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Steric Effects on the Solution Chemistry of Nickel(II) Complexes with N-Monomethylated 14-Membered Tetraaza Macrocycles. The Blue-to-Yellow Conversion and the Oxidation and Reduction Behavior

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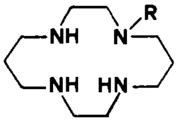
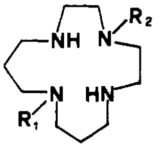
The three macrocycles **2**, **4**, and **5**, in which a methyl group has been introduced on a nitrogen atom of cyclam **1** or isocyclam **3**, have been prepared. The presence of a methyl group has substantial effects on the solution behavior of the corresponding Ni(II) complexes. In particular, it makes the blue (high-spin) to yellow (low-spin) conversion less endothermic and more exoentropic, compared to that of the unsubstituted ligand complexes, as demonstrated through temperature-dependence studies in aqueous solution. Moreover, N-methylation of the ligand makes the attainment of the Ni(I) state easier and the access to the Ni(III) more difficult, as shown by a cyclic voltammetry investigation in acetonitrile. Finally, the M(II) to M(III) oxidation process has been investigated in 10 M $HClO_4$ solution for both nickel and copper complexes. The different solution behavior of the complexes with the *N*-methyl-substituted macrocycles compared to the parent ligand analogues is interpreted in terms of (i) repulsive interactions with apically coordinated solvent molecules and (ii) weakening of the metal–nitrogen interactions. Mechanism i seems to be operative in the case of the Ni(II) blue-to-yellow conversion; mechanism ii is effective in the case of oxidation to Ni(III) and Cu(III) and reduction to Ni(I) processes.

Introduction

Tetraaza macrocycles have been developed in the early 1960s due to the pioneering independent contributions of Curtis and Busch.[2] Since then, tens of cyclic tetraaza ligands of varying structural features have been reported and the very versatile chemistry of their metal complexes has been described. Among 3d metal ions, Ni(II) has certainly been the most widely investigated, for several different reasons: (i) it is often very effective as a templating agent in many syntheses (in general to give 14-membered molecules); (ii) its complexes display unusually high solution stability, both kinetic and thermodynamic in nature; (iii) Ni(II) ion can exist in either the high-spin or the low-spin form according to the ligand's structural features, and the metal spin state gives clear indication on the in-plane coordination ability of the macrocycle. Among synthetic tetraaza macrocycles, the most popular is surely cyclam (**1**), whose simple and convenient synthesis has been described by Barefield in 1973,[3] which can be considered as a sophisticated and advanced representative of a class of coordinating agents, whose prototype is ammonia. The 14-membered saturated macrocycle cyclam is able to exert extremely strong coordinative interactions with 3d metal ions, compared to analogues of higher and lower atomicity, and is also stronger than the other 14-membered tetraaza ligand isocyclam (**3**), in which the donor nitrogen atoms are less symmetrically arranged.[4]



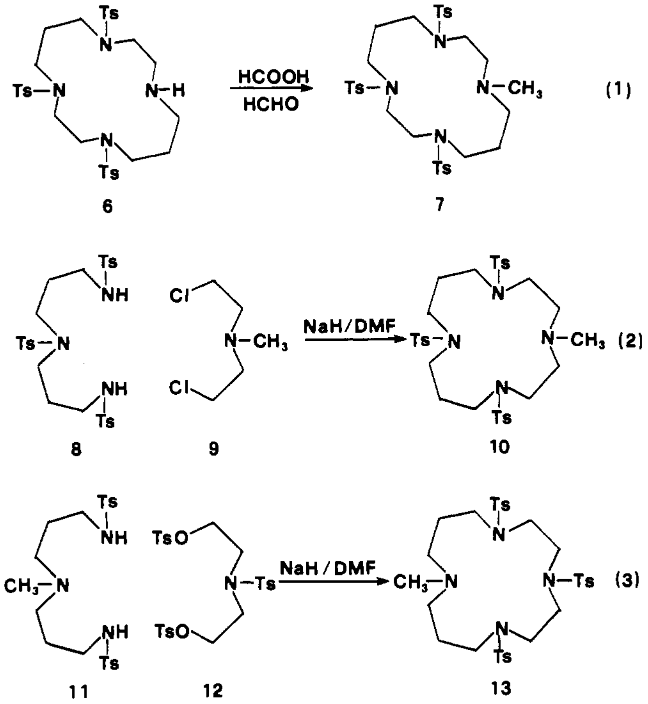
R = H : 1
$R = CH_3$: 2



$R_1 = R_2 = H$: 3
$R_1 = H$; $R_2 = CH_3$: 4
$R_1 = CH_3$; $R_2 = H$: 5

We describe here the synthesis of the *N*-monomethyl derivative of cyclam (**2**) and of two *N*-methyl derivatives of isocyclam (**4** and **5**) and their nickel(II) complexes. The investigation of the two distinctive aspects of their solution chemistry is described: (a) the temperature-dependent high-spin/low-spin conversion in water; (b) the one-electron-oxidation and -reduction processes to give Ni(III) and Ni(I) species, respectively. We demonstrate that the presence of a methyl group on donor atoms influences to some extent the equilibria of type a and b, substantially modifying their thermodynamic parameters ($\Delta H°$ and $\Delta S°$, and $E°$ respectively), compared to those of the unsubstituted cyclam and isocyclam frameworks. In particular, in the case of isocyclam derivatives, the position of the substituent (on the diethylamino, **4**, or on the dipropylamino group, **5**) has a remarkably different effect on the a and b processes.

Scheme I



The effect of N-methylation on the coordination chemistry of cyclam has been considered in the case of the fully substituted derivative Me_4cyclam.[5] In this case, however, steric effects by substituents are so heavy to favor, by a kinetic mechanism, the formation of a species in which the Ni(II) ion is displaced out of the four-nitrogen plane,[6] giving rise to a chemistry substantially

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[1] (a) University of Florence. (b) University of Pavia.
[2] Melson, G. A. *Coordination Chemistry of Macrocyclic Compounds*, Melson, G. A., Ed.; Plenum: New York, 1979; pp 2–6.
[3] Barefield, E. K. *Inorg. Chem.* **1972**, *11*, 2273–2274.
[4] Sabatini, L.; Fabbrizzi, L. *Inorg. Chem.* **1979**, *18*, 438–444.
[5] Barefield, E. K.; Wagner, F. *Inorg. Chem.* **1973**, *12*, 2435–2439.

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different than that found for complexes of cyclam and its analogues. Moreover, synthetic work on the partial alkylation of nitrogen atoms of cyclam, coordinated to Ni(II), to give disubstituted macrocycles has been described.[7]

Experimental Section

Synthesis of the Macrocycles. Formulas of some intermediates and crucial steps to the synthesis of macrocycles **2**, **4**, and **5** are sketched in Scheme I.

2 (Me-cyclam). The tritosylated cyclam (**6**)[8] (5 g, 7.5 mol) was dissolved in a mixture of 40% aqueous formaldehyde (5 mL) and formic acid (5 mL) and heated at 100 °C for 12 h. An excess of 40% aqueous sodium hydroxide was added to the cooled solution, and the resulting suspension was extracted with three 30-mL $CHCl_3$ portions. The combined $CHCl_3$ extracts, dried over Na_2SO_4, were evaporated on a rotary evaporator to give a white crystalline residue (**7**), which was recrystallized from toluene. Yield: 90%. **7** was deprotected through hydrolysis in H_2SO_4 (4 g of tosylate in 12 mL of acid, 105 °C, 3 days). To the dark brown ice-cooled solution were slowly added 100 mL of 95% ethanol and then 100 mL of diethyl ether. A brown solid formed, which was separated by filtration under nitrogen. The solid material was dissolved in 50 mL of 7 M NaOH and extracted with six 50-mL portions of $CHCl_3$. The combined extracts were dried over Na_2SO_4 and evaporated on a rotary evaporator to give a solid material, which was recrystallized from light petroleum (bp 40–70 °C): yield 85%; mp 70–72 °C.

4 (2.2-Me-isocyclam). Fragments for cyclization were obtained as follows.

9 (Methylbis(2-chloroethyl)amine). To a solution of 87 mL of $SOCl_2$ (1.2 mol) in 60 mL of $CHCl_3$ in a three-necked round-bottom flask was added dropwise a solution of 0.4 mol of methylbis(2-hydroxyethyl)amine (EGA) in 53 mL of $CHCl_3$, under vigorous stirring, over a period of 4 h. The solution was stirred for a further 2 h and concentrated on a rotary evaporator to give a solid, which was dissolved in hot ethanol. From the filtered solution, on addition of an acetone/light petroleum mixture, a white precipitate of the hydrochloride of **9** was obtained (yield 64%). The free amine **9** was prepared immediately before the cyclization step by the following procedure. The hydrochloride (0.2 mol) was dissolved in 15 mL of water and neutralized with a twofold excess of a concentrated solution of NaOH. A colorless oil was formed, which was separated from the aqueous layer and dried with some NaOH pellets. **8** (1,5,9-tris(*p*-tolylsulfonyl)-1,5,9-triazanonane) was obtained from dipropylenetriamine and tosyl chloride in a water/ether mixture, as previously described.[4]

10 (1-Methyl-4,8,12-tris(*p*-tolylsulfonyl)-1,4,8,12-tetraazatetradecane) (route 2 in Scheme I). To a stirred solution of **8** in DMF (0.1 mol in 800 mL) was added 15 g of NaH (80% suspension in oil) under nitrogen over a period of 2 h. The solution was then warmed to 50 °C and stirred for a further 3 h. The solution of the disodium salt of **8** was filtered under nitrogen through a glass frit, to eliminate unreacted NaH, into a three-necked round-bottom flask equipped with a mechanical stirrer and a condenser. To the solution, heated to 110 °C, was added a solution of **9** in DMF (0.1 mol in 75 mL) dropwise over 0.5 h. Heating and stirring were maintained for 4 h. During the reaction the solution turned pale brown and a fine white precipitate (NaCl) formed. The solution was concentrated under reduced pressure to 150 mL and then added dropwise with efficient stirring to 1 L of water to give a flocculent precipitate, which was dissolved in 1.2 L of hot $CHCl_3$. The solution was dried overnight over Na_2SO_4 and then concentrated on a rotary evaporator to 200 mL. A 700-mL aliquot of hot ethanol was added with stirring. A white precipitate of **10** slowly formed on cooling (yield 25 g, 37%). **10** was deprotected through hydrolysis in 96% H_2SO_4, according to the procedure described for **2**. **4** was obtained as an oily material and purified and characterized as the tetrahydrochloride (yield 50%).

5 (3.3-Me-isocyclam). The tritosylated macrocycle **13** was obtained by the same cyclization strategy (route 3 in Scheme I) as for **10** (yield 45%). In this case, tritosylated diethanolamine[4] was used as a fragment. Deprotection in concentrated sulfuric acid was carried out as described before. The free tetramine **5** was obtained as a yellowish semisolid, which was purified and characterized as its tetrahydrochloride (yield 55%).

Nickel(II) complexes were obtained as perchlorates on dropwise addition of $Ni(ClO_4)_2 \cdot 6H_2O$ in ethanol to a boiling ethanolic solution of the ligand. On cooling, an orange or orange-red (**5**) microcrystalline precipitate was obtained. The Cu(II) complexes were obtained through a similar procedure (yield 80–90%). Elemental analyses of described compounds (protected and free macrocycles, tetrahydrochlorides, metal complexes) gave satisfactory results.

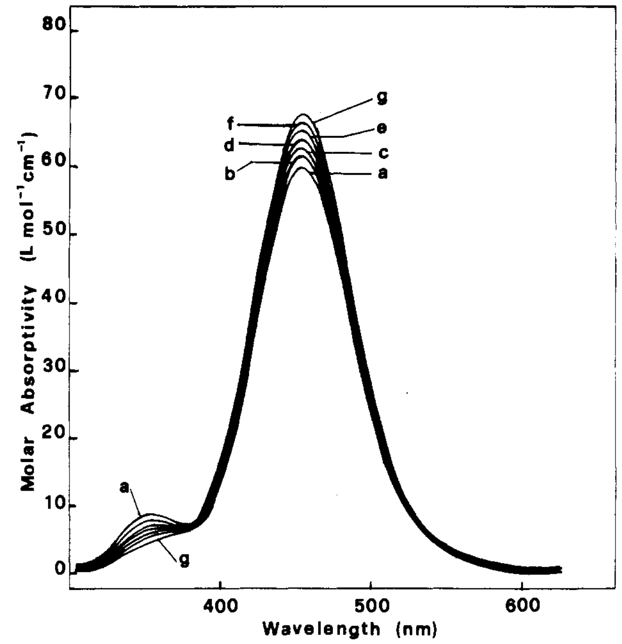

Figure 1. Absorption spectra of a 4.30 × 10^{-3} solution of $Ni(\mathbf{2})(ClO_4)_2$ adjusted to 0.1 M with $NaClO_4$, recorded at varying temperatures: a, 10 °C; b, 15 °C; c, 20 °C; d, 25 °C; e, 30 °C; f, 35 °C; g, 40 °C. The limiting absorbance value at 454 nm (yellow, planar species) determined in 7 M $NaClO_4$ solution is 85.2 L mol^{-1} cm^{-1}.

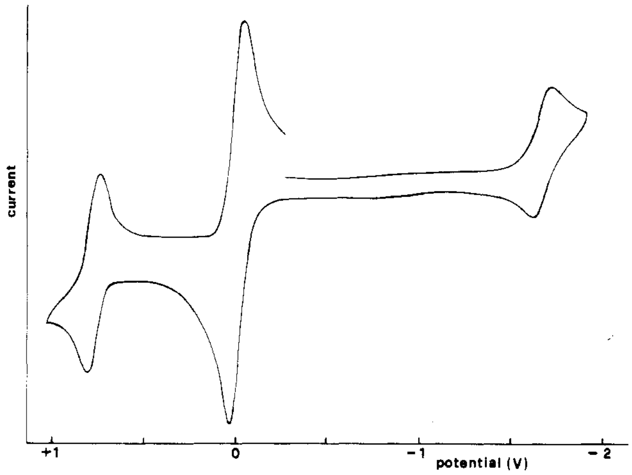

Figure 2. Cyclic voltammetry profile for a 5 × 10^{-4} M solution of $Ni(\mathbf{5})(ClO_4)_2$ in MeCN (made 0.1 M in Et_4BF_4) at 25 °C (platinum working electrode; potential scan rate 100 mV s^{-1}). The middle peak is due to the ferrocene internal standard.

Caution! Perchlorate salts are explosive, and due care must be employed when handling them. In particular, such compounds should never be heated as solids.

Spectrophotometric Measurements. Spectra were recorded on a Cary 2300 UV-VIS-NIR spectrophotometer (Varian). For variable-temperature measurements, a thermostated cell holder (Varian) was employed, connected to a Haake F3K circulating bath. Figure 1 shows a family of spectra of a 4.302 × 10^{-3} M solution of $[Ni(Me\text{-}cyclam)](ClO_4)_2$ adjusted to 0.1 M ionic strength with $NaClO_4$, recorded at varying temperatures, for the thermodynamic investigation of the blue-to-yellow conversion.

Electrochemistry. The apparatus used for electrochemical measurements has been previously described.[9] A conventional three-electrode cell was employed. The working electrode was a platinum microsphere. A silver wire was used as a pseudo reference electrode in both MeCN and 10 M $HClO_4$ solutions. In MeCN solution measurements, the reference electrode was calibrated with respect to the Fc^+/Fc redox couple:

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[6] D'Aniello, M. J.; Mocella, M. T.; Wagner, F.; Barefield, E. K.; Paul, I. C. *J. Am. Chem. Soc.* **1975**, *97*, 192–194.

[7] Wagner, F.; Barefield, E. K. *Inorg. Chem.* **1976**, *15*, 408–417.

[8] Ciampolini, M.; Fabbrizzi, L, submitted for publication.

[9] Fabbrizzi, L.; Forlini, F.; Perotti, A.; Seghi, B. *Inorg. Chem.* **1984**, *23*, 807–813.

Table I. Thermodynamic Parameters for the Blue-to-Yellow Conversion in 0.1 M $NaClO_4$ at 25 °C[a]

$$\underset{\text{blue, high-spin}}{[Ni^{II}L(H_2O)_2]^{2+}} \rightleftharpoons \underset{\text{yellow, low-spin}}{[Ni^{II}L]^{2+}} + 2H_2O$$

L	ν, cm^{-1}	ϵ_{lim}(yellow), L mol^{-1} cm^{-1}	% yellow	K[b]	$\Delta H°$,[c] kcal mol^{-1}	$\Delta S°$,[d] cal mol^{-1} K^{-1}
cyclam (**1**)	22 470	64.5	71.0	2.5	5.4	16.3
Me-cyclam (**2**)	21 980	85.2	78.2	3.6	3.2	8.2
isocyclam (**3**)	21 600	116.4	61.2	1.6	5.3	16.9
2.2-Me-siocyclam (**4**)	21 375	128.1	50.5	1.0	4.3	14.3
3.3-Me-isocyclam (**5**)	21 090	136.7	65.5	1.9	3.7	11.1

[a] Concentration of the metal complex (0.4–1.0) × 10^{-2}M. [b] ±0.1. [c] ±0.1 kcal mol^{-1}. [d] ±0.3 cal mol^{-1} K^{-1}.

in particular, an equimolar amount of ferrocene was added to the investigated solutions as an "internal standard"; a typical oxidation and reduction profile is reported in Figure 2.

In the case of $HClO_4$ solutions, the reference electrode was calibrated against the Fe^{3+}/Fe^{2+} redox couple:[10] in this case the Fe^{2+} was generated in solution on addition of an equimolecular amount of Fe (99.99%). Potential values were converted to NHE, by extrapolation of the formula of Ciavatta,[11] which relates $E(Fe^{3+}/Fe^{2+})$ to the $HClO_4$ molal concentration. Often, instead of Fe, $[Cu(cyclam)](ClO_4)_2$ or $[Ni(cyclam)](ClO_4)_2$ complexes were added as an internal reference to the solution of the electroactive species under investigation, their $E_{1/2}(M(III)/M(II))$ values vs. Fe^{3+}/Fe^{2+} (and NHE) being known.[10] MeCN (Carlo Erba) was purified through distillation from CaH_2 and stored over molecular sieves in a nitrogen atmosphere. Tetraethylammonium tetrafluoroborate (Carlo Erba, polarographic grade) was used without further purification. A 10 M $HClO_4$ solution was prepared by dilution of 70% $HClO_4$ (Fluka, puriss., p.a.).

Results and Discussion

Synthesis of the N-Methylated 14-Membered Tetraaza Macrocycles. Me-cyclam (**2**) has been simply obtained by exhaustive methylation in HCHO/HCOOH mixture of the cyclam molecule in which all but one of the nitrogen atoms have been protected by tosyl groups (see Scheme I, route 1). Detosylation in concentrated H_2SO_4 gave Me-cyclam.

A similar procedure could not be used for isocyclam derivatives, and synthesis was accomplished through cyclization of fragments already containing methyl-substituted nitrogen atoms (see Scheme I, routes 2 and 3). In the synthesis of 3.3-Me-isocyclam (**5**) the tritosylated diethanolamine (**12**) was employed, the tendency of –OTs to act as a leaving group being well-known.[12] In the synthesis of 2.2-Me-isocyclam (**4**) macrocycle, we were not able, in spite of several attempts, to obtain the ditosylated *N*-methyldiethanolamine derivative. Thus, we used the dichloro derivative (**9**), obtained by chlorination of *N*-methyldiethanolamine. The yield of the cyclization was satisfactory.

The Blue-to-Yellow Conversion. Jørgensen[13] first reported that the Ni(II) complex with the open-chain tetramine trien (1,4,7,10-tetraazadecane) exists in solution as an equilibrium mixture of the yellow, diamagnetic square species $[Ni(trien)]^{2+}$ and of the blue, high-spin, diaquo octahedral species $[Ni(trien)(H_2O)_2]^{2+}$, according to the following general equation:

$$[NiL(H_2O)_2]^{2+} \rightleftharpoons [NiL]^{2+} + 2H_2O \qquad (4)$$

Equilibrium (4) is displaced to the right by increasing either the concentration of supporting electrolyte (e.g. $NaClO_4$) or the temperature. This behavior was later found to be common to the Ni(II) complexes with open-chain tetramines of greater length, the value of the constant of the blue-to-yellow conversion being strictly dependent upon the ligand structure.[14] In the case of the complexes with the cyclic analogues of linear tetramines, the saturated tetraaza macrocycles, in dilute solutions (e.g. 0.1 M $NaClO_4$) and at room temperature, a balanced equilibrium mixture of high-spin and low-spin species was found to be present only in the case of the 14-membered macrocycles cyclam (**1**) and isocyclam (**3**), whereas for ligands of lower and greater atomicity a complete predominance of the blue octahedral complex was found to occur.[15]

In analogy with the parent unmethylated ligand complexes, the Ni(II) complexes with Me-cyclam (**2**), Me-2.2-isocyclam (**4**), and Me-3.3-isocyclam (**5**), isolated as perchlorates in the yellow low-spin form, also dissolve in water to give the typical equilibrium mixture of high- and low-spin species.[16] The intensity of the band at around 450 nm, ascribed to the yellow, low-spin chromophore, increases on addition of further amounts of $NaClO_4$ and with temperature. At a supporting electrolyte concentration of 3–4 M, ϵ reaches the limiting value, which does not further increase even on increasing the temperature. ν_{max}, the energy of the maximum of the absorption band and the limiting values of its molar extinction coefficient, ϵ_y, for the low-spin Ni(II) complexes with the investigated N-methylated macrocycles are reported in Table I. The equilibrium constants for the blue-to-yellow conversion (4) are obtained from the ratio $K = \epsilon/\epsilon_y - \epsilon$ where ϵ represents the molar extinction coefficient in 0.1 M $NaClO_4$ at 25 °C (concentration of the chromophore (0.5–1.0) × 10^{-2} M). Values of K as well as percentages of the yellow form are reported in Table I: it is seen that for the investigated *N*-methyl-substituted macrocycles the yellow species predominates over the blue one, as also observed in the case of the parent unsubstituted 14-membered ligands cyclam and isocyclam.[4]

Moreover, equilibrium constants values of the blue-to-yellow conversion (4) have been determined at different temperatures, and the corresponding $\Delta H°$ values have been obtained from a log K vs. $1/T(K)$ plot. $\Delta H°$ values and the corresponding $\Delta S°$ values, calculated from the appropriate combination of free energy and enthalpy data, are reported in Table I. In general, it is seen that the slightly favorable $\Delta G°$ term, which makes the concentration of the yellow square species predominant, results from the balance of two opposite contributions: the favorable entropy and the unfavorable enthalpy term.

Noticeably, both $\Delta H°$ and $\Delta S°$ values in the case of *N*-alkyl-substituted macrocycles are smaller in absolute value than those found for the parent unsubstituted ligands by a quantity ranging between 20 and 40%. The positive value of $\Delta S°$ observed for the blue-to-yellow conversion of nickel complexes of cyclam

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(10) Bisi Castellani, C.; Fabbrizzi, L.; Licchelli, M.; Perotti, A.; Poggi, A. *J. Chem. Soc., Chem. Commun.* **1984**, 806–808.

(11) Ciavatta, L. *Ann. Chim.* (*Rome*) **1980**, *70*, 551–567.

(12) Atkins, J. T.; Richman, J. E.; Oettle, W. F. *Org. Synth.* **1978**, *58*, 86–98.

(13) Jørgensen, C. K. *Acta Chem. Scand.* **1957**, *11*, 399–400.

(14) Anichini, A.; Fabbrizzi, L.; Paoletti, P.; Clay, R. M. *Inorg. Chim. Acta* **1977**, *24*, L21–L23 and references therein.

(15) Fabbrizzi, L. *J. Chem. Soc., Dalton Trans.* **1980**, 1857–1861.

(16) A reviewer raised the point that the temperature-dependent variation of the spectra of the aqueous solutions of the $[NiL](ClO_4)_2$ complexes (see Figure 2) could be ascribed to the existence of an equilibrium between different configurational isomers of the yellow diamagnetic species and not to the spin-state interconversion (4). While the presence of isomeric forms of the diamagnetic complex cannot be excluded, the presence at the equilibrium of the paramagnetic Ni(II) species is demonstrated by the following points: (i) an absorption band at about 350 nm (see Figure 2) is present in the visible region, belonging to the octahedral paramagnetic chromophore ($^3A_{2g} \rightarrow {}^3T_{1g}(P)$), and its intensity decreases when increasing the temperature, according to the endothermic nature of equilibrium 4; (ii) ^{13}C spectra of D_2O solutions of the investigated complexes, even at high concentration and after a large number of transients, do not show any distinguishable line, as expected in the presence of substantial amounts of paramagnetic species. This situation also makes it impossible to investigate possible configurational isomers of the diamagnetic complex.

Table II. Oxidation and Reduction Behavior of Ni(II) Complexes with 14-Membered Tetraaza Macrocycles in MeCN (0.1 M Et_4BF_4) at 25 °C

		$E_{1/2}$(III,II),[a] V	$E_{1/2}$(II,I),[a] V
$[Ni(cyclam)]^{2+}$	mixture[b]	0.600	−1.816
	blue	0.608	−1.824
	yellow	0.576	−1.794
$[Ni(N\text{-Me-cyclam})]^{2+}$	mixture[c]	0.696	−1.715
	blue	0.703	−1.708
	yellow	0.667	−1.744
$[Ni(isocyclam)]^{2+}$	mixture[d]	0.736	−1.730
	blue	0.748	−1.742
	yellow	0.708	−1.702
$[Ni(2.2\text{-Me-isocyclam})]^{2+}$	mixture[e]	0.845	−1.625
	blue	0.852	−1.632
	yellow	0.811	−1.591
$[Ni(3.3\text{-Me-isocyclam})]^{2+}$	mixture[f]	0.778	−1.663
	blue	0.785	−1.670
	yellow	0.738	−1.623

[a] Vs. Fc^+/Fc redox reference system. [b] yellow 22%; blue 78%. [c] yellow 19.5%; blue 80.5%. [d] yellow 18%; blue 82%. [e] yellow 17%; blue 83%. [f] yellow 14%; blue 86%.

and isocyclam has been ascribed to the increase in translational entropy due to the release of two water molecules from the octahedral species.[4] The endothermal nature of the blue-to-yellow conversion reflects the unfavorable contribution due to the breaking of the two $Ni-OH_2$ axial bonds in the high-spin complex, which is not compensated by the in-plane bond strengthening, which occurs during the high-spin to low-spin transition. Present results indicate that the presence of a methyl group on a nitrogen atom of the cyclam or isocyclam backbone makes the blue-to-yellow conversion both less endothermic and less exoentropic. This can be explained by admitting that the high-spin/low-spin conversion should involve the mobilization of a number of water molecules greater than two, i.e. those bound through hydrogen bonding to the apically coordinated molecules. The presence of a methyl group on the coordinating backbone may exert steric repulsion and make the "hydration" of the blue, octahedral species smaller. Therefore the "dehydration" process associated with the spin transition involves the breaking of a smaller number of hydrogen bonds (less endothermic process) and the neat liberation of a smaller number of particles (smaller increase of translational entropy). Present results would indicate that the "predehydration" effect among the two isomeric isocyclam derivatives is greater for the 2.2-Me-isocyclam species, in which the methyl group projects from the diethylamino moiety rather than from the dipropylamino portion of the 3.3-Me-isocyclam macrocycle.

Oxidation and Reduction Behavior in Acetonitrile Solution. The investigated Ni(II) complexes in MeCN solution undergo a reversible one-electron-redox change at the platinum electrode in oxidation and reduction scan (see Figure 2). This is a general behavior already observed for the Ni(II) complexes with fully saturated 14-membered tetraaza ligands, for which the formation of authentic solution-stable Ni(III) (d^7, low-spin) and Ni(I) (d^9) was demonstrated.[17] The $E_{1/2}$ values for the Ni(III)/Ni(II) and Ni(II)/Ni(I) redox changes for complexes of ligands **1**–**5** (MeCN solution made 0.1 M in Et_4BF_4, 25 °C) are reported in Table II. It should be considered that also in MeCN solution Ni(II) tetraaza macrocyclic complexes are present as a mixture of blue and yellow species: as a matter of fact, the absorption spectrum in the d–d region displays a mixed pattern of bands of the yellow (much more intense, at around 470 nm) and of the blue species, and increasing the temperature makes the intensity of the yellow band increase and that of the blue bands decrease. The limited solubility of the supporting electrolyte in MeCN prevented us from the determination of the $\epsilon_{\lim}$ value for the low-spin species, as described in the preceding paragraph. However, approximate values of $K_{\text{blue-to-yellow}}$ can be obtained by using the $\epsilon_{\lim}$ value for water, on the assumption that this value is not too seriously affected by the solvent change. The percentages of the blue and yellow species, calculated on the basis of this assumption, are reported in Table II. As a general behavior, the high-spin species predominates in MeCN solution over the low-spin one. Given the free energy change associated with the blue-to-yellow conversion ($\Delta G° = -RT \ln K$), the $E_{1/2}$ values which refer to the mixture of the two species have been corrected for the high-spin and the low-spin complexes. Corrections are, in any case, not dramatic (see Table II).

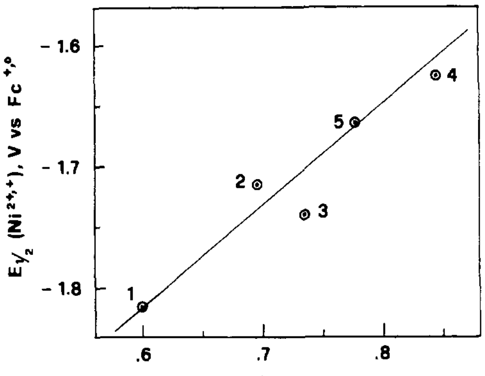

Figure 3. Linear inverse relationship between the $E_{1/2}$(Ni(III,II)) and $E_{1/2}$(Ni(II,I)) values for metal complexes with unsubstituted and *N*-methyl-substituted 14-membered macrocycles (**1**–**5**) in acetonitrile solution.

It is seen that substitution by a methyl group on a nitrogen atom of cyclam or isocyclam makes the oxidation to Ni(III) more difficult (more positive value of $E_{1/2}$(Ni(III)/Ni(II)) and the reduction to Ni(I) easier (less negative value of $E_{1/2}$(Ni(II)/Ni(I)). This can be explained very roughly, considering that the presence of a methyl group on a donor atom weakens the intensity of the metal–amine nitrogen atom interactions because of steric repulsion effects (compare for instance the Ni(II)(high-spin)–N distance in $[Ni(cyclam)]^{2+}$ (2.05–2.07 Å)[18] and in the coplanar $[Ni(Me_4cyclam)]^{2+}$ species (2.15–2.16 A)).[19] On the other hand, the intensity of the M–N interactions increases with the charge of the metal ion and is also very sensitive to perturbating effects (e.g. of steric origin) in the case of highly charged rather than small charged cations. On these bases, the perturbation exerted by the methyl group affects more heavily the Ni(III) complex, compared to Ni(II), and makes the oxidation of Ni(II) more difficult; on the other hand, the weaker Ni(I)–N bond is less disturbed, compared to Ni(II), and the reduction of Ni(II) to Ni(I) is made easier. The interdependence of the oxidation and reduction processes involving Ni(II) tetraaza macrocyclic complexes is pictorially expressed in Figure 3, where $E_{1/2}$(Ni(III)/Ni(II)) values are plotted against the $E_{1/2}$(Ni(II)/Ni(I)) values to display an inverse, roughly linear, pattern.

It can be observed that the disturbing effect is considerably greater when the methyl group is inserted in the diethylamino (2.2-Me-isocyclam) (**4**) rather than in the dipropylamino chain (3.3-Me-isocyclam) (**5**), with the oxidation to Ni(III) being more difficult and the reduction to Ni(I) easier in the former ligand's Ni complex. This state of affairs would suggest that the Ni–diethylamino bond (in the 2.2-Me-isocyclam system) is stronger than the Ni–dipropylamino bond (in the 3.3-Me-isocyclam system) and therefore more sensitive to steric effects. In this connection, it should be noted that the energy of the d–d band of the low-spin Ni(II) complex, which has been considered to give a measure of the intensity of the in-plane interactions,[20] is greater for the 2.2-Me-isocyclam complex (21 370 cm^{-1}) than in the 3.3-Me-isocyclam complex (21 090 cm^{-1}) (ν_{d-d} values for the low-spin

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Table III. Half-Wave Potential Values (vs. NHE[a]) for the $ML^{3+} + e^- \rightleftharpoons ML^{2+}$ Redox Equilibrium in 10 M $HClO_4$ at 25 °C

L	$E_{1/2}$, V	
	Ni	Cu
cyclam[b] (**1**)	0.89	1.01
Me-cyclam (**2**)	1.04	1.05
isocyclam (**3**)	0.93	1.11
2.2-Me-isocyclam (**4**)	1.14	1.20
3.3-Me-isocyclam (**5**)	1.04	1.14

[a] ±5 mV. [b] Reference 10.

Ni(II) complexes: cyclam, 22 470 cm^{-1}; Me-cyclam, 21 980 cm^{-1}; isocyclam, 21 600 cm^{-1}).

It should be noted that other steric/structural factors could influence to some extent the solution properties of the investigated metal complexes, such as for instance, differences in the configuration of the macrocycle coordinated to the metal in the considered oxidation state. In the above discussion, such effects are considered to be of secondary importance.

Formation of Ni(III) and Cu(III) Complexes in 10 M $HClO_4$ Solution. It is known that 14-membered tetraaza macrocycles are very special in stabilizing high oxidation states of the encircled metal ions.[21] Trivalent nickel is a particularly evident case, and Ni(III) complexes can be easily obtained in most solvents, including water. Trivalent copper is much more elusive, quickly decomposing, even in strictly anhydrous acetonitrile.[22] We have recently discovered that concentrated perchloric acid represents an excellent medium to permit formation of Cu(III) complexes with cyclic tetramines stable at least on the time scale of the voltammetry experiment.[10] This can be ascribed to the fact that a crucial step in the decomposition of trivalent tetramine complexes involves the formation of an M(III)–ligand radical species and liberation of a proton.[23] Massive amounts of strong acid quench or make slower the decomposition process.

In order to compare steric effects in the formation of 3d trivalent complexes, we have determined through cyclic voltammetry experiments at a platinum working electrode the $E_{1/2}$ values of the M(III)/M(II) redox change for nickel and copper complexes with *N*-methyl derivatives in 10 M $HClO_4$. $E_{1/2}$ values are reported in Table III. It is seen that the Ni(II)/Ni(III) redox change displays a similar pattern as observed in MeCN: N-methylation makes the attainment of the trivalent state more difficult, and in the isocyclam framework, the effect is more severe for 2.2-Me-isocyclam than for 3.3-Me-isocyclam. The same trend is observed for the Cu(II)/Cu(III) redox changes. The Ni(II)/Ni(III) and Cu(II)/Cu(III) processes can be represented as follows:[21]

$$\underset{\text{low-spin, square}}{[\mathrm{Ni^{II}(macrocycle)}]^{2+}} + 2H_2O \rightleftharpoons \underset{\text{low-spin, octahedral}}{[\mathrm{Ni^{III}(macrocycle)(H_2O)_2}]^{3+}} + e^-$$

$$\underset{\text{octahedral (elongated)}}{[\mathrm{Cu^{II}(macrocycle)(H_2O)_2}]^{2+}} \rightleftharpoons \underset{\text{low-spin, square}}{[\mathrm{Cu^{III}(macrocycle)}]^{3+}} + 2H_2O + e^-$$

Note that in the case of nickel complexes, due to the extremely high concentration of the supporting electrolyte, the divalent species exists as 100% of the yellow, low-spin form. It should also be noted that the Ni(II)/Ni(III) oxidation process involves the uptake of two water molecules (to occupy apical sites), whereas the Cu(II)/Cu(III) process involves the release of the two apical water molecules. Therefore, steric repulsion effects exerted by the methyl groups toward apically coordinated water molecules, already considered for the Ni(II) blue-to-yellow conversion, should induce a different behavior for nickel and copper complexes. In particular, N-methylation should favor the formation of the Cu(III) species and disfavor the formation of the Ni(III) species. The fact that N-methylation destabilizes the trivalent state both in copper and nickel cyclam and isocyclam complexes indicates that the apical solvent molecules/methyl group repulsion is a minor effect in the oxidation of divalent nickel and copper complexes, a far more important factor being the *N*-methyl-induced weakening of the M–N bonds, which is greater for the trivalent than for the divalent cation, as discussed in the previous paragraph on the redox behavior in MeCN solution.

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Registry No. **2**, 53118-99-3; **4**, 104395-68-8; **4**·4HCl, 104421-48-9; **5**, 95690-82-7; **5**·4HCl, 104395-67-7; **6**, 104395-69-9; **7**, 104395-70-2; **8**, 35980-64-4; **9**, 51-75-2; **10**, 104395-71-3; **11**, 95690-83-8; **12**, 16695-22-0; **13**, 104395-42-8; $[\mathrm{Ni^{II}}(\mathbf{1})(H_2O)_2]^{2+}$, 104485-30-5; $[\mathrm{Ni^{II}}(\mathbf{2})(H_2O)_2]^{2+}$, 104395-43-9; $[\mathrm{Ni^{II}}(\mathbf{3})(H_2O)_2]^{2+}$, 68317-92-0; $[\mathrm{Ni^{II}}(\mathbf{4})(H_2O)_2]^{2+}$, 104395-44-0; $[\mathrm{Ni^{II}}(\mathbf{5})(H_2O)_2]^{2+}$, 104395-45-1; $[\mathrm{Ni^{II}}(\mathbf{1})]^{2+}$, 46365-93-9; $[\mathrm{Ni^{II}}(\mathbf{2})]^{2+}$, 104485-31-6; $[\mathrm{Ni^{II}}(\mathbf{3})]^{2+}$, 68344-00-3; $[\mathrm{Ni^{II}}(\mathbf{4})]^{2+}$, 104395-46-2; $[\mathrm{Ni^{II}}(\mathbf{5})]^{2+}$, 95655-52-0; $\mathrm{Cu}(\mathbf{2})^{3+}$, 104395-47-3; $\mathrm{Cu}(\mathbf{3})^{3+}$, 104395-48-4; $\mathrm{Cu}(\mathbf{4})^{3+}$, 104395-49-5; $\mathrm{Cu}(\mathbf{5})^{3+}$, 104395-50-8; $[\mathrm{Cu^{II}}(\mathbf{2})(H_2O)_2]^{2+}$, 104395-51-9; $[\mathrm{Cu^{II}}(\mathbf{3})(H_2O)_2]^{2+}$, 104395-52-0; $[\mathrm{Cu^{II}}(\mathbf{4})(H_2O)_2]^{2+}$, 104395-53-1; $[\mathrm{Cu^{II}}(\mathbf{5})(H_2O)_2]^{2+}$, 104395-54-2; $[\mathrm{Ni^{III}}(\mathbf{2})(H_2O)_2]^{3+}$, 104395-55-3; $[\mathrm{Ni^{III}}(\mathbf{3})(H_2O)_2]^{3+}$, 104395-56-4; $[\mathrm{Ni^{III}}(\mathbf{4})(H_2O)_2]^{3+}$, 104395-57-5; $[\mathrm{Ni^{III}}(\mathbf{5})(H_2O)_2]^{3+}$, 104395-58-6; $[\mathrm{Ni^{III}}(\mathbf{1})]^{3+}$, 66199-97-1; $[\mathrm{Ni^{III}}(\mathbf{2})]^{3+}$, 104395-59-7; $[\mathrm{Ni^{III}}(\mathbf{3})]^{3+}$, 104395-60-0; $[\mathrm{Ni^{III}}(\mathbf{4})]^{3+}$, 104395-61-1; $[\mathrm{Ni^{III}}(\mathbf{5})]^{3+}$, 104395-62-2; $[\mathrm{Ni^{I}}(\mathbf{1})]^{+}$, 77076-74-5; $[\mathrm{Ni^{I}}(\mathbf{2})]^{+}$, 104395-63-3; $[\mathrm{Ni^{I}}(\mathbf{3})]^{+}$, 104395-64-4; $[\mathrm{Ni^{I}}(\mathbf{4})]^{+}$, 104395-65-5; $[\mathrm{Ni^{I}}(\mathbf{5})]^{+}$, 104395-66-6.

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