N-(Aminoethyl)cyclam: A Tetraaza Macrocycle with a Coordinating Tail (Scorpiand). Acidity Controlled Coordination of the Side Chain to Nickel(II) and Nickel(III) Cations

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Abstract: The novel functionalized macrocycle *N*-(aminoethyl)cyclam (**4**, L), in which a $NH_2CH_2CH_2-$ chain is appended to a tetraaza ring, has been prepared through a convenient route, whose key step involves the reaction of tritosylated cyclam and tosylaziridine. The nickel(II) ion is incorporated by the rigid basal tetraaza ring to give a species particularly resistant to demetalation, whereas the coordination by the amine group of the flexible side chain is controlled by the acidity. At pH >2.8 the $[Ni^{II}L]^{2+}$ species predominates, in which the side arm is apically bound (blue, high-spin complex); at pH <2.8 the predominant form is $[Ni^{II}LH]^{3+}$, in which the amine group of the side chain is protonated and which is a mixture of a blue high-spin form and of a yellow low-spin form. The nickel(II) complexes undergo a reversible one-electron oxidation process to give an authentic nickel(III) species in which the axial binding of the side arm is again controlled by the acidity. However, in this case the protonation of the side arm is sluggish, which allows the very unusual simultaneous voltammetric characterization of the $[Ni^{III}L]^{3+}$ and the $[Ni^{III}LH]^{4+}$ species. Comparison of the redox potential values with those of reference tetraaza macrocyclic systems demonstrates a stabilization effect on the Ni^{III} state, due to the apical binding by the primary amine group of the side chain.

Tetraaza macrocycles carrying a pendant side chain which contains an additional, potentially coordinating, nitrogen atom represent a novel class of quinquedentate ligands for transition-metal ions which couple two distinct properties: (i) the tendency of the rigid tetraaza ring to incorporate the metal (e.g., Ni^{II}, Cu^{II}) giving a kinetically stable species, especially resistant to demetalation; and (ii) the capability of the flexible pendant arm to further coordinate the metal ion in one of the axial positions of the octahedron, according to a labile binding mode.

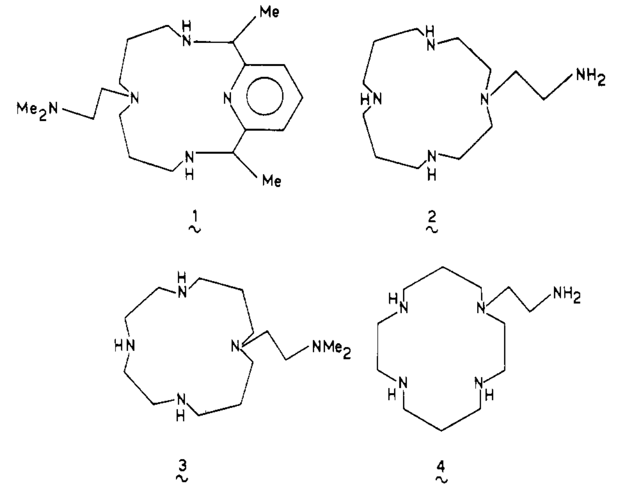
The first example of ligands of this type has been described by Kaden,[1] who prepared molecule **1** through metal template condensation of 2,6-diacetylpyridine with a diethylenetriamine moiety carrying the side chain, followed by hydrogenation of the imine bonds and demetalation in boiling cyanide solution. More recent approaches involved the N-substitution on the selectively protected isocyclam ring, followed by deprotection in concentrated sulfuric acid,[2] or the nontemplate condensation of tosylated polyamine fragments[3] (molecules of type **2** and **3**).

In the metal complexes with the above ligands, special attention has been paid to the effects of the coordination of the pendant arm on the properties of the cation incorporated by the basal ring. In particular, in the case of the nickel(II) complex of **1**, it has been observed that the species in which the side chain is coordinated is high spin (blue color), whereas the species with the uncoordinated side arm is low spin (yellow).[4]

The behavior in aqueous solution is spectacular since the neutral blue solution turns yellow on addition of strong acid, due to the competition of hydrogen ions for the amine group of the pendant arm. In this sense this nickel(II) complex behaves as an acid–base indicator, with a distinct pK_a value, its color changing back and forth from violet to yellow through consecutive additions of H^+ and OH^- ions.

In view of the active role of the tail, which can further "bite" an already chelated metal ion, and following the current trend to give ligands picturesque names recalling things of real life, one could suggest naming the above class of molecules *scorpiands*.

Chart I



A further, potentially very interesting aspect of the chemistry of metal scorpiate complexes, which has not yet been explored, is the modification of the redox activity of the encircled metal ion through the side arm coordination. As a matter of fact, it is well-known that incorporation of a 3d metal ion by a macrocyclic polyamine ring permits the access to unusually high and otherwise unstable oxidation states, due to a combined effect of kinetic and thermodynamic stabilization.[5] Of special interest is the case of the trivalent nickel cation. In fact, whereas the Ni^{III}, d^7 low-spin cation prefers six-coordination, according to a distorted octahedral stereochemistry,[6] the easiest access to the Ni^{III} state occurs with the quadridentate 14-membered macrocycle cyclam, rather than with ligands of greater denticity, i.e., penta- or hexaaza rings:[7] this apparent paradox has been explained considering the very special tendency of cyclam to exert a particularly strong in-plane field, a property precluded to quinque- and sexidentate macro-

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(1) Lotz, T. J.; Kaden, T. A. *J. Chem. Soc., Chem. Commun.* **1977**, 15; *Helv. Chim. Acta* **1978**, *61*, 1376.

(2) Hediger M.; Kaden, T. A. *J. Chem. Soc., Chem. Commun.* **1978**, 14; *Helv. Chim. Acta* **1983**, *66*, 861.

(3) Alcock, N. W.; Moore, P.; Pierpoint C. *J. Chem. Soc., Dalton Trans.* **1984**, 2371.

(4) Kaden, T. A. *Top. Curr. Chem.* **1984**, *121*, 157.

(5) Fabbrizzi, L. *Comments Inorg. Chem.* **1985**, *4*, 33.

(6) LoVecchio, F. V.; Gore, E. S.; Busch, D. H. *J. Am. Chem. Soc.* **1974**, *96*, 3109.

(7) Bencini, A.; Fabbrizzi, L.; Poggi, A. *Inorg. Chem.* **1981**, *20*, 2544.

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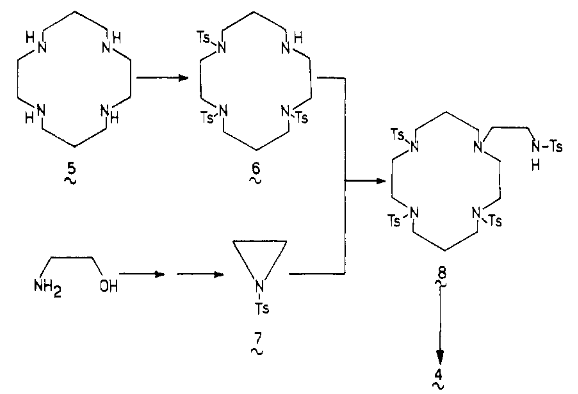
Scheme I



cycles, in which severe steric constraints arise when the ligand folds around the metal ion. The above arguments may suggest that a scorpiand molecule having the cyclam ring could facilitate oxidation to the Ni^{III} state due to the combined effects of a strong in-plane ligand field and the coordination by a fifth amine group in one of the axial sites of the distorted octahedron. Furthermore, the basal cyclam ring should impart the greatest kinetic stability and resistance to the extrusion of the metal, compared to tetraaza rings of the same or different atomicity.

The above considerations prompted us to develop the new scorpiand **4** in which a $-CH_2CH_2NH_2$ arm has been added on a nitrogen atom of the privileged cyclam ring: a primary amine group, rather than a secondary or tertiary one, has been chosen due to its greater coordinating tendency and to minimize steric repulsion effects. This work reports the convenient synthesis of **4** (*N*-(aminoethyl)cyclam) and the solution behavior of its nickel(II) complex, with a special regard to the oxidation process to the trivalent state in nonaqueous and aqueous solvents. In the latter medium we have discovered a singular kinetic effect in the competition of H^+ and Ni^{III} ions for the side chain amine group.

Experimental Section

Synthesis of 4. The synthetic route to the scorpiand **4** is outlined in Scheme I.

The preparation of the key intermediates *N,N',N''*-tritosylcyclam (**6**)[8] and tosylaziridine (**7**)[9] has been described. To a refluxing solution of **6** in MeCN (8 g, 0.012 mol in 300 mL), in a three-neck, round-bottomed flask equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel, was added dropwise a solution of **7** in MeCN (3.5 g, 0.018 mol in 120 mL). The course of the reaction was followed through TLC tests on silica (Stratocrom SI, Carlo Erba, Milan) with a CH_2Cl_2/*n*-hexane/CH_3OH mixture (8:4:1) as eluent. After 48 h of refluxing, the spot corresponding to **6** (R_f 0.35) had disappeared and only the spot of product **8** (R_f 0.7) was present. The reaction mixture was allowed to cool and rotary evaporated to a white powder which was purified by column chromatography on silica (Silica Gel 60, Fluka) with use of the same eluent as was used for TLC tests. **8** was obtained as a white microcrystalline solid (5.6 g, 54%). Calcd for $C_{40}H_{53}N_5S_4O_8$: C, 55.85; H, 6.21; N, 8.14. Found: C, 55.55; H, 6.16; N, 7.99.

The tetratosylated scorpiand **8** was deprotected through hydrolysis in concentrated H_2SO_4. **8** (3.26 g) was dissolved in 40 mL of 96% H_2SO_4. The solution was stirred at 105 °C in a nitrogen atmosphere for 3 days. Then to the vigorously stirred brown oily solution, cooled at 0 °C, were added 150 mL of ethanol, following 200 mL of diethyl ether. A whitish precipitate formed, which was dissolved in a small volume of water and made strongly basic through addition of 30 mL of 10 M NaOH. The solution was filtered to remove the copious white precipitate of Na_2SO_4 and extracted with 6 × 50 mL portions of chloroform. The chloroform solution was dried overnight on anhydrous $MgSO_4$ and then evaporated to yield *N*-(aminoethyl)cyclam (**4**) as a white oil (0.4 g, 45%). **4** was characterized as its pentahydrochloride (prepared by addition of excess 37% HCl to an ethanolic solution of the oil). Calcd for $C_{12}H_{34}N_5Cl_5$: C, 33.85; H, 8.05; N, 16.45. Found: C, 33.48; H, 8.18; N, 16.18.

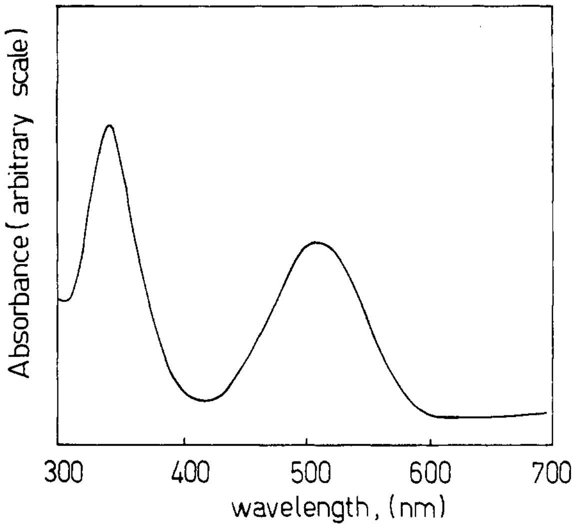


Figure 1. Absorption spectrum of solid $Ni(4)(ClO_4)_2$ spread on filter paper.

The $Ni(4)(ClO_4)_2$ complex was obtained by adding a butanol solution of $Ni(ClO_4)_2 \cdot 6H_2O$ (previously boiled to eliminate most of the water) to a refluxing solution of **4** (10% excess) in absolute ethanol. On cooling, a violet precipitate formed, which was collected by suction filtration. Calcd for $C_{12}H_{29}N_5O_8Cl_2Ni$: C, 28.76; H, 5.83; N, 13.97. Found: C, 28.46; H, 5.88; N, 13.63.

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

Solution Chemistry Studies.[10] UV-visible absorption spectra were measured on a Cary 2300 spectrophotometer (Varian) with use of 1 cm quartz cells. In the study of the pH dependent behavior of the nickel(II) scorpiate complex, a 5×10^{-3} M solution of $Ni(4)(ClO_4)_2$, made acidic with $HClO_4$, was titrated with standard NaOH solution, the pH being measured with a glass electrode. At selected pH values, 3-mL samples of the solution were transferred from the potentiometric cell to a quartz cuvette to record the absorption spectrum and then transferred back to the titration vessel. The pH value was found not to be affected by the above operation.

ESR spectra of the Ni^{III} complexes were recorded on a Varian E-109 spectrometer; *g* values were calibrated vs. DPPH. The solutions of the Ni^{III} complex were obtained through controlled potential electrolysis with use of a platinum gauze as anode (Me_2SO solution) or by chemical oxidation ($NOBF_4$ in Me_2SO; $Na_2S_2O_8$ in aqueous $HClO_4$ solutions) and then transferred to the quartz ESR tube and frozen at the liquid nitrogen temperature.

Voltammetry studies were performed in a three-electrode cell connected to either an AMEL (Milan, Italy) Model 563 (CV and AC measurements) or an AMEL 472 electrochemistry apparatus (DPV measurements). Voltammograms were recorded on a Hewlett-Packard 7040A X-Y recorder. For studies in Me_2SO solution the working electrode was a platinum microsphere and the pseudoreference electrode was a silver wire calibrated vs. the Fc/Fc^+ reference couple. In aqueous solution studies a carbon paste electrode was used as the working electrode and a saturated calomel electrode, connected to the cell through a salt bridge filled with NaCl solution, was used as the reference electrode.

In both spectrophotometric and voltammetric studies the temperature of the solution (25 °C) was controlled by circulating thermostated water.

Results and Discussion

1. Design of the Ligand. Synthesis of the scorpiand **4** is based on the reaction of Ts_3cyclam, **5**, a cyclam ring having all but one protected amine groups, with the electrophilic moiety tosylaziridine **7** (see Scheme I). The synthesis is particularly convenient due

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[8] Ciampolini, M.; Fabbrizzi, L.; Perotti, A.; Poggi, A.; Seghi, B.; Zanobini, F., submitted for publication.

[9] Dietrich, B.; Hosseini, M. W.; Lehn, J. M.; Sessions, R. B. *Helv. Chim. Acta* **1985**, *68*, 289.

[10] It should be noted that, since each of the nitrogen atoms of **4** represents a chiral center, the nickel(II) complex of **4** could give rise to eight isomers. However, spectra of both acidic and alkaline solutions of $[Ni(4)](ClO_4)_2$ at 50 °C did not show any change; a spectral change usually occurs when several different isomers are present and they convert to the most stable form.[3] In any case, when preparing standard solutions to be used in spectrophotometric or electrochemical studies, the $[Ni(4)](ClO_4)_2$ complex was dissolved in 0.1 M NaOH and kept at 80 °C for 20 min. Then the cooled solution was neutralized with standard $HClO_4$ and adjusted to the desired pH. It is believed that the above procedure would ensure, through N-H isomerization, the conversion of the isomers hypothetically present in solution to the most stable form and, in any case, to the same state.

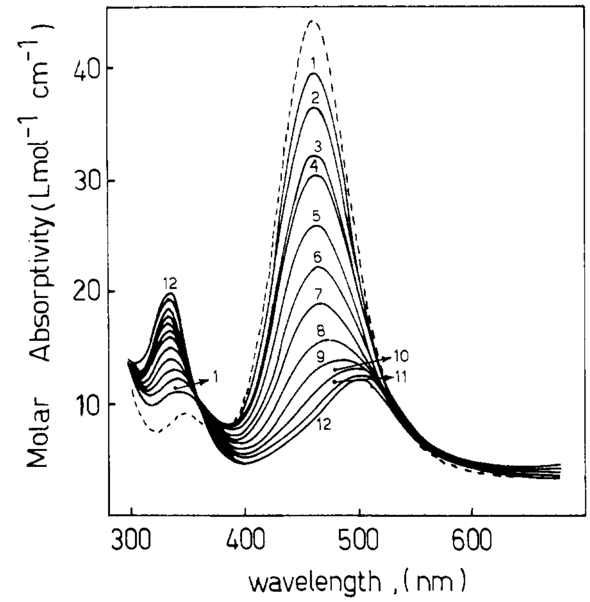


Figure 2. Absorption spectra of a 9×10^{-3} M solution of $Ni(4)(ClO_4)_2$, made 0.1 M in $NaClO_4$, measured at varying pH values: (1) 2.00; (2) 2.20; (3) 2.30; (4) 2.45; (5) 2.65; (6) 2.80; (7) 3.00; (8) 3.20; (9) 3.40; (10) 3.60; (11) 3.60; (12) 4.20. At higher pH values (up to pH 12) the spectrum did not show further changes. The dotted line refers to a solution made 0.1 M in $HClO_4$ in which the complex should exist as 100 % of the $[Ni^{II}LH]^{3+}$ form.

to the ready availability of the Ts_3cyclam synthon, which is simply obtained through reaction of cyclam with stoichiometric tosyl chloride.[8] It should be noted that the analogous synthon Ts_3-isocyclam, used by Kaden in the synthesis of type **2** and **3** scorpiand molecules, had to be prepared through a tedious procedure involving several consecutive steps of selective protection and deprotection of the tetraaza macrocyclic ring.[2]

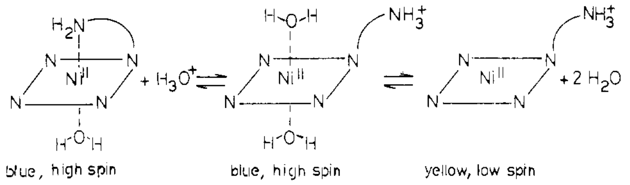
2. Solution Behavior of the $[Ni^{II}$(scorpiand)$]^{2+}$ Complex. The pH Controlled Blue-to-Yellow Equilibrium. The Ni^{II} scorpiate complex is obtained as a blue–violet microcrystalline solid whose elemental analysis corresponds to the formula $NiL(ClO_4)_2$. The absorption spectrum of the powder spread on filter paper (see Figure 1) shows two bands centered at 340 and 510 nm, as expected for a high-spin pseudooctahedral chromophore. Thus for the Ni^{II} scorpiate complex in the solid state, apical coordination by the amine group must be hypothesized, the second axial site probably being occupied by an oxygen atom of a perchlorate ion. The presence of two absorption bands, due to the perchlorate group, at 1120 and 1050 cm^{-1} in the infrared spectrum of a Nujol mull of the well-anhydrified complex further indicates apical coordination of the anion.[11]

If the solid blue $NiL(ClO_4)_2$ complex is dissolved in water, a blue solution is obtained whose absorption spectrum strictly resembles that measured for the solid. However, on addition of strong acid, the blue solution turns yellow, the color change being quickly reversible on consecutive additions of base and acid. This behavior is consistent with the model already proposed by Kaden[4] for scorpiate complexes of type **1** and described by the following equation

$$\underset{\text{blue, high spin}}{NiL^{2+}} + H^+ \rightleftharpoons \underset{\text{yellow, low spin}}{NiLH^{3+}} \qquad (1)$$

According to eq 1, protonation of the apically coordinated amine group induces formation of a square tetraaza macrocyclic complex and stabilizes the singlet state of Ni^{II}. The effect of the pH change on the blue-to-yellow equilibrium of the presently investigated scorpiate complex is illustrated in detail in Figure 2. It is seen that in neutral or slightly acidic solution only the two absorption bands of the "octahedral" high-spin chromophore (at 508 and 350 nm) are present and that below pH 4 a band at 464 nm begins to appear. This band, typical of a low-spin Ni^{II} tetramine complex, becomes more intense with decreasing pH, whereas the intensity of the bands centered at 508 and 350 nm simultaneously decreases.

Scheme II



If an aqueous solution of $[Ni(4)](ClO_4)_2$ containing an excess of strong acid, is titrated with standard base, the pH vs. moles of NaOH plot displays the profile expected for a weak acid ($NiLH^{3+}$), for which a pK_a value of 2.8 can be calculated ($K_a = 1/K_H$, K_H being the constant of equilibrium 1).

It is useful to consider the pK_a value as being made up by two distinct contributions, according to eq 2

$$pK_a = pK_a(-NH_2) - \log K(Ni^{II} + -NH_2) \qquad (2)$$

$pK_a(-NH_2)$ refers to the process in which the side arm $-NH_3^+$ group is deprotonated, whereas $\log K(Ni^{II} + -NH_2)$ refers to the apical coordination of the $-NH_2$ group to the macrocycle-encircled metal.

One could guess that the $pK_a(-NH_2)$ value is not too distant from the pK_{a2} value of ethylenediamine: 6.8 (assuming that the basal amine group bound to the Ni^{2+} exerts the same repulsive effect of a $-NH_3^+$ group).[12] On this basis a value of 4 log units is calculated for $\log K(Ni^{II} + -NH_2)$. This value is much greater than that observed for the addition of a fifth ammonia molecule to Ni^{II}, $\log K_5 = 0.8$.[13] However, it should be considered that the coordination of the side arm $-NH_2$ group is favored, compared to that of the NH_3 molecule, by the chelate effect. Chelate effect contributions of 3 log units are typically observed in the solution chemistry of metal–amine complexes.

Moreover, a closer inspection of Figure 2 may indicate that the simple equilibrium 1 is not adequate to justify the pH dependence of the visible absorption spectrum of the Ni^{II}–scorpiate complex. As a matter of fact, (i) at pH 2.8, where 50% of the nickel complex is present as the $[NiLH]^{3+}$ species, the measured value of the molar extinction coefficient, ϵ, of the band at 464 nm is 23 mol^{-1} L cm^{-1}, a value much lower than the half of the limiting ϵ value for low-spin yellow nickel(II) tetraaza macrocyclic complexes (typically ranging from 70 to 100 mol^{-1} L cm^{-1}),[14] and (ii) in 0.1 M $HClO_4$, where the nickel(II) scorpiate complex should exist as 100% of the protonated form, $[Ni(LH)]^{3+}$, the ϵ value at 464 nm (45 L mol^{-1}cm^{-1}) is still very low. Moreover, the band at 350 nm of the high-spin nickel(II) complex is still present. This state of affairs can be explained by admitting that the protonated species $[NiLH]^{3+}$ exists as an equilibrium mixture of the blue, high-spin complex and of the yellow, low-spin species, a situation that is typical for nickel(II) complexes with 14-membered tetraaza macrocycles.[15] The above hypothesis is confirmed by the following evidence: (i) further additions of inert electrolyte to the acidic solution (0.1 M $HClO_4$) of the scorpiate complex make the intensity of the band at 464 nm increase; (II) a further increase is observed if the solution is heated. It is well-known that the blue-to-yellow interconversion equilibrium involving Ni^{II}–tetramine complexes is displaced to the right by an increase of both ionic strength and temperature.[15] Thus, the pH induced color change

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[11] Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*; John Wiley & Sons: New York, 1978; p 242.

[12] $pK_a(-NH_2)$ value for the complex could be directly compared to the corresponding quantity for the scorpiand **4**. However, while it is possible to determine through pH-potentiometric titration the pK_a values for the pentaprotic ligand, it is not possible, on the simple basis of the potentiometric experiment, to assign unambiguously the correct pK_a value to each one of the five basic sites.

[13] Sillen, L. G.; Martell, A. E. *Stability Constants of Metal-ion Complexes*; The Chemical Society: London, 1971; Special Publication No. 25.

[14] Ciampolini, M.; Fabbrizzi, L.; Licchelli, M.; Perotti, A.; Pezzini, F.; Poggi, A. *Inorg. Chem.* **1986**, *25*, 4131.

[15] Sabatini, L.; Fabbrizzi, L. *Inorg. Chem.* **1979**, *18*, 438.

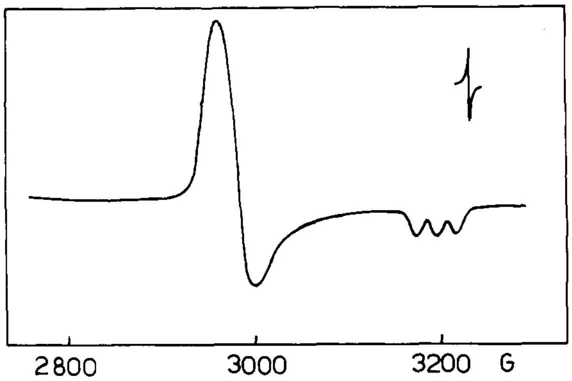

Figure 3. ESR spectrum (recorded at 77 K) of a 1 × 10^{-3} M solution of $Ni(4)^{3+}$ in Me_2SO (made 0.1 M in Et_4NBF_4) generated through controlled potential electrolysis. $g_\perp = 2.16$, $g_\parallel = 2.03$.

observed in solution of the scorpiate complex here investigated should be better interpreted on the basis of the equilibria depicted in Scheme II.

In the definitively acidic conditions (pH <2.8) we perceive the solution as yellow due to the much greater extinction coefficient of the low-spin species compared to the high-spin one.

3. The Ni^{II}/Ni^{III} Redox Change in Nonaqueous Solution. A further aspect of the solution chemistry of nickel(II) scorpiate complexes that deserves special attention is the investigation of the Ni^{II}/Ni^{III} oxidation process and the evaluation of any stabilization effect on the Ni^{III} state due to the side chain coordination. First, the Ni^{II}/Ni^{III} redox change has been studied in a nonaqueous medium. Dimethyl sulfoxide has been chosen for the following reasons: as an aprotic medium it will not induce any complication of the redox equilibria due to the protonation of the amine group of the pendant arm; moreover, the oxygen coordinating fragment does not cause any hyperfine splitting of the ESR signals of the Ni^{III} complex and does not compete with the ligand's nitrogen atoms ($I = 1$).

The $[Ni(4)]^{2+}$ complex in Me_2SO solution undergoes a reversible one-electron oxidation process, as shown by cyclic voltammetry experiments at a platinum microsphere. The one-electron stoichiometry has been confirmed through coulometric measurements performed during controlled potential electrolysis with a platinum gauze as working electrode. During the experiment, the blue–violet solution of the Ni^{II} in the working electrode compartment turns green, the typical color of trivalent nickel polyamine complexes.

The UV–vis spectrum of the blue Ni^{II} solution presents the typical bands of the high-spin complex ($\nu_2 = 530$ nm, $\epsilon = 10.8$ L mol^{-1} cm^{-1}; $\nu_3 = 340$, $\epsilon = 21.9$). No band is observed at 450–470 nm, where the absorption of the yellow chromophore is expected. Furthermore, increasing the temperature up to 60 °C does not cause any change of the spectrum. The above findings are consistent with a pseudooctahedral stereochemistry of the high-spin Ni^{II} complex, in which the axial sites are occupied by the amine group of the pendant arm and by a solvent molecule. On the other hand, pieces of information on the electronic and stereochemical properties of the Ni^{III} complexes are given by the ESR experiment.

As a matter of fact, the ESR spectrum of the frozen green solution obtained through controlled potential electrolysis or by oxidation with $NOBF_4$ (see Figure 3) presents an axial symmetry with $g_\perp$ considerably greater than $g_\parallel$. This is consistent with the formation of an authentic Ni^{III} complex, d^7 low-spin.[6] Moreover, the $g_\parallel$ feature is split into three lines of equal intensity, as expected for coordination by a nitrogen atom (that of the pendant arm) in one of the axial positions. Therefore, the redox change in Me_2SO seems to occur according to an uncomplicated mechanism involving species of similar stereochemistry (the distorted octahedron) in which the scorpiand exerts full coordination, as shown in eq 3.

$$\underset{d^8,\ \text{high spin}}{[Ni^{II}L(\text{solvent})]^{2+}} \rightleftharpoons \underset{d^7,\ \text{low spin}}{[Ni^{III}L(\text{solvent})]^{3+}} + e^- \qquad (3)$$

Table I. Half-Wave Potential, $E_{1/2}$ (V), Values for the Ni^{III}/Ni^{II} Redox Change in Polyaza Macrocyclic Complexes, at 25 °C

ligand	Me_2SO^a	aq solution (1 M $HClO_4$)^b
scorpiand (**4**)	0.28	0.96
cyclam	0.26	0.75
Me-cyclam	0.39	0.88
[16]aneN$_5$	0.32	0.76

^{a}0.1 M Et_4NBF_4; vs. the Fc^+/Fc internal reference standard. ^{b}vs. SCE.

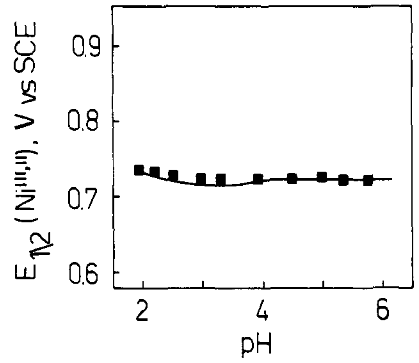

Figure 4. Plot of $E_{1/2}(Ni^{III}/Ni^{II})$ vs. pH for complexes of **4** in aqueous solution made 0.1 M in $NaClO_4$. The solid line corresponds to eq 6.

In order to assess possible stabilization effects on the Ni^{III} state due to the side-chain coordination we have measured $E_{1/2}$ values for the Ni^{II}/Ni^{III} redox change also for a series of complexes with cyclam and some related polyamine macrocycles. $E_{1/2}(Ni^{III,II})$ values associated to the reversible redox change in Me_2SO solution are reported in Table I. .

It is seen that the $E_{1/2}(Ni^{III,II})$ value for the scorpiate complex is slightly more positive than that observed for the reference cyclam complex. Thus, side arm apical coordination apparently would not induce any stabilization effect on the formation of the trivalent state of nickel. However, it should be considered that cyclam is not the appropriate reference system. In fact, cyclam presents a donor set of four secondary amine nitrogen atoms, rather than the three secondary amine groups and one tertiary amine group found in the scorpiand **4**. On the other hand, it is well-established that substitution of a secondary nitrogen atom by a tertiary one in a tetraaza ring induces a relative destabilization of the Ni^{III} state, by a quantity corresponding to at least 100 mV.[14,16] Thus, the proper reference system should be N-monomethylated cyclam, Me-cyclam, rather than cyclam. Table I shows that the $Ni(N\text{-}Me\text{-}cyclam)^{3+}$ complex is formed at a distinctly more positive potential than $Ni(4)^{3+}$, demonstrating the existence of a moderate stabilization effect due to the pendant arm coordination. The $E_{1/2}(Ni^{III,II})$ value for the quinquedentate scorpiand complex is also slightly less positive (more favorable access to the trivalent state) than that observed for the complex with the pentaaza macrocycle [16]ene N$_5$, a system in which the ring folds to occupy an apical site with a secondary nitrogen atom.[7]

4. The Ni^{III}/Ni^{II} Redox Change in Aqueous Solution of Varying Acidity. Due to the affinity of the pendant arm toward the proton, it is reasonable to expect that the oxidation behavior of the $Ni(4)^{2+}$ complex is strongly influenced by the acidity. Therefore, a voltammetric investigation on the Ni^{III}/Ni^{II} redox change, using a carbon paste electrode, has been performed on neutral to strongly acidic solutions. In particular, it has been found that in the zone of measurable pH (to pH 2) a reversible one-electron wave appears on the oxidation scan (attributable to the Ni^{II}/Ni^{III} process), whose $E_{1/2}$ value remains almost constant (see Figure 4).

It has been shown in subsection 2 that the nickel(II) complex of the scorpiand **4** exists in aqueous solution in two forms: the NiL^{2+} form (side arm coordinated, predominant species for pH

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(16) Barefield, E. K.; Freeman, G. M.; Van Derver, D. G. *Inorg. Chem.*, **1986**, *25*, 552.

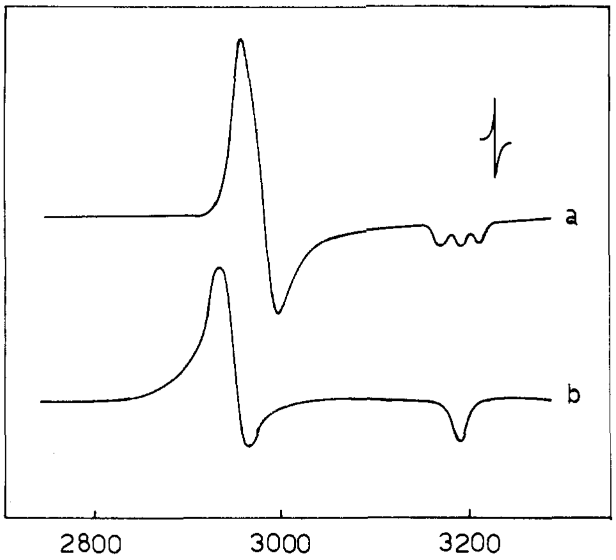
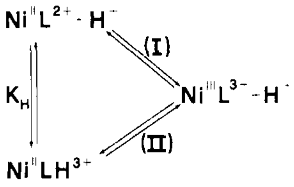


Figure 5. ESR spectrum of aqueous frozen solutions (77 K) of Ni(**4**)$^{3+}$ at varying concentrations of $HClO_4$: (a) $C(HClO_4)$ = 0.01 M, the signal is due to the $[Ni^{III}L]^{3+}$ species, $g_\perp$ = 2.16, $g_\parallel$ = 2.03; (b) $C(HClO_4)$ = 0.2 M, the signal is due to the $[Ni^{III}LH]^{4+}$ species, $g_\perp$ = 2.23, $g_\parallel$ = 2.02; compare to $[Ni^{III}(cyclam)]^{3+}$ values.[15]

Scheme III



>2.8) and the $NiLH^{3+}$ form (side arm protonated, predominant form at pH <2.8). On the other hand ESR spectra of the oxidized aqueous solutions, frozen at 77 K, in the pH range from 7 to 2, display the same profile (Figure 5, spectrum a).

The spectrum is similar to that observed in frozen Me_2SO solution (see Figure 3) and is indicative of the presence, in the investigated pH zone, of only one trivalent species, in which the side chain is axially coordinated.

Thus, two redox active divalent species are present: $[Ni^{II}L]^{2+}$, which is oxidized to the trivalent form through the half-reaction I in Scheme III, whose formal potential is E^*_I; and $[Ni^{II}LH]^{3+}$, which is oxidized to the trivalent form through the half-reaction II, whose formal potential is E^*_{II}. As a consequence, each of the two half-reactions I and II should originate an individual wave, whose $E_{1/2}$ value should vary with the hydrogen ion concentration according to the following equations

$$E_{1/2}(I) = E^*_I + 0.05916 \log (1 + K_H[H^+]) \qquad (4)$$

$$E_{1/2}(II) = E^*_{II} + 0.05916 \log ([H^+] + K_H^{-1}) \qquad (5)$$

Since the protonation/deprotonation equilibrium involving the side arm in divalent complexes is fast compared to the time scale of the voltammetry experiment, a single wave (e.g., a single peak in the AC or DPV profiles) is obtained, whose $E_{1/2}$ value results from the contributions of $E_{1/2}(I)$ and $E_{1/2}(II)$, weighted according to the relative concentrations of $[Ni^{II}L]^{2+}$ and $[Ni^{II}LH]^{3+}$ at a given pH value. Through the weighted combination of eq 4 and 5, the following general equation is obtained

$$E_{1/2} = \frac{1}{1 + K[H^+]}\{E^*_I + 0.05916 \log (1 + K_H[H^+])\} + \frac{K[H^+]}{1 + K_H[H^+]}\{E^*_{II} + 0.05916 \log (K_H^{-1} + [H^+])\} \qquad (6)$$

To E^*_I is ascribed the value of $E_{1/2}$ measured in neutral solution. The value for E^*_{II} is calculated from eq 5, using the $E_{1/2}$ value measured at the lowest pH ($[H^+] = 10^{-2}$ M). Now, it can be seen in the $E_{1/2}$ vs. pH diagram in Figure 4 that the general eq 6 (represented by the solid line) fits quite well the measured $E_{1/2}$ values. Thus, independence of $E_{1/2}$ upon pH is explained on the basis of balanced contributions of two mutually related pH dependent redox equilibria.

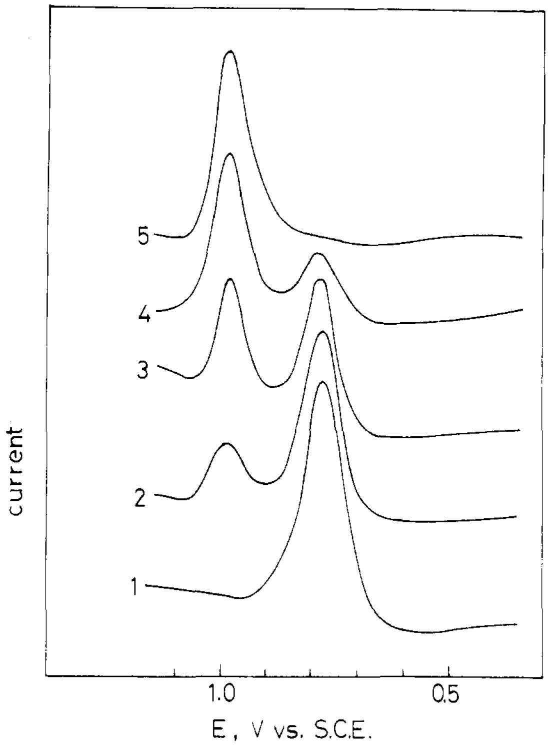
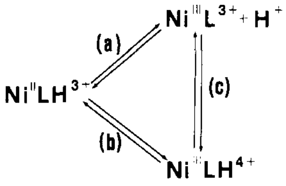


Figure 6. Alternating current voltammetry profiles (oxidation scan) obtained for aqueous solutions of Ni(**4**)$(ClO_4)_2$ of varying concentrations of $HClO_4$: (1) $C(HClO_4) = 1 \times 10^{-2}$ M; (2) 3×10^{-2} M; (3) 6×10^{-2} M; (4) 1×10^{-1} M; (5) 2×10^{-1} M.

Scheme IV



At concentrations of strong acid greater than 10^{-2} M, due to the variation of junction potentials, the acidity effects on the redox behavior cannot be expressed in terms of pH. Thus, voltammetry profiles (Figure 6) refer to solutions of varying analytical concentration of $HClO_4$. At moderate acidity levels ($C(HClO_4) = 10^{-2}$ M) only one peak is observed. However, on increasing the acidity, the intensity of this peak decreases and a new peak at a potential 200 mV more positive begins to form. In particular, at $C(HClO_4) = 6 \times 10^{-2}$ M the two peaks exhibit the same intensity. Finally, at $C(HClO_4) = 2 \times 10^{-1}$ M the first peak has disappeared and the second peak has reached its limiting value.

Pieces of information about the stereochemical nature of the oxidized scorpiate complexes can be obtained from the ESR experiments (see Figure 5). The ESR spectrum of the solution of $C(HClO_4) = 10^{-2}$ M, for which only the first peak is present in the voltammetry profile (spectrum a in Figure 5), corresponds to the previously described $[Ni^{III}L]^{3+}$ species, in which the side arm is axially bound to the metal. On the other hand, in definitively acidic conditions, $C(HClO_4) = 2 \times 10^{-1}$ M and more, for which only the second, higher potential peak is observed, a totally different spectrum (b in Figure 5) is obtained, still exhibiting axial symmetry, but displaying g values substantially different than those of spectrum a and close to those observed for $[Ni(cyclam)]^{3+}$ in the same conditions.[17] Moreover, the $g_\parallel$ feature appears as a single line. The above findings are consistent with the formation of the $[\mathrm{Ni^{III}LH}]^{4+}$ species, in which the pendant arm is protonated and both apical positions are occupied by water molecules. Thus, the one-electron oxidation process involving the $[\mathrm{Ni}(\mathbf{4})]^{2+}$ complex at pH <2 can be described by Scheme IV.

The fact that two waves are observed in the oxidation scan indicates that equilibrium c, which involves the protonation/deprotonation of the side arm in the trivalent complex, is slow compared to the time scale of the voltammetric investigation. Thus, the employed technique is able to simultaneously detect the two distinct redox events and does not give the weighted single response as observed for solutions of lower acidity as previously described. The result is singular and surprising and the interpretation does not seem straightforward. In fact, there is no previous experimental evidence nor theoretical support for sluggish substitution reactions at the axial sites of the d^7 cations. However, it is possible that the abstraction of one electron from the metal center of the $[\mathrm{Ni^{II}LH}]^{3+}$ complex induces, through changes of the metal–nitrogen bond distances, a rearrangement of the macrocyclic backbone, which makes sterically difficult the binding of the side chains to one of the axial sites. Further investigations on the acidity dependence of the solution behavior of $\mathrm{Ni^{II}}$ and $\mathrm{Ni^{III}}$ complexes with scorpiands of varying structural features may help to throw light on this novel and singular aspect of the redox chemistry of macrocyclic complexes.

5. Electrostatic Influence of the Protonated Side Chain on the $\mathrm{Ni^{II}/Ni^{III}}$ Oxidation Process. In Table I are reported the $E_{1/2}$ values associated with the $\mathrm{Ni^{II}/Ni^{III}}$ oxidation process for the complexes of **4** and related polyaza macrocycles, measured in 1 M $\mathrm{HClO_4}$ aqueous solution. Comparison to the reference Me-cyclam system shows a behavior opposite to that observed in $\mathrm{Me_2SO}$ solution: the access to the trivalent state in the Me-cyclam complex is favored by 140 mV compared to the scorpiate complex. However, it should be considered that in the present conditions the redox equilibrium for the scorpiand system is represented by

$$[\mathrm{Ni^{II}LH}]^{3+} \rightleftharpoons [\mathrm{Ni^{III}LH}]^{4+} + e^- \qquad (7)$$

Thus, any favorable axial coordination effect (observed in $\mathrm{Me_2SO}$ solution) is excluded. Moreover, the process of the increase of the charge of the metal center from 2+ to 3+ is made more difficult due to the presence of a positive charge (of the ammonium group of the side chain) at a distance of 5.31 Å (as calculated by molecular models).[18]

Finally, we have observed a singular phaenomenon that may be related to the presence of a positively charged group ($-\mathrm{NH_3^+}$) at a relatively short distance from the metal center. We have described in subsection 2 that addition of $\mathrm{NaClO_4}$ to an acidic (e.g., 0.1 M $\mathrm{HClO_4}$) solution of $\mathrm{Ni}(\mathbf{4})(\mathrm{ClO_4})_2$ causes the intensity of the band of the yellow planar species to increase. However, if made strongly saline ($C(\mathrm{NaClO_4}) \geq 3$ M), the solution turns an intense yellow–green color and the typical smell of chlorine develops. The color is due to a strong absorption band at 290 nm (with a shoulder at 360 nm), which is typical for $\mathrm{Ni^{III}}$–tetramine complexes,[19] which is observed in the $\mathrm{Ni}(\mathbf{4})^{3+}$ complex generated through chemical oxidation of a diluted solution ($[\mathrm{ClO_4^-}] = 0.1$ M). As judged from the molar extinction coefficient at 290 nm, only part of the $\mathrm{Ni^{II}}$ complex is oxidized to $\mathrm{Ni^{III}}$ and the concentration of the trivalent complex increases when the concentration of $\mathrm{NaClO_4}$ is increased. Noticeably, the intense yellow–green color (and the chlorine smell) also develops when solid $\mathrm{Ni}(\mathbf{4})(\mathrm{ClO_4})_2$ is dissolved in an $\mathrm{HClO_4}$ solution of concentration ≥ 3 M. The above preliminary evidence suggests that at sufficiently high perchlorate concentration the following process takes place.

$$\mathrm{ClO_4^-} + 7[\mathrm{Ni^{II}(LH)}]^{3+} + 8\mathrm{H^+} \rightleftharpoons 0.5\mathrm{Cl_2} + 7[\mathrm{Ni^{III}(LH)}]^{4+} + 4\mathrm{H_2O} \qquad (8)$$

Usually, the aqueous $\mathrm{ClO_4^-}$ ion for kinetic reasons does not exert its very strong oxidizing power ($\mathrm{ClO_4^-} + 7e^- + 8\mathrm{H^+} = 0.5\mathrm{Cl_2(g)} + 4\mathrm{H_2O}$, $E^\circ = 1.392$)[20] and most reducing agents persist indefinitely in acidic perchlorate solutions. For instance, the $\mathrm{Ni^{II}(cyclam)^{2+}}$ complex is stable in concentrated perchloric acid (11.56 M). Thus, the protonated side chain of the presently investigated complex should play an essential role in the activation of the $\mathrm{ClO_4^-}$ ion. It is possible that this occurs through the formation of an ion pair with the $-\mathrm{NH_3^+}$ group, which activates the $\mathrm{ClO_4^-}$ ion, at a favorable distance from the reducing metal center. Reducing tendencies of the metal are obviously required, as demonstrated by the fact that the analogous $\mathrm{Cu^{II}}$ scorpiate complex does not give any reaction even in concentrated perchloric acid.

6. Conclusions. Encircling of a 3d cation by a tetraaza macrocycle makes its redox behavior more rich, in particular favoring the access to unusually high, otherwise unstable, oxidation states (e.g., $\mathrm{Ni^{III}}$). It has been shown that the formation of the trivalent nickel complex can be made more or less easy by varying the ring size of the tetraaza ring (the cyclam framework being the most favorable).[7] This work has shown that insertion of a side chain carrying an amine group on the cyclic framework adds additional elements of selectivity. In particular, when the side chain is coordinated to the metal, the attainment of trivalent nickel is made relatively easier. On the other hand, if the side arm is protonated, the $\mathrm{Ni^{II}/Ni^{III}}$ oxidation process becomes substantially more difficult due to electrostatic repulsive effects. Moreover, the ammonium group of the pendant arm is able to activate, through an ion pair interaction, the otherwise kinetically stable perchlorate ion, which oxidizes the divalent metal center.

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Registry No. 4, 109151-85-1; **4**·5HCl, 109151-86-2; $\mathrm{Ni}(\mathbf{4})(\mathrm{ClO_4})_2$, 109151-89-5; Ni(**4**), 109151-90-8; **6**, 104395-69-9; **7**, 3634-89-7; **8**, 109151-87-3.

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[17] $[\mathrm{Ni(cyclam)}]^{3+}$, 0.1 M $\mathrm{HClO_4}$ solution frozen at 77 K: $g_\perp = 2.22$; $g_\parallel = 2.02$.

[18] Taking 2.00 Å for the M–N distance and standard values for the C–C and C–N distances and bond angles.

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