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Metal Complexes of Macrocyclic Ligands Containing Pyridine

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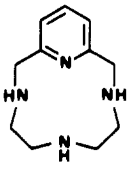
Some macrocyclic compounds containing pyridine have been synthesized: 3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene (**1**), 3,7,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**2**), 3,7,11,17-tetraazabicyclo-[11.3.1]heptadeca-1(17),13,15-triene (**3**), and 7-methyl-3,7,11,17-tetraazabicyclo[11.3.1]heptadeca-1(17),13,15-triene (**4**). The protonation reactions of these ligands were studied by potentiometric and ^{1}H NMR techniques, and it was found that all of them present two very basic and the other two very acidic nitrogen atoms. The stability constants of the complexes of **1–4** with some divalent first-series transition metal ions, Cd^{2+}, and Pb^{2+} were determined by potentiometric methods. The constants for the Co^{2+} complexes were impossible to determine due to their rapid reaction with dioxygen, followed by degradation of the species formed. The Irving–Williams order of stability is obeyed for all the complexes of those ligands, and the values of stability constants decrease with the increasing ring size of the macrocycle, with the exception of those of the copper complexes. The latter complexes present a different trend with stability constants of similar values, but the complex of **2** shows a lower stability. The Ni^{2+} complexes were studied by electronic and NMR spectroscopies, and the Cu^{2+} complexes, by electronic and ESR spectroscopies. The structures adopted by the complexes in aqueous solution are discussed, and comparison with the behavior of the corresponding complexes of the tetraaza macrocyclic ligands (without a pyridine nitrogen) is undertaken.

Introduction

Four ligands have been synthesized in the present work, one of them, **2**, for the first time. Ligand **1** has been prepared before,[1,2] but studies on its metal complex properties have never been undertaken. Stetter *et al.*[1] were interested in this macrocycle as a starting material for the synthesis of a triacetate derivative. Studies of some metal complexes with compounds **3** and **4** have been made, especially Cu^{2+}, Ni^{2+}, and Co^{2+} complexes,[3–6] and also with some N-functionalized derivatives.[3–14] However, the protonation constants of these ligands and their stability constants with several divalent metal ions are determined in the present work for the first time.



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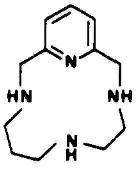

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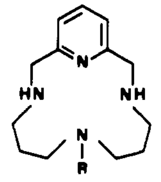
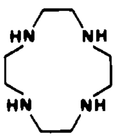


3-R=H

4-R=CH_3

1: 3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene (py[12]aneN$_4$)
2: 3,7,10,16-tetraazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (py[13]aneN$_4$)
3: 3,7,11,17-tetraazabicyclo[11.3.1]heptadeca-1(17),13,15-triene (py[14]aneN$_4$)
4: 7-methyl-3,7,11,17-tetraazabicyclo[11.3.1]heptadeca-1(17),13,15-triene (*N*-Mepy[14]aneN$_4$)

It is well-known that tetraaza macrocyclic compounds (**5–8**) present very peculiar properties on complexation, forming complexes with remarkable stability and inertness, even in very acidic media. Nevertheless, a restrictive property of many of these complexes for practical applications is the slow kinetics of their formation.[15]



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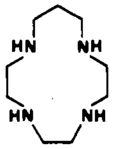

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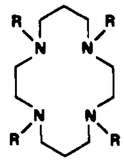
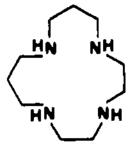


7-R=H

9-R=CH_3



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5: 1,4,7,10-tetraazacyclododecane ([12]aneN$_4$ or cyclen)
6: 1,4,7,10-tetraazacyclotridecane ([13]aneN$_4$)
7: 1,4,8,11-tetraazacyclotetradecane ([14]aneN$_4$ or cyclam)
8: 1,4,7,11-tetraazacyclotetradecane (isocyclam)
9: 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (tetramethylcyclam)

Searching for complexes with faster formation reactions, and also with high stability constants, especially presenting particular

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selectivity for some divalent metal ions, we have decided to undertake the study of some complexes of ligands containing a pyridine nitrogen in the macrocyclic ring. Compounds **1**–**4** were synthesized, their protonation properties studied, and the stability constants determined for their complexes with metal ions of different ionic radii, such as some first-series metal ions, Cd^{2+} and Pb^{2+}. To have some insight into the properties of the metal complexes in aqueous solution some spectroscopic studies were made.

Experimental Section

Reagents. Diethylenetriamine, *N*-(2-aminoethyl)-1,3-propanediamine, 3,3′-diaminodipropylamine, 3,3′-diamino-*N*-methyldipropylamine, and 2,6-pyridinedimethanol were obtained from Aldrich Chemical Co.; selenium dioxide, sodium borohydride, and sodium hydride were from Merck; triethylenetetramine (tren) was from BDH. All of them were used as supplied, without further purification.

2,6-Pyridinedicarbaldehyde was prepared by refluxing 2,6-pyridinedimethanol (1 g) with selenium dioxide (0.8 g) in dioxane (16 cm^3) during 3 h; the product obtained after evaporation of the solvent was recrystallized from chloroform–petroleum ether.[7]

2,6-bis(bromomethyl)pyridine was obtained by refluxing 2,6-pyridinedimethanol (5 g) with 47% hydrobromic acid for 2 h; after neutralization with NaOH (10 M), the product precipitated was recrystallized from petroleum ether.[16]

All the ligands were synthesized and purified in our laboratory. The other chemicals used were of reagent grade, and organic solvents were purified by standard methods.[17]

Synthesis and Characterization of the Ligands. Compounds **1** and **2** were synthesized by following the method of Richman and Atkins,[18] with some modifications. Ligands **3** and **4** were synthesized by a template method, using copper(II).[6]

2 was prepared by condensation of the disodium salt of *N*-(2-((*p*-tolylsulfonyl)amino)ethyl)-*N*,*N*′-bis(*p*-tolylsulfonyl)-1,3-propanediamine (0.011 mol, 6.38 g) with 2,6-bis(bromomethyl)pyridine (0.011 mol, 2.89 g) in 125 cm^3 of dry dimethylformamide (dmf) at 110 °C for 5 h. The disodium salt was obtained immediately before the reaction by addition of NaH (0.033 mol) in dry dmf (15 cm^3) to a solution of *N*-(2-((*p*-tolylsulfonyl)amino)ethyl)-*N*,*N*′-bis(*p*-tolylsulfonyl)-1,3-propanediamine (0.011 mol) in dmf (55 cm^3), under nitrogen. The solution of the 2,6-bis(bromomethyl)pyridine in dmf (55 cm^3) was added slowly, dropwise, during a period of 3 h. At the end of the reaction, the solution was filtered off and concentrated to one-tenth of the initial volume. The product then precipitated and was washed with warm water (60 °C), NaOH (5 M), and water again. The pure tristosylated cyclic amine (tosyl ≡ *p*-tolylsulfonyl) was obtained after recrystallization from methanol (yield 30%). The tosyl groups were removed by reductive cleavage, refluxing the tosylated cyclic amine (1.0 g, 0.0015 mol) with a mixture of glacial acetic acid, 48% hydrobromic acid (9:16 v/v), and phenol (0.85 g) for 7 h. The mixture was concentrated and extracted with chloroform (4 × 30 cm^3); the aqueous layer was concentrated, and the required cyclic amine was precipitated by diethyl ether and obtained in the hydrobromide form, **2**·4HBr (yield 80%). Mp: 122–4 °C. ^1H NMR (D_2O, DSS): δ (ppm) 7.88 (1H, t), 7.45 (2H, m), 4.53 (2H, s), 4.47 (2H, s), 3.60 (4H, m), 3.27 (4H, m), 2.25 (2H, q). ^{13}C NMR (D_2O, dioxane): δ 150.31, 150.08, 140.07, 125.06, 124.76, 49.60, 49.07, 43.49, 42.52, 41.99, 41.08, 20.38 ppm. Anal. Calc for $C_{12}H_{24}N_4Br_4 \cdot H_2O$: C, 25.7; H, 4.7; N, 10.0. Found: C, 25.4; H, 4.6; N, 9.8.

1 was synthesized by the procedure described for **2** but using the disodium salt of *N*,*N*′,*N*″-tris(*p*-tolylsulfonyl)diethylenetriamine instead of disodium salt of *N*-(2-((*p*-tolylsulfonyl)amino)ethyl)-*N*,*N*′-bis(*p*-tolylsulfonyl)-1,3-propanediamine,[1,2] followed also by the removal of the tosyl groups by refluxing with a mixture of glacial acetic acid, 48% hydrobromic acid, and phenol, and obtained in the hydrobromide form, **1**·3HBr (yield 70%). Mp: 250–4 °C dec. ^1H NMR (D_2O, pD 8.66, DSS): δ (ppm) 7.915 (1H, t), 7.417, 7.391 (2H, d), 4.482 (4H, s), 3.142 (4H, t), 2.908 (4H, t). ^{13}C NMR (D_2O, pD 2.8, dioxane): δ 149.18, 139.59, 122.29, 49.25, 47.26, 44.39 ppm. Anal. Calc for $C_{11}H_{21}N_4Br_3$: C, 29.4; H, 4.7; N, 12.5. Found: C, 29.4; H, 4.5; N, 12.2.

3 was synthesized by the addition of 3,3′-diaminodipropylamine (in ethanol) to a solution of 2,6-pyridinedicarbaldehyde and copper nitrate (in a mixture of ethanol/water, 1:1 v/v). The copper(II) diimine complex formed was reduced by sodium borohydride, and the copper was removed by precipitation of its sulfide (yield 86%). Mp: 83–5 °C. ^1H NMR ($CDCl_3$, TMS): δ (ppm) 7.50 (1H, t), 6.97 (2H, d), 3.85 (4H, s), 2.88 (3H, br), 2.72 (4H, t), 2.62 (4H, t), 1.71 (4H, m). ^{13}C NMR ($CDCl_3$): δ (ppm) 159.13, 136.50, 120.63, 54.26, 47.50, 46.30, 28.90. Anal. Calc for $C_{13}H_{22}N_4$: C, 66.6; H, 9.5; N, 23.9. Found: C, 66.5; H, 9.3; N, 23.6.

4 was prepared by a procedure analogous to that for **3**, replacing the 3,3′-diaminodipropylamine by 3,3′-diamino-*N*-methyldipropylamine.[6] (yield 75%). Mp: 79–80 °C. ^1H NMR ($CDCl_3$, TMS): δ (ppm) 7.43 (1H, t), 6.90 (2H, d), 3.77 (4H, s), 3.14 (2H, br s), 2.44 (4H, t), 2.27 (4H, t), 1.96 (3H, s), 1.63 (4H, m). ^{13}C NMR ($CDCl_3$): δ (ppm) 159.16, 136.21, 120.25, 56.09, 54.30, 46.44, 40.70, 26.89. Anal. Calc for $C_{14}H_{24}N_4$: C, 67.7; H, 9.7; N, 22.6. Found: C, 67.7; H, 9.8; N, 22.9.

Other Reagents and Standard Solutions. Metal nitrates of analytical grade were used and solutions prepared in demineralized water (obtained by a Millipore/Milli-Q system) and standardized with Na_2H_2EDTA.[19] Carbonate-free solutions of the titrant, KOH, were prepared by dilution of a commercial ampule of Titrisol (Merck) analytical concentrate with demineralized water under a stream of purified nitrogen gas. The solutions were standardized by titration with hydrochloric acid and discarded when the concentration of carbonate reached 0.5% of the KOH present.

Potentiometric Equipment and Measurements. For the potentiometric titrations an Orion 720 measuring instrument was used together with an Orion 91-01 glass electrode, an Orion 90-05 Ag/AgCl reference electrode, and a Wilhelm-type salt bridge containing 0.1 M KNO_3 solution. Titrations were carried out in a thermostated cell kept at 25.0 ± 0.1 °C by circulating water through the jacketed titration cell from a Grant W6 thermostat, and the ionic strength of the solutions was kept at 0.10 M with KNO_3, as described previously.[20]

The emf of the cell is given by $E = E'^{\circ} + Q \log [H^+] + E_j$, and both E'° and Q were determined by titrating a solution of known hydrogen ion concentration at the same ionic strength, using the acid pH range of titration. The term pH is defined as $-\log [H^+]$. E_j, the liquid-junction potential, was found to be negligible under the experimental conditions used. The ionic product of water, $K_w = [H^+][OH^-]$, was determined from data obtained in the alkaline range of the titration, considering E'° and Q valid for the entire pH range, and found equal to $10^{-13.78}$.

The potentiometric equilibrium measurements were made on 20.00 cm^3 of ligand ≈2.50 × 10^{-3} M diluted to a final volume of 30.00 cm^3, first in the absence of metal ions and then in the presence of each metal ion for which the m_L:m_M ratios were 1:1 or 2:1. The E data were collected after additions of 0.025- or 0.050-cm^3 increments of standard KOH solution.

Formation Constant Studies. Equilibration of ligands **1**–**4** with most of the metal ions is fairly rapid, and automatic titrations were possible, with the exception of the case of the Ni^{2+} complexes of all the ligands studied in this work, which required several days for the equilibration (45, 17, and 6 days for complexes of **1**–**3**, respectively). For these cases of slow equilibration "out-of-cell" titrations were used.[21]

Calculation of Equilibrium Constants. Protonation and stability constants were calculated by fitting the potentiometric data to the SUPERQUAD program.[22] The initial computations were obtained in the form of overall protonation constants

$$\beta^{H}_{i} = \frac{[H_iL]}{[L][H]^i}$$

or overall stability constants

$$\beta = \frac{[M_mL_lH_h]}{[M]^m[L]^l[H]^h}$$

Differences between the various log β^H_i or the log β values provide the stepwise protonation constants or the stepwise formation and protonation constants of the complex reactions. The species introduced were limited

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Table I. Protonation (log K_i^H) Constants of Ligands **1**–**4** (T = 25.0 °C; I = 0.10 M (KNO_3))

	equilibrium quotient (log units)			
ligand	[HL]/ [L][H]	$[H_2L]$/ [HL][H]	$[H_3L]$/ $[H_2L]$[H]	$[H_4L]$/ $[H_3L]$[H]
py[12]aneN_4 (**1**)	10.33(4)	7.83(5)	(1.27)	<1
py[13]aneN_4 (**2**)	9.79(2)	8.49(1)	2.85(5)	<1
py[14]aneN_4 (**3**)	9.92(1)	8.56(3)	4.66(4)	<1
N-Mepy[14]aneN_4 (**4**)	9.74(4)	8.67(5)	4.67(6)	<1

to those which can be justified by established principles of coordination chemistry. Species distribution curves were generated with the aid of the program SPE.[23]

A minimum of two titrations, performed by the automated system, for which the m_L:m_M ratios were 1:1 and 2:1, was used, 1:1 being the only ratio for the titrations performed by the "out-of-cell" procedure. In the case of the reaction of Cu^{2+} with compound **1**, a ligand–ligand competition titration was performed using a 1:1:1 m_L:$m_{L'}$:m_M ratio (L being the ligand **1**, L′ the reference ligand, and M the Cu^{2+} ion), as the complex was already completely formed in the beginning of a direct potentiometric titration. The reference ligand used for the competition was trien.

The errors quoted are the standard deviations of the overall stability constants given directly by the program. In the case of the stepwise formation and protonation constants, the standard deviations were determined by the normal propagation rules and do not represent the total experimental errors.

Spectroscopic Studies. Proton NMR spectra were recorded with a Varian Unity 300 spectrometer. The adjustment in pD for the NMR titrations was made with an Orion 420A instrument fitted with a combined Ingold microelectrode. The –log [H^+] was measured directly in the NMR tube, after the calibration of the microelectrode with buffered aqueous solutions, and the final pD calculated by the equation pD = pH + 0.40.[24] Solutions of the ligands for the NMR measurements (≈0.01 M) were made up in D_2O, and the pD was adjusted by adding DCl or CO_2-free KOD. Sodium 3-(trimethylsilyl)propane-1 sulfonate (DSS) was used as an internal reference. ^{13}C NMR spectra were recorded with the same spectrometer, and dioxane was used as internal reference.

Electronic spectra were measured with a Perkin-Elmer Model Lambda 9 spectrophotometer for UV–vis–near-IR, using aqueous solutions of the complexes prepared by the addition of the metal ion to the ligand at the appropriate pH value (corresponding to the total formation of the metal complex). The solutions of the nickel(II) complex of ligand **1** were prepared in 1 M KNO_3, those of the copper(II) complexes with all ligands were prepared in 0.1 M KNO_3, but the nickel(II) complexes with **2**–**4** were prepared without inert electrolyte. The nickel complexes were also studied by ^1H NMR spectroscopy using a maximum spectral width of 10^5 Hz, and ^{13}C NMR spectra of the diamagnetic complexes were recorded.

The copper(II) complexes were also studied by ESR spectroscopy, using a Bruker ER 200-SRC spectrometer equipped with an Oxford Instruments continuous-flow cryostat. The spectra of the complexes (1.2×10^{-3} M in 1.0 M $NaClO_4$) were recorded at 77 K (in liquid nitrogen). For higher concentrations of the complexes and lower ionic strength, only one broad resonance is observed. The concentration of the copper complexes used is well below the range where ion–ion dipolar broadening can be detected. The computer simulation of the ESR spectra was carried out with a program for a microcomputer.

Results

Protonation Constants. In Table I are summarized the protonation constants for ligands **1**–**4**. These ligands present two high and two low values of protonation constants (log units). The last constant was not determined due to its very low value, which prevents the determination by potentiometric measurements. ^1H NMR spectroscopy titrations of ligands **1** and **3** were carried out to understand the sequence of the protonation. Figure 1 shows a spectrum of **1** at pD 8.70, and Figure 2, the spectrum of **3** at pD 5.96 and also the titration curves for the entire pD range for the two ligands.

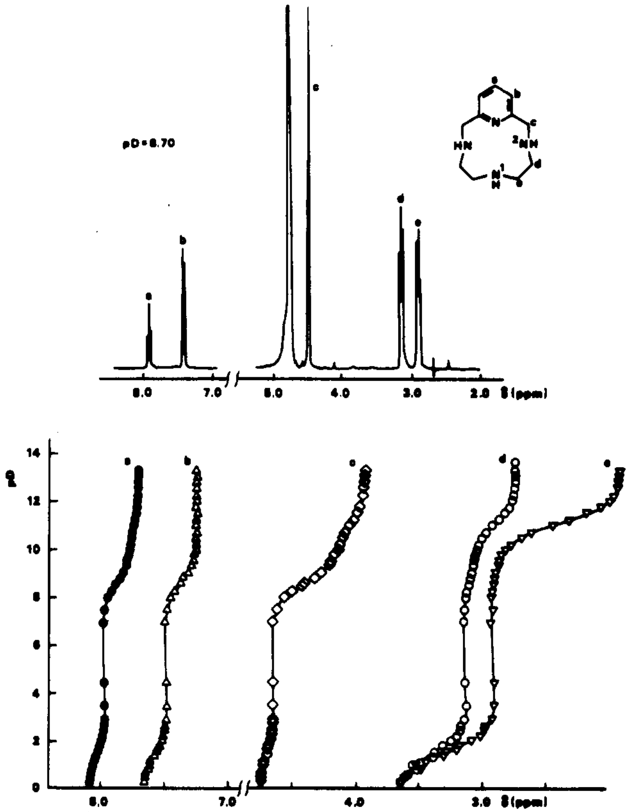

Figure 1. ^1H NMR spectrum of ligand **1** at pD = 8.70 and titration curve for pD *versus* δ (ppm).

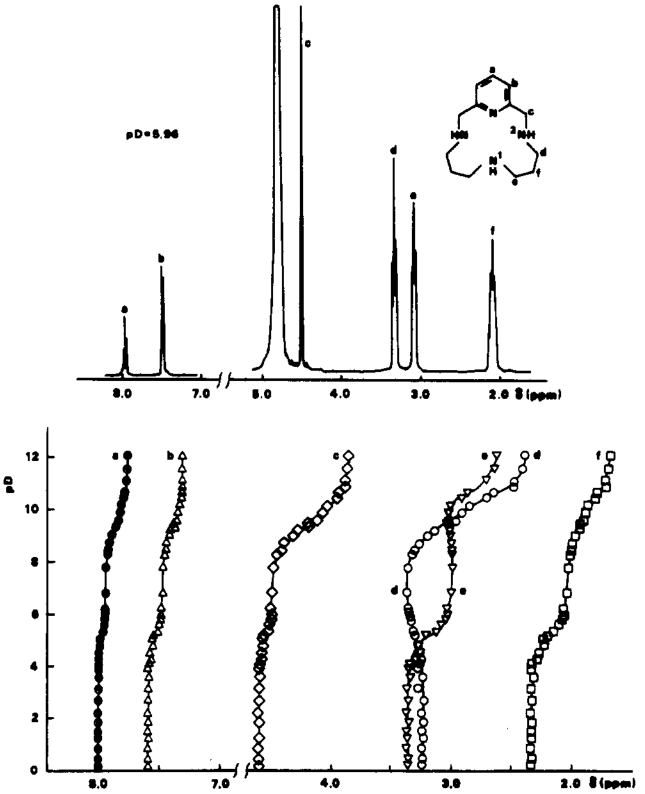

Figure 2. ^1H NMR spectrum of ligand **2** at pD = 5.96 and titration curve for pD *versus* δ (ppm).

The spectra of **1** exhibit five resonances over almost the entire pD range, but the resonances assigned to e and d overlap for pD values below 1.0. The assignment of the resonances is straightforward for a–c, taking into account the area ratio and the pattern of each absorption. The two resonances at low field were assigned to the protons of the pyridine ring: the triplet to the a protons

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and the doublet to the b protons. At high field, three resonances appear: the singlet readily assigned to the methylenic protons c and two triplets of the methylenic protons d and e. The assignment of these last two resonances was made using the technique of selective INEPT (intensive nuclei enhanced by polarization transfer), followed by a 2D carbon/proton correlation. The experiment was performed at pD 2.8. At this pD, the ^{13}C NMR spectrum exhibits resonances at δ (ppm) 149.18, 139.59, 122.29, 49.25, 47.26, and 44.39 and the correspondent ^{1}H NMR spectrum resonances at δ (ppm) 7.97 (t), 7.50 (d), 4.64 (s), 3.18 (t), and 2.95 (t). Selective irradiation of protons c (4.64) resulted in the enhancement of ^{13}C signals at δ (ppm) 149.18 (two-bond J_{CH} coupling, ortho carbon of the pyridine ring), 122.29 (three-bond J_{CH} coupling, meta carbon of the pyridine ring), and 47.26 (three-bond J_{CH} coupling). A J_{CH} value for the long-range coupling of 4 Hz was used. Correlation of the resonances at 47.26 ppm in the ^{13}C NMR spectrum with the d protons at 3.18 ppm in the ^{1}H NMR spectrum was observed in a two-dimension experiment. The ^{1}H NMR titration curves show the effect of the successive protonation of the various basic centers of the molecule: the first equivalent of acid added to the basic form of the ligand **1** (pD 12.0–9.5) protonates mainly the nitrogen atom opposite the pyridine nitrogen, since only resonances d and e shift downfield; resonance c has a very small shift in this pD range, meaning a small percentage of protonation in nitrogen atoms N^2. The second equivalent of acid added (pD 9.0–7.0) protonates the pyridine nitrogen, as resonances a–c move downfield. The addition of one more equivalent of acid (pD <3.0) seems to change the conformation of the ligand, involving a redistribution of charges in the ring. Similar effects were observed in the tetraaza macrocyclic compounds when the third nitrogen was protonated and were attributed to the modifications of the conformation of the tetraaza rings to minimize repulsions between two positively charged nitrogen atoms at short distance.[25,26] In the case under study, the differences in behavior of the macrocycle in the basic and acidic regions are more remarkable due to the asymmetry of the macrocyclic ring caused by the pyridine moiety. In fact, it seems that for low pD values (between 3.0 and 1.0) the first two centers already protonated are deprotonated in favor of the other two basic centers (the nitrogen atoms N^2) and nitrogen atoms N^1 are again protonated. This sequence explains the fact that resonance c does not shift for pD values below 6, as these protons are simultaneously affected by the deprotonation of the pyridine nitrogen and the protonation of nitrogen atoms N^2 and the shift of resonance e is almost similar to that of resonance d. At the end of the titration, at pD = 0, only three protonations have occurred, meaning that one nitrogen center is not protonated even for very low pD values.

The spectra of **3** exhibit six resonances over the entire pD range, whose assignment was carried out as described for **1**. Triplet a and doublet b at low field were assigned to the protons of the pyridine ring; the quintuplet at high field was assigned to protons f; the singlet at high field was readily assigned to the methylenic protons c and two triplets of the methylenic protons d and e. The assignment of protons d and e was made by two different experiments: an ^{1}H NMR titration of ligand **4** (*N*-Mepy[14]aneN$_4$) and a selective INEPT experiment. The ^{1}H NMR titration curve of **4** presents a pattern exactly the same as that of **3**, but the first ligand exhibits one resonance more (a singlet at high field) readily assigned to protons of the methyl group bonded to the nitrogen atom opposite the pyridine one. This resonances has the same profile as resonance e, which can be assigned by comparison. The selective INEPT experiment was made at pD 8.66. At this pD, the ^{13}C NMR spectrum exhibits resonances at δ 152.17, 139.07, 122.22, 50.41, 47.09, 46.49, and 24.76 ppm and the correspondent ^{1}H NMR spectrum resonances at δ (ppm) 7.93 (t), 7.44 (d), 4.37 (s), 3.25 (t), 3.03 (t), and 2.00 (q). Selective irradiation of protons c (4.37 ppm) resulted in the enhancement of ^{13}C signals at 152.17 (two-bond J_{CH} coupling), 122.22 (three-bond J_{CH} coupling), and 47.09 ppm (three-bond J_{CH} coupling). Correlation of the resonance at 47.09 ppm in the ^{13}C NMR spectrum with the d protons at 3.25 ppm in the ^{1}H NMR spectrum was observed in a two-dimension experiment. The ^{1}H NMR titration curves show a profile different from that of **1** (Figure 2): the first 2 equiv of acid added to the basic form of **3** (pD 11.0–10.0) spreads over to all nitrogen atoms of the ring, but in a larger percentage to the nitrogen atom N^2, since all resonances shift downfield; resonances c and d shift more and shift continuously in this entire range of pD; the third equivalent of acid added (pD 5.8–4.0) protonates mainly N^1, opposite the pyridyl group, as resonances e and f move downfield, although the slight shifts of resonances c and b reveal a small percentage of protonation of the pyridine atom; the addition of more acid till pD = 0 does not lead to any alteration of the shift parameters of the resonances, meaning that, in spite of the increase of the cavity size of the ring, one nitrogen center is not protonated even for very low pD values and, contrary to what happens with **1**, it is the pyridine nitrogen that is the nonprotonated center in this ligand.

The ^{1}H NMR titrations allowed also the determination of the protonation constants in D_2O: for **1**, $\log K_1(D) = 11.52(2)$, $\log K_2(D) = 8.99(1)$, and $\log K_3(D) = 1.41(4)$, and for **3**, $\log K_1(D) = 10.84(8)$, $\log K_2(D) = 9.58(3)$, and $\log K_3(D) = 5.26(8)$. These values are in agreement with the equation for the correlation between the protonation constants determined in H_2O and D_2O obtained before:[24] $pK(D) = 0.11 + 1.10pK(H)$.

Stability Constants. The values of the stability constants for the complexes of the four ligands with some divalent first-series transition metal ions, Cd^{2+} and Pb^{2+}, determined in water, are shown in Table II. In most cases only 1:1 complexes are formed; but hydroxo complexes are also found with some metal ions. We have checked the possibility of formation of other species like protonated (MH_iL) or ML_2, but they do not appear to be formed under the conditions used, according to the best set of stability constants determined by the SUPERQUAD program.

The copper(II) complexes with these ligands have very high stability constants, the value of the constant for the complex with ligand **1** being impossible to determine by direct potentiometry, as this ligand is the least basic of the four studied in this work, and the metal complex was completely formed even at low pH. However, a competition reaction with another ligand (trien) enables the determination of the constant, using the SUPERQUAD program:

$$ML' + H_nL \rightleftarrows ML + (n - m)H^+ + H_mL'$$

where L′ is trien, L is ligand **1**, and M is Cu^{2+}. The values of the protonation and stability constants of trien were taken from the literature:[27] protonation constants, $\log \beta_1 = 9.48$, $\log \beta_2 = 18.35$, $\log \beta_3 = 24.89$, $\log \beta_4 = 28.32$; stability constants, $\log \beta_{ML} = 20.10$, $\log \beta_{MHL} = 23.60$, $\log K_{MLOH} = 10.8$ (the equilibrium quotient for the last constant being $[ML]/([MLOH][H])$). Figure 3 shows the species distribution diagram of this competition reaction obtained with the SPE program.[23]

It was, however, impossible to determine the stability constants for the Co^{2+} complexes with ligands **2**–**4**, due to a continuous drifting of the pH readings, as oxidation of the complexes occurs in water solution, even with a strong stream of nitrogen gas. It seems that the inclusion of the pyridine ring into the macrocycle creates special electronic and steric effects on oxygenation of the cobalt complexes, as no similar effects were observed with the tetraaza macrocycles, **5** to **9**. The Co^{2+} complex of ligand **1** seems more stable, and a value for stability constant was

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Table II. Stability Constants (log *K*) for the Metal Complexes of Ligands 1–4 with Several Divalent Metal Ions (T = 25.0 °C; I = 0.10 M (KNO_3))

		value (log units)			
metal ion	equilibrium quotient	py[12]aneN_4 (**1**)	py[13]aneN_4 (**2**)	py[14]aneN_4 (**3**)	*N*-Mepy[14]aneN_4 (**4**)
Mn^{2+}	[ML]/[M][L]	8.81(1)	7.29(2)	5.477(5)	3.70(2)
	[ML]/[MLOH][H]		9.93(9)		9.10(3)
Fe^{2+}	[ML]/[M][L]	12.547(7)	10.76(2)	9.34(1)	
	[ML]/[MLOH][H]			10.91(7)	
Ni^{2+} [a]	[ML]/[M][L]	17.05(8)	16.81(3)	16.267(6)	
Cu^{2+}	[ML]/[M][L]	20.14[b]	18.62(3)	19.76(2)	20.23(2)
	[ML]/[MLOH][H]	7.48[b]	10.4(9)		
Zn^{2+}	[ML]/[M][L]	14.40(1)	14.27(2)	12.816(5)	11.91(1)
	[ML]/[MLOH][H]	8.5(2)	7.83(5)	8.48(6)	8.06(3)
Cd^{2+}	[ML]/[M][L]	12.670(2)	11.64(1)	9.759(3)	8.77(1)
	[ML]/[MLOH][H]	10.44(4)	10.02(4)	10.30(3)	9.62(2)
Pb^{2+}	[ML]/[M][L]	15.422(4)	12.275(8)	9.715(3)	9.029(8)
	[ML]/[MLOH][H]	10.58(1)	9.99(1)	10.948(6)	

[a] "Out-of-cell" titration. [b] Values obtained by a competition titration, using trien.

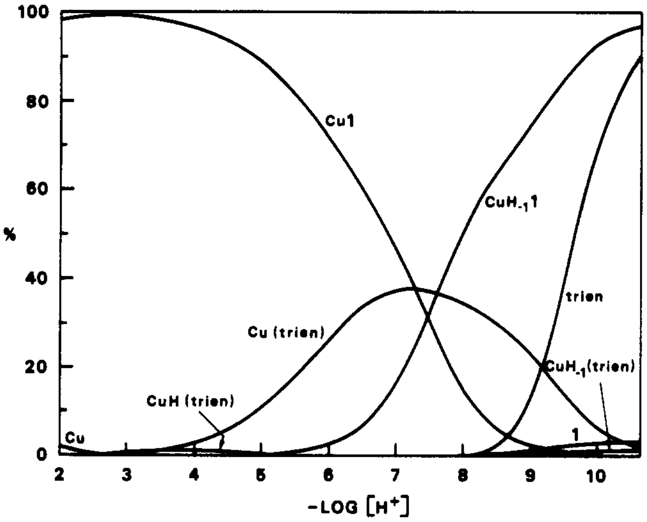

Figure 3. Species distribution curves calculated for the aqueous solution containing **1**, trien, and Cu^{2+} at a molar ratio of 1:1:1. Percent values represents concentrations relative to the total amount of copper(II) at an initial value of 1.667 × 10^{-3} M.

determined by an automated titration (log K_{ML} = 15.69(4) was obtained). The yellow solution of the cobalt(II) complex turns to brown when left in air at pH 3.12 and light pink in some hours. The Co^{2+} complex of ligand **2** presents the same degradation and the same colors, but the stability constant could not be determined, as it was impossible to obtain stable values of pH; however the formation of the dioxygen species and further decomposition of the complex were followed by visible spectroscopy. The yellow solution of the complex, Co^{2+}/**2**, exhibits two bands 5 min after preparation [λ_{max}/nm (ϵ/M^{-1} cm^{-1}) 560 (156.0), and 360 (2438.0)]; both bands increase with time, exhibiting maximum absorptivity values 12 h later (225.0 and 3125.0 M^{-1} cm^{-1}, respectively), which points to the formation of the μ-peroxo binuclear complex; after that time, both bands start to decrease, while a new band appears at 440 nm, which increases with time; the spectrum of the solution exhibits three bands 15 days after preparation: λ_{max}/nm (ϵ/M^{-1} cm^{-1}) 560 (187.5), 440 (687.5), 360 (1688.0), characteristic of the formation of the oxidized Co(III) species.[28,29] The cobalt complex of **3** did not show any alteration of the initial yellow color when exposed to the air, but the irreversible autoxidation of the complex could be verified by electronic spectroscopy: A solution of the Co^{2+} complex at pH 4.8 shows an electronic spectrum with three bands 3 min after preparation [λ_{max}/nm (ϵ/M^{-1} cm^{-1}) 460 (12), 368 (103), 320 (119.6)]; absorption at 320 nm increases (ϵ = 214.7 and 365.0 M^{-1} cm^{-1} 22 min and 21 h later, respectively), and bands at 368 and 460 nm increase slightly in the first 2 h and then decrease, corresponding to the formation of the μ-peroxo binuclear complex; 3 days after the formation of the complex, the band at 320 μm disappears, the other two remaining at 368 nm (ϵ = 37.0 M^{-1} cm^{-1}) and 460 nm (ϵ = 18.0 M^{-1} cm^{-1}) for the Co(III) species.

The greenish Ni^{2+} complex of **2** has, at 23 °C, an electronic spectrum typical of a high-spin octahedral complex with three bands (915, 550, and 410 nm, of low absorptivity; cf. Table III). The increase of the temperature decreases the bands at 915 and 550 nm, increasing the band at 410 nm. The ^1H NMR spectrum of this complex in D_2O reveals some broad resonances characteristic of a paramagnetic species and some sharp resonances in the region 1.20–7.83 ppm characteristic of a diamagnetic species. This spectrum is consistent with rapid equilibrium between the paramagnetic diaqua species (blue) and the diamagnetic square-planar species (yellow), in a proportion 2:1. When the solution is heated to 45 °C or when the ionic strength is increased by addition of an inert electrolyte like KNO_3, the solution becomes yellow, and the area of the broad resonances decreases while the area of the resonances of diamagnetic species increases (in a ratio 1:1 at 45 °C). A ^{13}C NMR spectrum of the mixture of complexes at 45 °C shows one species with 12 resonances, easily assigned (ppm): 161.26, 159.00 (two ortho C's of the pyridine ring); 141.90 (one para C of the pyridine ring); 120.78, 120.03 (two meta C's of the pyridine ring); 61.07, 56.74 (two C's of the N=$CHCH_2N$ moiety); 55.33, 50.14, 49.75, 48.95 (four C's, NCH_2C); 28.50 (one C of the propane chain, CCH_2C). The Ni^{2+} complex of **1** is blue and exhibits a visible–near-IR spectrum characteristic of a high-spin six-coordinate complex, showing two absorption bands at 960 and 560 nm (the peak at high energy can be obscured by the intense charge-tranfer absorption). The ^1H NMR spectrum, at 23 °C, of this complex shows five broad resonances of a paramagnetic species and some very small peaks in the region 7.83–2.26 ppm which can be assigned to a small amount of a diamagnetic species (by the relation of areas, for a solution in 1 M KNO_3, it seems that the diamagnetic species exists in about 20% of the total amount). An increase of the temperature to 45 °C does not cause a sensible change in the spectrum, and it was impossible to record a ^{13}C NMR spectrum of the small amount of diamagnetic species. The nickel(II) complexes of the two ligands with the same cavity size, **3** and **4**, exhibit very similar electronic spectra and probably have similar structures, although completely different from those already mentioned. The visible–near-IR spectrum of the Ni^{2+} complex of **3**, which is brown, exhibits five bands, those which appear at low energies having low intensities characteristic of a high-spin five-coordinate complex. The spectrum is similar to that of [Ni(tetramethylcyclam)(H_2O)]$^{2+}$, well characterized in solution,[30,31] and

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Table III. Spectroscopic UV–Vis–Near-IR Data for the Ni^{2+} and Cu^{2+} Complexes of **1**–**4** and EPR Data for the Cu^{2+} Complexes

complex	pH; color	UV–vis–near-IR λ_{max}/nm (ϵ/M^{-1} cm^{-1})	EPR: g_x; A_x (10^4 cm^{-1}) $x = 1$	$x = 2$	$x = 3$
$Ni(py[12]aneN_4)^{2+}$	3.3; blue-purple	960 (63.7), 560 (33.1) (in 1 M KNO_3)			
$Ni(py[13]aneN_4)^{2+}$	7.05; greenish	915 (5.0), 550 (2.2), 410 (5.3)			
$Ni(py[14]aneN_4)^{2+}$	7.11; brown	920 (3.0), 790 (7.4), 735 (7.7), 460 (33.6), 320 (sh, 43.5)			
$Ni(N\text{-}Mepy[14]aneN_4)^{2+}$	7.06; yellow-brown	900 (4.5), 792 (10.3), 750 (11.3), 466 (78.0), 330 (sh, 110.0)			
$Cu(py[12]aneN_4)^{2+}$	3.47; blue	695 (161)	2.033; 26.6	2.084; 38.9	2.210; 161.0
$Cu(py[13]aneN_4)^{2+}$	6.89; purple	580 (192)	2.040; 23.8	2.052; 43.1	2.188; 197.7
$Cu(py[14]aneN_4)^{2+}$	8.0; purple	560 (187)	2.040; 4.8	2.110; 9.8	2.178; 199.3
$Cu(N\text{-}Mepy[14]aneN_4)^{2+}$	6.0; purple	550 (119)			

Table IV. ^1H and ^{13}C NMR Data for the Ni^{2+} Complexes of the Ligands **1**–**4** (ppm)

complex	^1H NMR (23 °C) paramagnetic species	diamagnetic species	^{13}C NMR (45 °C)
$Ni(py[12]aneN_4)^{2+}$	201.0, 114.7, 61.4, 15.11, −5.23	7.83–7.30 (m), 4.25 (s), 3.21–2.26 (m)	
$Ni(py[13]aneN_4)^{2+}$	128.6, 113.3, 62.8, 41.1, 15.8, −1.9, −3.3, −9.4, −18.7	7.831 (t), 7.186 (d), 4.334–4.045 (m), 2.961 (m), 2.639 (m), 2.468 (m), 1.862 (d), 1.203 (q)	161.26, 159.00, 141.90, 120.78, 120.03, 61.07, 56.74, 55.33, 50.14, 49.75, 48.95, 28.50
$Ni(py[14]aneN_4)^{2+}$	81.5, 62.0, 36.5, 31.8, 26.2, 13.2, 12.0, 11.5, 8.5, 3.8, 3.1, 1.1, 0.6, −1.6, −6.8, −16.6		
$Ni(N\text{-}Mepy[14]aneN_4)^{2+}$	68.1, 42.5, 35.6, 26.4, 17.9, 14.3, 11.6, 3.4, 1.9, 0.3, −6.4		

in the solid state by X-ray crystallography,[32] as having a high-spin, five-coordinate square-pyramidal configuration, with the nitrogen donors coplanar with all the four methyl groups on one side of the macrocycle. When the ionic strength or the temperature of the complex is increased, the bands at 320 and 460 nm also increase. The Ni^{2+} complex of **4** is similar to that of **3**, although with slightly higher values of molar absorptivity, indicating a greater degree of distortion of this last complex. Both of these complexes are paramagnetic, their ^1H NMR spectra exhibiting a large quantity of broad resonances (cf. Table IV), but the complex of **3** seems to present two isomers, as the spectrum has two kinds of broad resonances, some of them with a smaller area. Increasing the temperature to 45 °C causes all resonances to move to lower field and other small broad resonances to appear at 7.9, 7.5, 6.8, 6.1, 4.2, 3.8, 3.4, and 2.9 ppm, two other larger resonances to appear at 6.15 and 5.33 ppm, and a broad triplet to appear centered at 1.4 ppm, indicating an equilibrium between two paramagnetic species.

The electronic spectra of the copper(II) complexes with ligands **1**–**4**, in aqueous solution, exhibit only a single broad band in the visible region, due to the copper d–d transition. However, complexes of **2**–**4** have ill-defined shoulders, the first one at ≈700 nm and the last two at ≈350 nm. In the ESR spectra of all the complexes, shown in Figure 4, four lines are observed due to the copper coupling, and no hyperfine coupling due to the coupling with the four nitrogen atoms is observed. The simulation of the ESR spectra leads to three different principal values of g. This fact indicates that the copper(II) ions of these complexes are present in rhombically-distorted ligand fields. Nevertheless, the difference between the values of g_1 and g_2 for the complex with **2** is very small.

The data obtained are summarized in Tables III and IV.

Discussion

Protonation Studies. The protonation constants of these compounds, determined in the present work, show a behavior similar to that of the tetraaza macrocyclic compounds: two very basic and the other two very acidic nitrogen atoms. The higher values of protonation constants (in log units) correspond to the protonation of nitrogen atoms in opposite positions, minimizing the electrostatic repulsion between positive charges of the ammonium groups formed. However, the second protonation constant of **1** is lower than the corresponding constant of the other three ligands. The reason for this seems to be related to the size of this macrocycle, as shown by the sequence of protonation followed by ^1H NMR. While in **1** the second protonation involves the pyridine nitrogen, in **3** and probably in the other ligands, due to the similarity of constants, the second protonation occurs at secondary nitrogens. It is interesting to note that the conformation adopted by the ring of **1** when the pyridine nitrogen is protonated could not be retained for low pH values, when the third protonation occurs, and an alteration of the conformation seems to be adopted by the macrocycle with a redistribution of the charged nitrogen atoms. The third and fourth values ($\log K_3$ and $\log K_4$) correspond to the protonation of nitrogen atoms at short distances from another already protonated nitrogen and the strong repulsions then aroused in the molecule, where the motion is limited by the skeleton of the ring, make the protonation difficult. When the size of the chain between contiguous nitrogen atoms increases (with the number of methylenic groups), the third protonation constant in log values also increases (1.27 for **1**, 2.85 for **2**, and 4.66 for **3**). The introduction of the methyl substituent on the

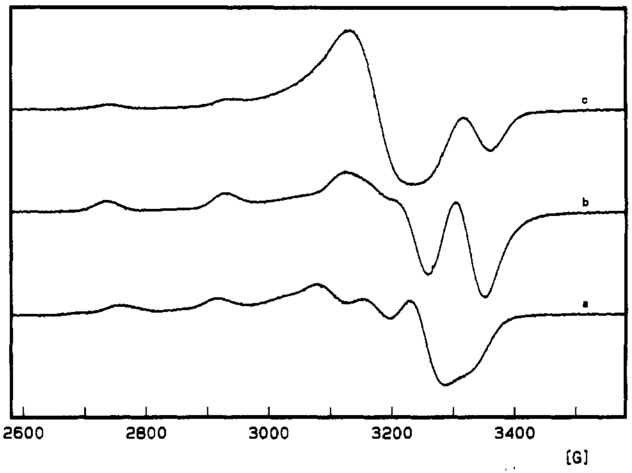

Figure 4. ESR spectra of Cu^{2+} complexes of **1** (a), **2** (b), and **3** (c).

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nitrogen atom opposite the pyridine nitrogen has practically no effect on the values of protonation constants.

The overall basicity of these ligands containing pyridine is smaller than that of corresponding tetraaza macrocycles,[21] as expected. In fact, the replacement of a pyridine ring by an alkylamino group of a polyamine when they are similarly positioned results in the lowering of the basicity, as also observed for linear polyamines.[33-37]

Metal Complexation Studies. The Irving–Williams order of stability is obeyed for all the ligands, and the values of stability constants decrease with increasing ring size of the macrocycle, with the exception of those of the copper complexes. These last complexes present a different trend with stability constants of similar values, but the complex of **2** shows a lower stability.

The introduction of one methyl group as a substituent on the nitrogen atom opposite the pyridine nitrogen slightly decreases the value of the stability constants of the metal complexes compared to those formed with the parent ligand, except for the copper complexes, which both present about the same values. As the overall basicities of the two 14-membered ligands are similar, the differences in the complexation behavior of the ligands may be attributed to steric crowding in the structure of the complexes of the *N*-methyl derivative.

When the values of stability constants of the metal complexes of the ligands containing pyridine (Table II) are compared with those of the corresponding tetraaza macrocyclic ligands, **5** to **8** (Figure 5),[21,38] it can be observed that the complexes formed with the last series of macrocyclic ligands present higher stability constants in most cases, except for the Ni^{2+} complex of **5**, which has a stability constant lower than that of **1**. However, *three* groups of behavior can be distinguished in the comparison of the complexes of these two series of ligands. In the *first* one, the differences in stability observed for the corresponding complexes of both series are slightly smaller than could be predicted by the differences in the basicity of the ligands. This is what happens with the complexes of ligands **1** and **2** with Ni^{2+}, Zn^{2+}, Cd^{2+}, and Pb^{2+} (the differences in overall basicities are, in log units, about 3 for the 12-membered macrocycles and about 2 for the 13-membered one; the differences in stability for the corresponding metal complexes are between −0.6 and +1.8). Probably the same happens with the Co^{2+} complexes, for which we do not have values, and also for the complexes of Mn^{2+} and Fe^{2+}, for which there are no stability values for the tetraaza series. The *second* group of behavior includes the complexes of the 14-membered ligands with Zn^{2+} and Cd^{2+}, where the differences in stability of the complexes are slightly higher than could be expected by taking into account only the effect of the differences in basicities (1.66 log units is the difference in basicity; 2.62 is the difference for the zinc and 2.08 that for the cadmium complexes). The Pb^{2+} complexes of the 14-membered ligands present a difference of 1.14 log units and can be included more appropriately in the first group. The *last* group of behavior is found for the Cu^{2+} complexes with all the ligands, where the complexes formed with the tetraaza macrocyclic ligands are markedly more stable than those formed with the corresponding ligands containing pyridine (the differences, in log units, are 3.16–4.66 for the 12-membered ligands, 5.74–10.18 for the 13-membered ligands, and 7.54 for the 14-membered ligands; the large range of values arises from differences in the literature values for the complexes of the tetraaza macrocycles).[21] The Ni^{2+} complexes of the 14-membered ligands probably may be included in this last group; although no value of stability constant is found for the complex of isocyclam. If the comparison is made with the corresponding value of cyclam, a difference of 4.32–6.74 log units is observed.[21,38]

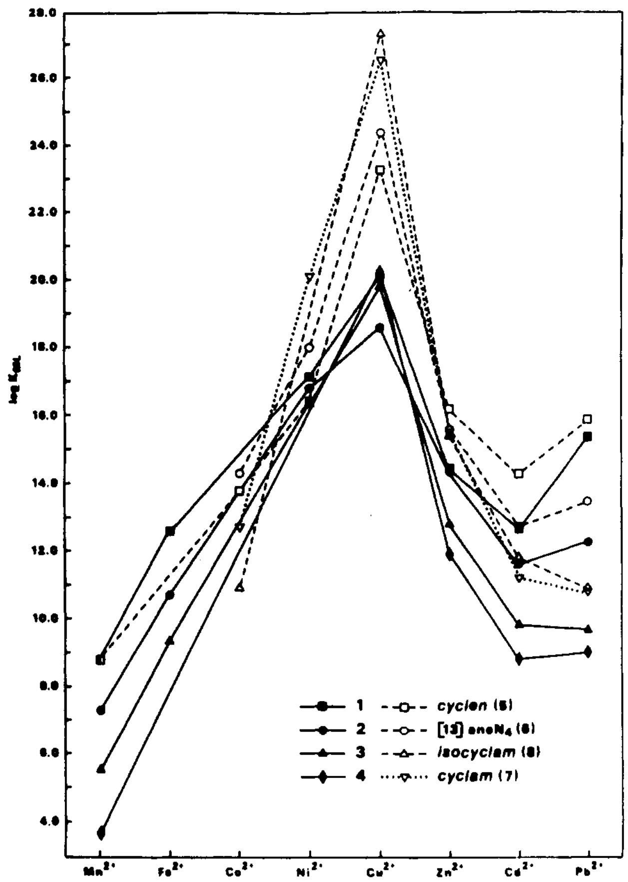

Figure 5. Variation of the stability constants (log K_{ML}) of the metal complexes of the ligands **1–8** with the atomic number of the metal ion. Values for the stability constants of the metal complexes of ligands **5–8** were taken from refs 21 and 38.

Nevertheless, a comment needs to be made about the range of the values of stability constants for the complexes of copper and nickel with the tetraaza macrocyclic ligands obtained by different authors (the values chosen for Figure 5 were taken from the same authors, when possible). In fact, the difficulty of the determination of those values arises from the slowness of the formation of the complexes; for instance, the Ni^{2+}/cyclam complex required 2 years[39] and Ni^{2+}/cyclen needed 6 months[40] for equilibration. Due to the time required for the stabilization of these complexes, the values of the constants are less accurate and discrepancies are found for different authors.[21] It is interesting to emphasize that the complexes formed by macrocyclic ligands containing pyridine have faster kinetics of formation when compared with those of the corresponding tetraaza macrocyclic ligands. In our case, only the nickel(II) complexes have longer equilibration reactions, the slowest case requiring 45 days.

The behavior of the complexes of the first group mentioned above seems to be similar to what is generally found for linear ligands, if it is taken into account that in the series of macrocycles under study only one of the secondary nitrogen atoms of the tetraaza macrocyclic series is replaced by a pyridine nitrogen and no remarkable differences in the overall basicities between the two series are found. In fact, the stability constants for metal complexes of linear ligands containing pyridyl donors tend to be higher than one would predict on the basis of the weak σ-donating properties of the pyridine nitrogens, if it is assumed that the

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ligand protonation constants reflect this ability.[33–37] The enhanced stabilities of these complexes was partially attributed to π-bonding interactions between the pyridyl π or π^* orbitals and appropriate metal d orbitals and also (in the case of Zn^{2+} ion, for instance) a lower ring strain for the formation of chelate rings involving pyridine-containing ligands.[36] However, the differences found for the Cu^{2+} complexes of the two series of macrocyclic ligands and those found for the 14-membered ligands cannot be explained in the same way. If any evidence could be found for the effect of π-bonding interactions, smaller differences would be expected. The low values of stability constants for the complexes with macrocyclic ligands containing pyridine of the last two groups mentioned above when compared with the tetraaza series could, in part, be found in the particular conformation adopted by these ligands upon complexation.

The spectroscopic measurements suggest that the Ni^{2+} complexes formed with **1** and **2** (Tables III and IV) exist in aqueous solution as an equilibrium mixture of high-spin, six-coordinate octahedral species and low-spin, four-coordinate planar species, the percentage of the four-coordinate complex being higher in the case of the complex of **2**. The nickel(II) complexes of **3** and **4** seem to exist in a high-spin, five-coordinate square-pyramidal configuration. The structure of the Ni^{2+} complex of **1** seems to be similar to that of the corresponding complex of cyclen, which in the solid state is in a folded *cis*-octahedral configuration;[41] a similar equilibrium occurs, in aqueous solution, between a yellow diamagnetic and a blue high-spin complex, the amount of the diamagnetic complex being 19% at 22 °C (in 6 M $NaClO_4$),[42] and the agreement of the constants of both complexes is understandable. The same happens with the Ni^{2+} complexes of the 13-membered ligands, although few structural studies of the tetraaza macrocycle exist for comparison, to our knowledge. The X-ray structure of the complex of a dimethyl derivative of [13]aneN$_4$ (12,12-dimethyl-1,4,7,10-tetraazacyclotridecane) shows the donor atoms in a planar coordination to the Ni^{2+}, in a *trans*-III configuration (*R,S,S,R*)[43], with the central five-membered chelate ring eclipsed[44] and no reason for a different structure is expected for the complex of [13]aneN$_4$. However, a dissimilar situation seems to occur with the 14-membered macrocycles, the structures adopted by Ni^{2+} complexes with **3** and cyclam or isocyclam are different, and so is their behaviour in solution. In fact, the complex of Ni^{2+} with cyclam exists also in solution as a mixture of a six-coordinate octahedral species and a four-coordinate planar species,[45] adopting in the solid state a strain-free *trans*-III conformation, in which the metal ion is inside the ring in a planar coordination, with *trans* chlorides completing an octahedral arrangement, the two six-membered chelate rings being in a chair conformation and the five-membered rings in a *gauche* conformation.[46] In our case, the spectroscopic studies have pointed out that Ni^{2+} seems to form with the 14-membered ligand containing pyridine a pentacoordinate complex with a high-spin, square-pyramidal arrangement similar to that found for the *N*-methyl derivative of cyclam[30–32] or for the dimethyl derivative of **3**, 2,12-dimethyl-3,7,11,17-tetraazabicyclo[11.3.1]heptadeca-1(17),13,15-triene.[47] For the latter two complexes a square-pyramidal arrangement was found with the donor atoms in a planar coordination and some displacement of the metal ion from the N_4 plane toward an anion coordinated in the apical position.

Complexes of **3** would be more appropriately compared with those of isocyclam than of cyclam. Nevertheless, only one structure of the complex with isocyclam is known,[48] [Ni(isocyclam)]$(ClO_4)_2$, where Ni^{2+} is coordinated to the four nitrogens of the macrocycle in a square-planar arrangement, with the nitrogen atom situated between the two propane chains above the coordination plane. With respect to the comparison of the behaviors of the metal complexes of this ligand and cyclam, no agreement is found in the literature. Hancock *et al.* have determined the stability constants for several metal complexes of this ligand and have found values identical with those for cyclam complexes, suggesting that the ring sequence in isocyclam does not have an unfavorable effect on the stability of its complexes.[38] On the other hand, it was found before, on the basis of thermodynamic and spectroscopic studies, that the complexes of isocyclam were less stable than those formed by cyclam, and this was attributed to the sequence of the chelate ring which leads to greater steric strain in the M–N bonds.[49] For the complexes of tetramethylcyclam stability constants lower than those obtained for the corresponding cyclam complexes were found (differences of 10 log units were found for some complexes).[50,51] These results show that the square-pyramidal arrangement of the ligand leads to much strain in the complex and also to some loss in crystal field stabilization energies and to lower stability constants, as is the case for the Ni^{2+} complex of **3** compared with that of cyclam.

While the nickel(II) complexes of **1** and **2** present similar structures but differ from **3** and **4**, the increase of the ionic radius of the metal ion from nickel to copper seems to increase the similarity of the complexes of **2**–**4**, leaving the complex of **1** in a different arrangement. In fact, the electronic spectra of aqueous solutions seem to show that the copper(II) complex of ligand **1** adopts a structure with a more octahedral (elongated-tetragonal) copper(II) ion environment and the complexes of **2**–**4** adopt a more square-planar geometry (*cf.* Table III). The Cu^{2+} complex of **1** has the largest g_3 value and the smallest A_3 value of the four complexes studied, and its electronic spectrum shows a band in the red region. It has been a generally-accepted rule that the g values increase as the planar ligand field becomes weaker, or as the axial ligand field becomes stronger, and that this behavior of the ligand field is accompanied by a red shift of the d–d absorption bands.[52–54] The low-energy d–d band in the complex $[Cu(\mathbf{1})]^{2+}$ is characteristic of five- or six-coordinated Cu(II) and is similar to what was found for [Cu(tetramethylcyclam)]$(ClO_4)_2$ in water, λ_{max}/nm (ϵ/M^{-1} cm^{-1}) 627 (227) and 583 (214), for which a five-coordinate geometry was proposed.[55]

For all the Cu^{2+} complexes $g_3 > g_2$ (or g_1), typical of tetragonal Cu(II) where the tetragonal distortion takes the form of elongation of the axial bonds. So it appears that it is possible to exclude a trigonal-bipyramidal geometry or a tetragonal structure involving compression of axial bonds.[53,54–56] On the basis of spectroscopic data, Blinn *et al.* suggested a square-pyramidal structure for a Cu(II) complex of cyclen, [Cu(cyclen)$(NO_3)_2$], for which they found in aqueous solution an electronic spectrum with a band at λ_{max} 590 nm (ϵ 257 M^{-1} cm^{-1}) and an ESR spectrum with $g_\parallel$ = 2.172 ($A_\parallel$ = 175 G) and $g_\perp$ = 2.089 ($A_\perp$ = 32 G).[57]

The ESR parameters for copper complexes are determined by the chemical composition and the physical constraints on the

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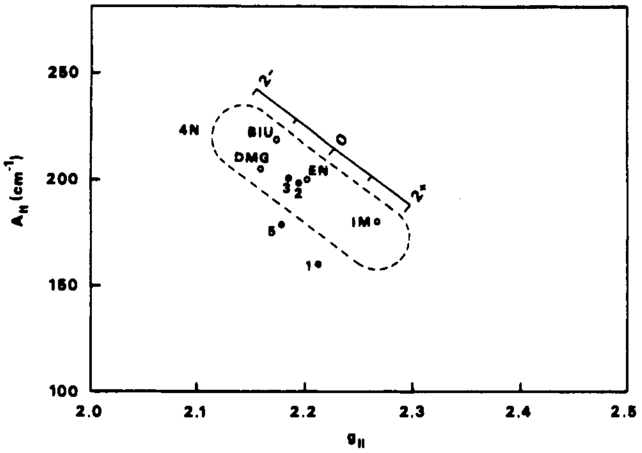

Figure 6. Diagram of the relation between the magnetic parameters $g_{\parallel}$ and $A_{\parallel}$ for a series of Cu^{2+} complexes where the close-lying ligands on the metal are four nitrogen atoms. Points 1, 2, 3, and 5 are the positions for the Cu^{2+} complexes of **1**, **2**, **3** and cyclen. Points IM, EN, BIU, and DMG are the positions of the tetrakis(imidazole), bis(ethylenediamine) (pH 8), bis(biuret) (pH 12), and bis(dimethylglyoxime) complexes of Cu^{2+}, respectively.

atoms nearest to the metal ion. Using diagrams of $g_{\parallel}$ and $A_{\parallel}$ values, compiled by Peisach and Blumberg,[58] for a series of model compounds in which the structure and charge were known for the case of four nitrogen donor atoms, it was found that the copper complexes of **2** and **3** fall inside the model area (Figure 6), whereas the Cu^{2+} complex of **1** and also that of cyclen lie outside that area (considering $g_{\parallel}$ as g_3), confirming the square-planar character of the complexes of **2** and **3**. However, these two complexes are located in a position of the diagram corresponding to neutral complexes, a situation found for some complexes of aromatic ligands and explained as increasing delocalization.[58] Using the approximated equation taken from ligand field theory[52,59] for the g values

$$g_{\parallel} = 2.0023\left(1 - \frac{4\alpha_{\parallel}^{2}\lambda}{E(d_{x^2-y^2} - d_{xy})}\right)$$

where λ is the spin–orbit coupling constant of the copper ion (-828 cm^{-1}), $\alpha_{\parallel}^2$ is the orbital reduction factor, caused by a spreading of the unpaired electron out to the ligands, and E is the energy corresponding to the split between the two sets of molecular orbitals, taken from the electronic spectra, it is possible to determine approximate values for $\alpha_{\parallel}^2$, about 0.68 for the three complexes. The magnitude of this value suggests considerable covalent character for the bonding to copper.[52]

The copper(II) complex $[Cu(cyclam)(ClO_4)_2]$ has shown a planar structure in a *trans*-III configuration, with the *trans* perchlorates weakly interacting in axial positions,[60] an arrangement which seems similar to that adopted by the copper(II) complexes of **2**–**4**.

In conclusion, it can be said that the structures of the copper complexes of the two series of tetraaza macroccylic ligands (containing or not containing a pyridine nitrogen) seem to be very similar and so the differences in stability of the complexes of the two series are difficult to understand. However, caution must exercised with regard to the stereochemical assignments based on electronic properties, namely their ESR and electronic spectra, which can hardly be considered conclusive. The electronic spectra of copper(II) complexes are not especially good indicators of geometry.[56] Another complicated factor in the comparison of these copper complexes, especially with regard to results from different laboratories, is related to the determination of their stability constants. These values are so high that they generaly prevent the use of direct potentiometric measurements; the equilibrium of the formation of the complex also takes a much longer time to attain in the case of the tetraaza macrocyclic series, and less accurate techniques, such as "out-of-cell" titrations, are required. In such cases, molecular structural determinations of the complexes by X-ray crystallography could provide some insight. These studies are in progress in our laboratory.

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