (2)	63.55 (2)
L + 10H					65.0 (1)
HL + H	9.52	9.59	9.77	9.72	9.72
H_2L + H	8.84	8.94	9.28	9.35	9.27
H_3L + H	6.54	8.05	8.61	8.70	8.72
H_4L + H	3.80	4.75	6.68	7.93	8.24
H_5L + H	2.51	3.37	4.44	5.10	6.58
H_6L + H		2.45	3.31	3.88	4.54
H_7L + H			2.93	2.94	3.50
H_8L + H				2.74	2.71
H_9L + H					1.46

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

in such a way that electrostatic repulsions are minimized. Open-chain polyamines with even numbers of nitrogen can take up $k/2$ protons (k = total number of nitrogens in the macrocycle) without great repulsion between same sign charges (see Chart Ia). The $(k/2 + 1)$th proton will necessarily be placed next to one ammonium group, which would considerably increase electrostatic repulsion and, therefore, yield a drop in basicity. All the other protons will bind nitrogens located between two ammonium groups, producing a further decrease in basicity. This situation will produce, as observed in Figure 1, two groups of constants separated by an intermediate constant. Polyamines with odd numbers of nitrogens present a slightly different protonation pattern. For these compounds, the intermediate situation does not occur and just two groups of constants can be observed (see Chart Ia). The first $[(k + 1)/2]$th constants are much more basic than the following ones, since, in the latter, the protons, as indicated above, would be placed between polyammonium groups. The protonation behavior of cyclic polyamines with odd numbers of protons follows the pattern of open-chain ones with even numbers of nitrogens. In the same way, cyclic polyamines with even numbers of nitrogens will follow the pattern of open-chain counterparts with odd numbers.

^{13}C NMR Spectroscopy. ^{13}C NMR spectra recorded at different pH values confirm the above-mentioned protonation patterns. ^{13}C NMR spectra of cyclic $[3k]aneN_k$ ligands just consist of one resonance. Upon protonation this signal undergoes an upfield shift

Chart I



a

b

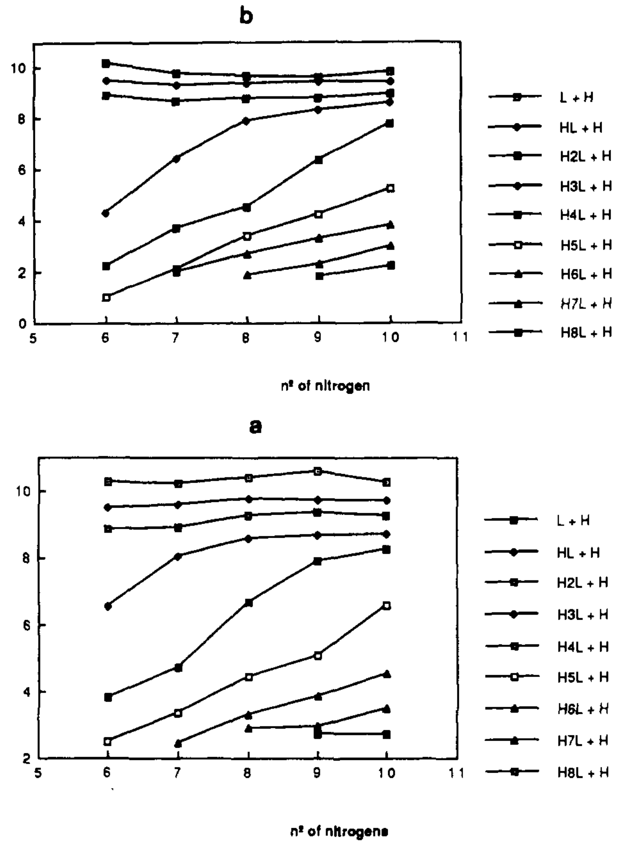


Figure 1. Plot of the stepwise protonation constants versus the number of nitrogens for (a) acyclic ligands (L_{acy}) and (b) cyclic [3k]aneN$_k$ ligands (L_{cy}).

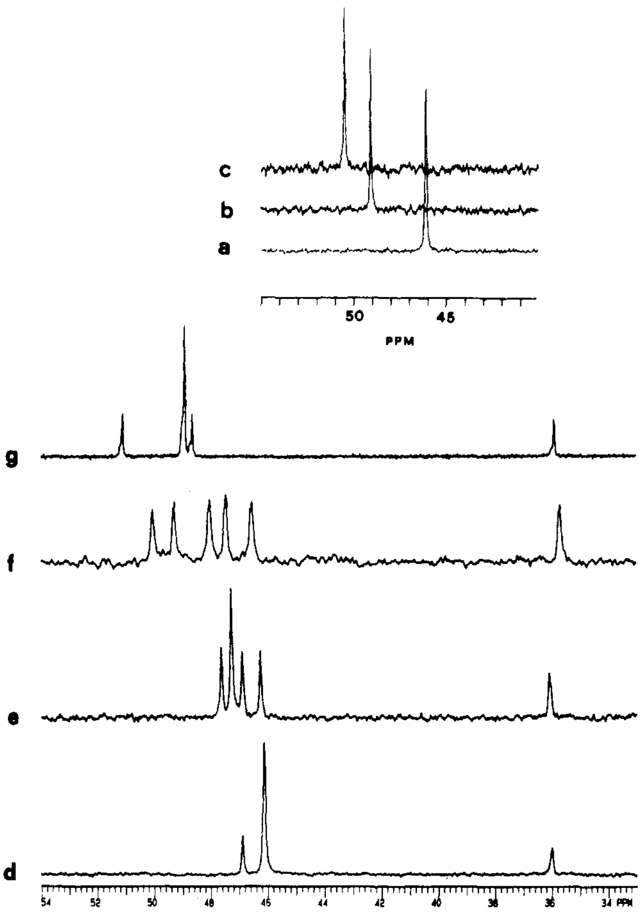


Figure 2. ^{13}C NMR spectra at different pH values for [18]aneN$_6$ and Me$_2$pentaen. The top three spectra are for [18]aneN$_6$ with (a) pH = 2.0, (b) pH = 6, and (c) pH = 10. The bottom four spectra are for Me$_2$pentaen with (d) pH = 1, (e) pH = 4, and (f) pH = 6. Spectrum g is of the free amine recorded in CDCl$_3$.

of about 4–5 ppm without any splitting. So, independently of the pH, all the carbons remain magnetically equivalent (see Figure 2).

The ^{13}C NMR spectra of the free amines, both for Me$_2$pentaen and Me$_2$hexaen, display four signals, which can be assigned to the methyl carbons (ca. 36 ppm), to the carbons in the β (C2, ca. 52 ppm) and in γ-positions with respect to the methyl groups (C3, ca. 49 ppm), and to all the remaining carbons (ca. 50 ppm). When protonation of the nitrogens occurs, the carbons become nonequivalent and ^{13}C NMR spectra recorded at pH values corresponding to an intermediate degree of protonation show six signals for Me$_2$pentaen (Figure 2) and seven signals for Me$_2$hexaen. At more acidic pH the carbons recover their magnetic equivalence and the spectra for the fully protonated species consist of only three signals integrating as 2:8:2. These resonances, although upfield shifted, can be assigned in way similar to those for the free amine.

An analysis of the variation of ^{13}C chemical shifts with pH allows a full understanding of the protonation pattern of these polyamines.

First of all, it has to be noted that the maximum number of magnetically nonequivalent carbons is half of the overall carbons present in the molecule. Therefore, all the different protonated species should present C_{2v} symmetry (see Chart Ib; the labeling of the nitrogens corresponds to the protonation order). By means of the empirical formula deduced by Reilley et al.[24] for aliphatic amines, we have calculated the theoretical chemical and protonation shifts for a variety of supposed protonation patterns, obtaining the best agreement pattern already suggested by the thermodynamic data. In Figure 3 the variations in the chemical shifts for both Me$_2$pentaen and Me$_2$hexaen are presented. The assignation of any resonance for individual carbons is based on the fitting between experimental and theoretical values and is confirmed by the ^{2}D ^1H–^1H- and ^1H–^{13}C-correlated NMR spectra recorded at intermediate pH, which show that methylene protons appear as different A_2B_2 patterns (see Figure 4).

On the other hand, it is interesting to analyze the variation in the chemical shift of the carbon in the β-position with respect to the methyl group (C2). It can be observed that it shifts slightly at pH values 9–11 when the first two protons attack Me$_2$pentaen, presenting its maximum variation at pH values 4–6, corresponding to the binding of the fifth proton to Me$_2$pentaen. These observations clearly indicate that protonation takes first place on both terminal nitrogens, in agreement with the maximum shift for the carbons in the β-position to these nitrogens (C3).[25] The contiguous nitrogens (N3) would be the last ones in bearing protonation accordingly with the variation in chemical shifts for C2 and C5.

A similar pattern can be deduced for Me$_2$hexaen, but in this case the last proton would bind the central nitrogen (N4) in the molecule (see Chart Ib).

Copper(II) Complexes. In Table II the stability constants related to the formation in aqueous solution of mono- and binuclear copper(II) complexes of the ligands Me$_2$pentaen, Me$_2$hexaen, Me$_2$heptaen, Me$_2$octaen, and Me$_2$nonaen are shown. First of all, it can be noticed that all the ligands studied form nonprotonated mononuclear complexes, [CuL]$^{2+}$. The stability of these complexes remains unaffected along the series (see Figure 5). This fact establishes the first difference with the behavior of the corresponding cyclic amines, for which mononuclear complexes were only detected in the cases of [18]aneN$_6$ and [21]aneN$_7$.[26] On

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Table II. Formation Constants of Copper(II) Complexes of the Long Polyazaalkanes Me_2pentaen, Me_2hexaen, Me_2heptaen, Me_2octaen, and Me_2nonaen in 0.15 mol dm^{-3} $NaClO_4$ Aqueous Solution at 298.15 K

reacn[a]	Me_2pentaen	Me_2hexaen	Me_2heptaen	Me_2octaen	Me_2nonaen
$Cu + L = CuL$	21.58 (1)[b]	20.73 (2)	21.80 (3)	22.24 (3)	21.81 (3)
$Cu + L + H = CuHL$	30.171 (5)	30.31 (2)	31.58 (2)	31.87 (2)	31.93 (3)
$Cu + L + 2H = CuH_2L$	34.075 (4)	36.59 (1)	39.44 (2)	40.56 (2)	40.91 (3)
$Cu + L + 3H = CuH_3L$	37.155 (6)	40.15 (1)	44.31 (1)	47.09 (2)	48.49 (2)
$Cu + L + 4H = CuH_4L$			47.04 (2)	51.10 (2)	53.53 (2)
$Cu + L + 5H = CuH_5L$			50.47 (2)	54.09 (2)	56.89 (3)
$Cu + L + 6H = CuH_6L$					59.60 (3)
$CuL + H = CuHL$	8.59	9.58	9.78	9.63	10.12
$CuHL + H = CuH_2L$	3.90	6.28	7.86	8.69	8.98
$CuH_2L + H = CuH_3L$	3.08	3.56	4.87	6.53	7.58
$CuH_3L + H = CuH_4L$			3.09	4.01	5.04
$CuH_4L + H = CuH_5L$					2.70
$Cu + HL = CuHL$	19.89	20.09	21.19	21.29	21.66
$Cu + H_2L = CuH_2L$	14.27	16.77	19.28	20.26	20.92
$2Cu + L = Cu_2L$	28.031 (7)[b]	31.99 (1)	35.67 (2)	38.70 (3)	41.17 (3)
$2Cu + L + H = Cu_2HL$		35.79 (3)	40.10 (2)	43.87 (2)	46.84 (2)
$2Cu + L + 2H = Cu_2H_2L$			43.21 (6)	47.72 (2)	50.82 (2)
$2Cu + L + 3H = Cu_2H_3L$					54.06 (3)
$2Cu + L + H_2O = Cu_2L(OH) + H$	22.081 (8)	23.47 (2)	25.79 (3)		
$Cu_2L + H = Cu_2HL$		3.80	4.43	5.17	5.67
$Cu_2HL + H = Cu_2H_2L$			3.10	3.85	3.98
$Cu_2H_2L + H = Cu_2H_3L$					3.24
$Cu_2L + H_2O = Cu_2L(OH) + H$	−6.03	−8.52	−9.88		
$Cu_2L + OH = Cu_2L(OH)$	7.70	5.21	3.85		
$2Cu + HL = Cu_2HL$		25.57	29.71	33.29	36.57
$2Cu + H_2L = Cu_2H_2L$			23.05	27.42	30.83
$2Cu + H_3L = Cu_2H_3L$					24.80
$CuL + Cu = Cu_2L$	6.45	11.26	13.87	16.46	19.36

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

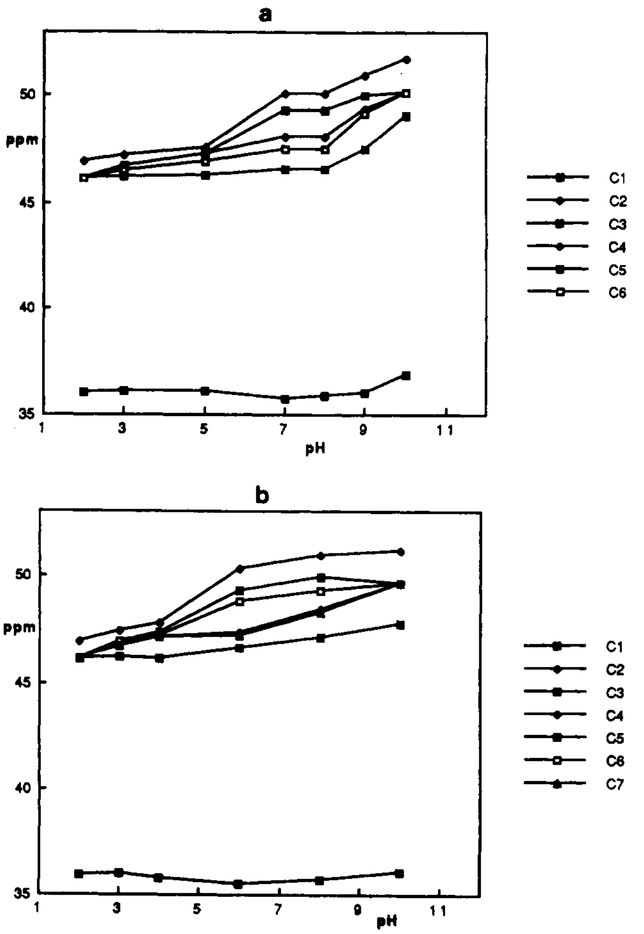

Figure 3. ^{13}C experimental chemical shifts as a function of pH for (a) Me_2pentaen and (b) Me_2hexaen.

Table III. Thermodynamic Parameters for the Formation of Copper(II) Complexes of Azaalkanes and [3*k*]aneN_k Polyazacycloalkanes at 298.15 K in 0.15 mol dm^{-3} $NaClO_4$ Unless Otherwise Noted.

reacn	$-\Delta G°$, kcal/mol	$-\Delta H°$, kcal/mol	$T\Delta S°$, kcal/mol
Cu^{2+} + Me_2pentaen	29.4[a]	25.4 (2)[a,b]	4.0[a]
Cu^{2+} + Me_2hexaen	28.3[a]	25.9 (2)[a]	2.4[a]
Cu^{2+} + Me_2heptaen	29.7[a]	24.5 (2)[a]	3.7[a]
Cu^{2+} + Me_2nonaen	29.7[a]	25.4 (3)[a]	4.9[a]
Cu^{2+} + $[Cu(Me_2nonaen)]^{2+}$	26.4[a]	21.1 (2)[a]	5.3[a]
Cu^{2+}+ [18]aneN_6	33.3[c]	23.9[c]	9.4[c]
Cu^{2+} + [21]aneN_7	26.6[c]	19.7[c]	6.9[c]
Cu^{2+} + Me_2trien	28.6[d]	21.1[d]	7.5[d]
Cu^{2+} + tetren	31.1[e]	25.0[e]	6.1[e]

[a] Values in parentheses are standard deviations in the last significant figure. [b] This work. [c] From ref 26. [d] From ref 28 (0.5 mol dm^{-3} KNO_3). [e] From ref 27 (0.1 mol dm^{-3} KCl).

the other hand, the stabilities of these complexes undergo a sharp decrease when the series from $[Cu([18]aneN_6)]^{2+}$ (log K = 24.27) to $[Cu([21]aneN_7)]^{2+}$ (log K = 19.48) is examined (see Figure 5), which is usually attributed to the formation of highly membered chelate rings (eight or more). For long open-chain polyamines such a decrease is not observed, so the nitrogens coordinating the copper(II) ions have to present a similar disposition along the polyamine chain in all the ligands. Furthermore, the formation enthalpies for the species $[CuL]^{2+}$ remain roughly constant (Table III), while for their cyclic counterparts a marked decrease was observed when [18]aneN_6 and [21]aneN_7[26] are examined.

Another interesting feature to be analyzed is the magnitude of the first protonation constant of the complexes $[CuL]^{2+}$ to give $[CuHL]^{2+}$. The values of these equilibrium constants are very high and close to the corresponding ones for the third protonations of the free ligands, $H^+ + H_2L^{2+} \rightleftarrows H_3L^{3+}$ (Tables I and II), pointing out that at least one nitrogen remains uncoordinated throughout all the members of the series. The same conclusion can be drawn if the stability constants for the following equilibria are considered: $Cu^{2+} + HL^+ \rightleftarrows [Cu(HL)]^{3+}$ and $Cu^{2+} + L \rightleftarrows [CuL]^{2+}$ (see Table II). For Me_2pentaen the second stepwise protonation constant of the complex, $[CuHL]^{3+} + H \rightleftarrows [CuH_2L]^{4+}$, is, however, much lower (log K = 3.90) than the constant for the fourth protonation of the free ligand (log K = 6.54). Therefore, five out of the six nitrogens in the Me_2pentaen

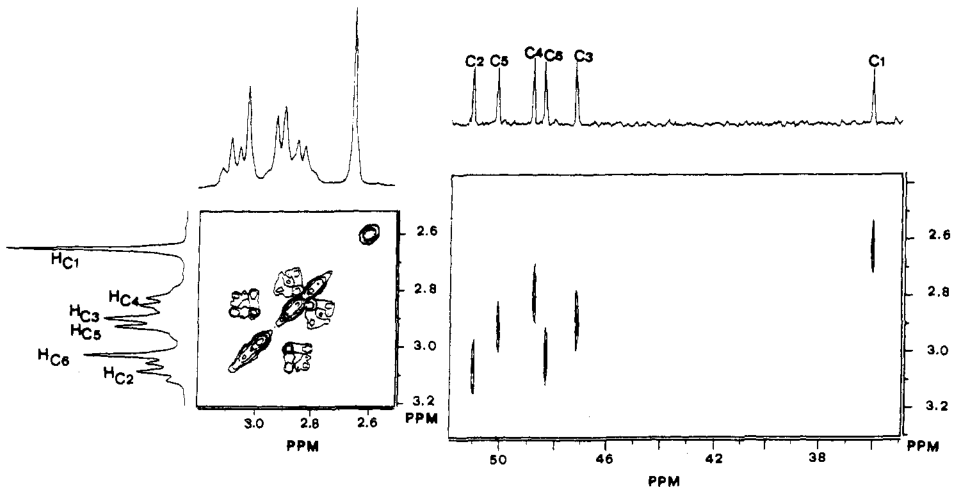

Figure 4. ^1H-^1H- and ^1H-^{13}C-correlated NMR spectra for H_3Me_2pentaen.

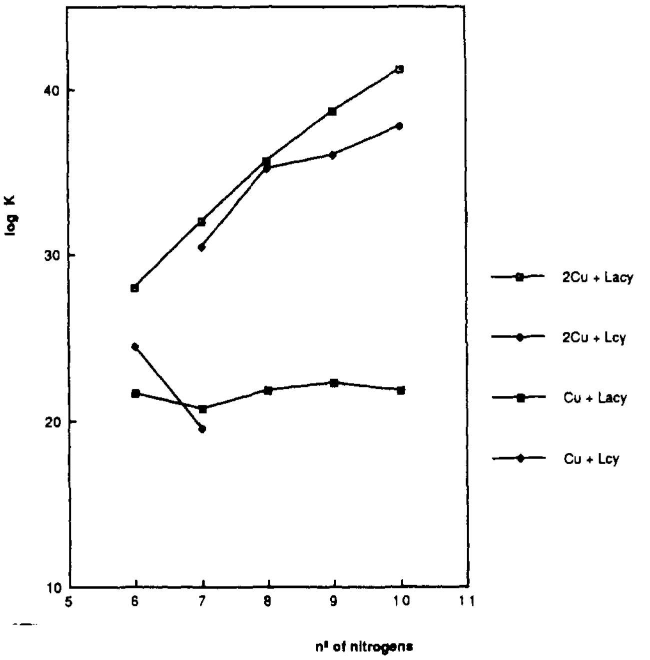

Figure 5. Plot of the equilibrium constants for the reactions Cu + L ⇄ CuL and 2Cu + L ⇄ Cu_2L, versus the number of nitrogens, both for acyclic (L_{acy}) and cyclic (L_{cy}) ligands.

are presumably binding the copper(II) ion. This fact, together with the steady values of the stability constants for the formation of the species $[CuL]^{2+}$ along the series, allows one to assume a coordination number of 5 for all these complexes. This hypothesis based on the stability constants is fully confirmed by the formation enthalpies of the $[CuL]^{2+}$ species. In fact, the values obtained (see Table III) are quite similar to those reported for the linear tetraethylenepentamine ($\Delta H° = -25.0$ kcal mol^{-1}, which acts as a pentadentate ligand toward copper(II).[27] However, as previously mentioned, this ligand could not be considered as the most appropriate counterpart, since it presents terminal primary nitrogens. On the other hand, for the analogous ligand 1,10-dimethyl-1,4,7,10-tetraazadecane an enthalpy contribution of −21.0 kcal mol^{-1} was found, accounting for the coordination of just four nitrogens.[28] This pentacoordination of copper(II) by the nitrogens of the ligand is also evidenced by the visible spectra of the complexes $[CuL]^{2+}$, displaying a band at ca. 15 000 cm^{-1} and a shoulder at ca. 11 500 cm^{-1}, which are characteristic of this type of geometry.[29]

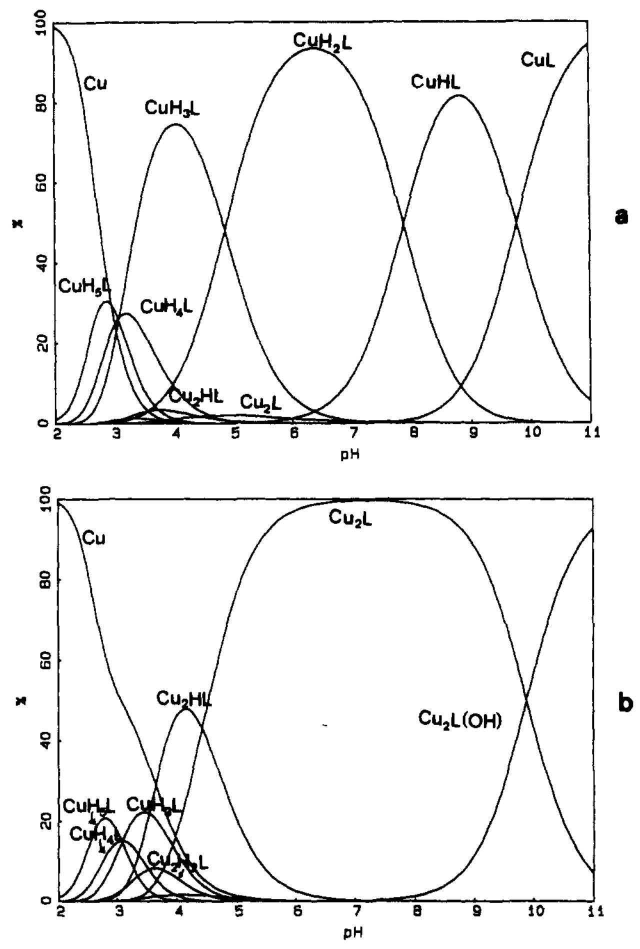

Figure 6. Calculated distribution diagram for the species existing in solution for the system Cu^{2+}–Me_2heptaen: (a) $[Cu^{2+}] = 10^{-3}$ mol dm^{-3}, $[Me_2heptaen] = 10^{-3}$ mol dm^{-3}; (b) $[Cu^{2+}] = 2 \times 10^{-3}$ mol dm^{-3}, $[Me_2heptaen] = 10^{-3}$ mol dm^{-3}. Charges have been omitted.

Some protonated species of the mononuclear complexes are formed (Table II). For a given degree of protonation of the complexes, the values of the stepwise protonation constants increase with the ligand size. This is usually attributed to the smaller repulsions between positive charges in the complexes of the longer ligands.

All the linear polyamines under study form binuclear complexes. The stability of these complexes increases with the number of

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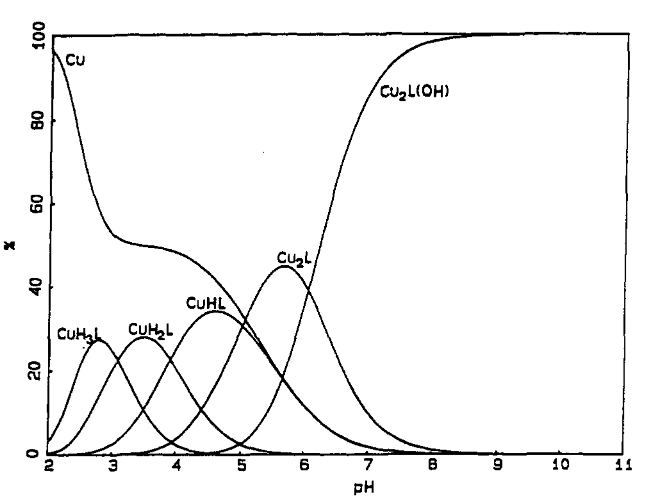

Figure 7. Calculated distribution diagram for the species existing in solution for the system Cu^{2+}–Me_2pentaen with $[Cu^{2+}] = 10^{-3}$ mol dm^{-3} and [Me_2pentaen] = 10^{-3} mol dm^{-3}. Charges have been omitted.

nitrogens in the ligands, varying from log $K = 28.03$ for $[Cu_2(Me_2pentaen)]^{4+}$ to log $K = 41.17$ for $[Cu_2(Me_2nonaen)]^{4+}$. These constants are higher than those found for their cyclic counterparts (see Figure 5). With Me_2hexaen, and the longer ligands, the formation of protonated binuclear complexes is also observed.

The first aspect to be remarked is that the smallest ligand of the series, Me_2pentaen, forms a binuclear complex, while its cyclic counterpart, [18]aneN_6, failed to form such a species.[26] If a symmetric coordination of Me_2pentaen is assumed, both copper(II) ions would be bound by just three nitrogens. As is well-known, two copper(II) sites with three nitrogens may readily incorporate an exogen ligand to complete the 4-coordination. In Figure 6, it can be seen that the hydroxylated species $[Cu_2L(OH)]^{3+}$ is the main species in solution from pH 7.5. The magnitude of the constant for the equilibrium $[Cu_2L]^{4+} + H_2O \rightleftarrows [Cu_2L(OH)]^{3+} + H^+$ (log $K = -6.03$) suggests that the OH^- is bridging both metal centers. For the complex $[Cu(den)]^{2+}$ (den = 1,4,7-triazaheptane) the constant for such a reaction is 3 orders of magnitude lower (log $K = -9.16$).[30] Also, for the following terms of the series, Me_2hexaen and Me_2heptaen, these constants are considerably lower (see Table II).

The increase in the values of the stability constants for the complexes $[Cu_2L]^{4+}$, together with the low values of their protonation constants, suggests that in these complexes all the nitrogens of the ligand are involved in the coordination to the metal ion. In fact, the stepwise constants related to the addition of the second copper(II) ion increase with the number of nitrogen donors in the ligand. For Me_2nonaen, in which 10 nitrogens are available for coordinating the copper(II) ions, the values of the first and second stepwise stability constants are similar enough to assume pentacoordination for both metal ions. The close $\Delta H°$ values for both coordination steps are also confirming this assumption.

In Figure 7 are shown the calculated distribution diagrams for the equilibrium species formed in the system copper(II)–Me_2heptaen for 1:1 and 2:1 metal–ligand ratios. It can be seen that for the 1:1 metal–ligand ratio the mononuclear species are almost the only species in solution, while for the 2:1 metal–ligand ratio the binuclear species largely predominate. The two longer ligands Me_2octaen and Me_2nonaen behave similarly.

For analysis of the macrocyclic effect, the metathetical reaction $[Cu_nL_{cy}] + L_{oc} \rightleftarrows [Cu_nL_{oc}] + L_{cy}$ ($n = 1$–2; cy = cyclic, oc = open chain) has to be considered.[15] This reaction presents negative log K values just for the mononuclear complexes of the ligands with six nitrogen donors, [18]aneN_6 and Me_2pentaen. This greater stability of the macrocyclic complex is due to a larger entropic contribution, even though the enthalpy is slightly more favourable for the formation of the open-chain complex. For the following terms of these series, Me_2hexaen and [21]aneN_7, the enthalpy term for the formation of the macrocyclic complex decreases to such extent that the macrocyclic effect vanishes, although the entropic term favors the formation of the macrocyclic complex (Table III). For all the other terms of both series, positive log K values are found for the metathetical reaction above mentioned, independent of the mono- or binuclear nature of the complexes formed. In the case of the binuclear complexes of the ligands Me_2nonaen and [30]aneN_{10}, both the enthalpic and entropic contributions favor the open-chain ligand complex. Currently we are extending these studies to other metal ions to elucidate the extent of this "antimacrocyclic" effect.

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Mechanism of Oxidation of the 2-Hydroxycyclohexyl Radical to Cyclopentanecarbaldehyde by Copper Ions in Aqueous Solutions

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Copper ions are known to catalyze the oxidation of cyclohexene by persulfate to yield cyclopentanecarbaldehyde. The mechanism suggested in the literature for this process involves the reaction of 2-hydroxycyclohexyl free radicals with Cu^{2+}(aq). In the present study the kinetics of reaction of these free radicals with copper ions were studied by the pulse-radiolysis technique. The results indicate that the mechanism of the catalytic process involves the following reactions: The reaction of the free radical with Cu^+(aq), and not with Cu^{2+}(aq), yields the transient complex 1-cuprio-2-hydroxycyclohexane(1+). This transient complex rearranges in a reaction that involves the ring contraction step to form 6-hydroxy-7λ^2-cuprabicyclo[3.2.0]heptane. The latter intermediate decomposes via heterolysis of one of the copper(II)–carbon σ bonds to form (1-cupriocyclopentyl)methanol(1+), which reacts with Cu^{2+}(aq) to form the final product, cyclopentanecarbaldehyde. The rates of the first three reactions in this sequence and the spectra of the first two intermediates are reported. The results thus point out the possibility to use the pulse-radiolysis technique to elucidate the mechanisms of complex catalytic processes.

Olefins are oxidized by persulfate ions, in aqueous solutions, to form a mixture of products. Thus, for example, the oxidation of cyclohexene yields a mixture of I–III.[2] It was suggested[2] that these products are formed via the reaction sequence