# Chemistry of Structurally Developed Macrocycles. Part 1. Complexation Properties of *NN'N''N'''*-Tetra(2-cyanoethyl)-1,4,8,11-tetra-azacyclotetradecane with Nickel(II)

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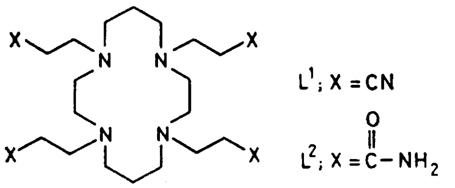
Reaction of 1,4,8,11-tetra-azacyclotetradecane (cyclam) with excess of acrylonitrile yields quantitatively the tetracyanoethylated product. In the presence of donor anions this potentially eight-co-ordinate ligand behaves as a quadridentate ligand towards nickel(II) binding through the tertiary amine donors alone. The resulting complexes are generally five-co-ordinate (six-co-ordinate with $NCS^-$) having the ligand in a partially folded configuration. With perchlorate as anion a polymeric nickel(II) complex is formed which consists of five-co-ordinate metal centres linked together by intermolecularly bridging nitriles. Attempts to hydrolyse the nitrile groups of the free ligand to produce the tetra-amide or tetracarboxylic acid were unsuccessful. However, hydrolysis of the tetranitrile when co-ordinated to nickel(II) proceeds at neutral pH producing an octahedral complex containing the co-ordinated tetra-amide.

A study of the interaction that occurs between a metal ion locked within a non-labile, macrocyclic co-ordinating array of donor atoms, and other donor groups which are pendant from the macrocycle, provides a likely means for gaining an understanding of the importance of this type of metal environment to living systems, where it is commonly observed. An obvious approach to the synthesis of the requisite type of ligand, which has largely gone unexplored, and yet which has the advantage of avoiding the preparative difficulties associated with *ab initio* macrocycle synthesis,[1] is to attach the required pendant donors to the periphery of an easily synthesised, pre-prepared macrocycle by means of flexible hydrocarbon chains. It is the purpose of this series of papers to discuss the synthesis and properties of macrocyclic systems derived from reactions of this type. In this, the first of these, the reaction between 1,4,8,11-tetra-azacyclotetradecane (cyclam) and acrylonitrile, which leads to ligand $L^1$, is considered, together with the properties of the nickel(II) complexes of this ligand.



Although $L^1$ is readily synthesised (see below) its geometry does not immediately allow the observation of co-ordinative interactions between the pendant donor groups and the parent metal ion, owing to the linear configuration of the cyano-group, which prevents it from coming within the required bonding distance. In order to permit this the hybridisation pattern at the terminal carbon atom of a three carbon pendant chain must be $sp^2$ or $sp^3$, and thus it is necessary to be able to convert the nitrile into a non-linear co-ordinating moiety. There appear to be two possible ways of doing this: (*i*) hydrolysis, leading either to the tetra-amide or tetracarboxylic acid, or (*ii*) reduction yielding pendant primary amines. However, extensive investigations in this laboratory into the hydrolysis of free $L^1$ have failed to produce more than trace amounts of any characterisable product. Similarly, reduction of $L^1$ with lithium aluminium hydride or diborane produces only mixtures of partially reduced material. This apparent impasse in what is potentially a high-yield synthetic route to macrocycles carrying pendant donor groups, capable of intramolecular co-ordination, can be avoided, however, since it has been observed during the course of this work that hydrolysis, preceded by co-ordination of $L^1$ to nickel(II), proceeds cleanly to yield the co-ordinated tetra-amide, $L^2$, in which the pendant donor groups are bound to the parent metal.

## EXPERIMENTAL

Hydrogen-1 n.m.r. spectra were recorded at 60 MHz on a JEOL JNM-PMX60 continuous-wave spectrometer. Natural abundance $^{13}C$ n.m.r. spectra were recorded using a Brucker WH90 Fourier-transform spectrometer at 22.63 MHz and are proton noise decoupled. Infrared spectra were determined as Nujol mulls using a Perkin-Elmer 577 spectrometer. Conductance data were obtained using an M.E.L. conductance bridge. Magnetic moments were measured on a Newport Gouy balance and were corrected for ligand and inner-core diamagnetism using Pascall's constants. Electronic spectra were from a Unicam SP700A spectrometer. Molecular weights were measured in solution using a Mechrolab vapour pressure osmometer. Mass spectra were from an A.E.I. MS902 spectrometer. Microanalyses were performed by the Analytical Department of the Queen's University of Belfast.

Cyclam was prepared in accordance with the procedure of Barefield and Wagner.[2] All other reagents were obtained commercially and used without special purification.

NN'N''N'''-*Tetra*(2-*cyanoethyl*)-1,4,8,11-*tetra-azacyclotetradecane*, $L^1$.—Cyclam (3 g, 15 mmol) was dissolved in boiling acrylonitrile (60 $cm^3$). After refluxing the solution for 4 h the excess of acrylonitrile was removed by distillation under reduced pressure. The resulting sticky residue was recrystallised twice from an ethanol–chloroform (9 : 1) mixture yielding white prisms of the pure product (5.7 g, 94%), m.p. 127—128 °C. Hydrogen-1 n.m.r. spectrum in $CDCl_3$ (p.p.m. downfield from $SiMe_4$): 2.62 (12 line multiplet, 32 H) and 1.66 (quintet, $J = 7.0$ Hz, 4 H). Carbon-13 n.m.r. spectrum in $CDCl_3$ (p.p.m. downfield from $SiMe_4$): 119.3, 51.7, 51.3, 50.2, 24.8, and 16.4. Infrared spectrum in Nujol: 2 248s, 1 298m, 1 158m, 1 052m, 977m, 880m, 792m, and 772m cm$^{-1}$. Mass spectrum: *m/e* for parent ion 412 (calc. 412).

NN′N″N‴-*Tetra*(2-*cyanoethyl*)-1,4,8,11-*tetra-azacyclotetradecanenickel*(II) *Diperchlorate*, (1).—Ligand L$^1$ (412 mg, 1 mmol) was dissolved in refluxing ethanol (20 cm$^3$). A solution of hexa-aquanickel(II) diperchlorate (366 mg, 1 mmol) in ethanol (5 cm$^3$) was added dropwise to the solution over a period of 5 min. Refluxing was continued for a further 15 min before collecting the fine green product, which had precipitated, by filtration. Recrystallisation, once, brought about by the slow addition of ethanol to a solution of the crude material in acetonitrile gave the pure product (600 mg, 90%).

*Complexes* (2)—(4).—These compounds were all prepared by the same general procedure: The sodium salt of the appropriate anion (1 mmol) was added, as a solid, to a well stirred solution of compound (1) (412 mg, 1 mmol) in refluxing acetone (50 cm$^3$). After refluxing the mixture for 4 h it was allowed to cool and concentrated to *ca.* one half of its original volume. The precipitated product was collected by filtration, washed with methanol (2 × 10 cm$^3$), and dried *in vacuo*. Yield: 80%.

*Complexes* (5)—(7).—These compounds were all prepared by the same general procedure. Ligand L$^1$ (412 mg, 1 mmol) was dissolved in ethanol (20 cm$^3$) together with the sodium salt of the appropriate anion (2 mmol). The solution was brought to reflux before adding dropwise a solution of hexa-aquanickel(II) diperchlorate (366 mg, 1 mmol) in ethanol (5 cm$^3$) over a period of 5 min. The resulting suspension was refluxed for a further 15 min before allowing it to cool and collecting the product by filtration. Yield: 80—90%.

NN′N″N‴-*Tetra*(2-*carbamoylethyl*)-1,4,8,11-*tetra-azacyclotetradecanenickel*(II) *Diperchlorate*, (8).—Compound (1) (0.8 g, 1.2 mmol) was suspended in water (30 cm$^3$) at room temperature. The temperature of the water was raised to boiling point and the resulting deep green solution was refluxed for 48 h, over which time it became mauve in colour. The mauve solution was cooled, concentrated to *ca.* 5 cm$^3$, and then diluted with ethanol (30 cm$^3$) before allowing it to stand in a refrigerator for 24 h. After this time the product (0.25 g, 28%) was collected by filtration as fine mauve crystals.

NN′N″N‴-*Tetra*(2-*carbamoylethyl*)-1,4,8,11-*tetra-azacyclotetradecane*, L$^2$.—A solution of sodium cyanide (294 mg, 6 mmol) in water (5 cm$^3$) was added to the mauve solution obtained in the preparation of (8) (see preceding synthesis). The resulting straw coloured solution was refluxed for 10 min, allowed to cool, and adjusted to *ca.* pH 13 by the addition of a few drops of 10 mol dm$^{-3}$ sodium hydroxide. The solution was then evaporated to dryness and the residue extracted with chloroform (3 × 50 cm$^3$). The chloroform extracts were combined, dried ($Mg[SO_4]$), and evaporated under reduced pressure, leaving the product as a sticky oil which could not be crystallised (0.5 g, 87%). Carbon-13 n.m.r. spectrum in $H_2O$ (p.p.m. downfield from $SiMe_4$, internal dioxan being used as the chemical-shift reference): 179.2, 49.7, 49.6, 46.9, 32.1, and 25.4. Infrared spectrum in Nujol: ν(C=O) 1 660s and 1 628m cm$^{-1}$. Mass spectrum: *m/e* for parent ion 484 (calc. 484).

## RESULTS AND DISCUSSION

The synthesis of tetracyanoethylcyclam, L$^1$, has been briefly alluded to in an earlier publication by Barefield.[3] No preparative details or properties were given. However, it is found here that it may be obtained, virtually quantitatively, by refluxing cyclam in neat acrylonitrile. Under these conditions the cyanoethylation reaction[4] proceeds readily to give exclusively the per-cyanoethylated compound, which is remarkable, amongst compounds of this type, for its crystallinity and ease of purification.[5] Attempts to isolate other compounds by this method, in which the cyclam residue was cyanoethylated to a lesser extent, were unsuccessful. Combination of cyclam and acrylonitrile in the molar ratio 1 : 1, for example, even under mild conditions, produced the complete range of addition products, which were readily observable by mass spectroscopy, but which could not be separated.

Complexation of L$^1$ with nickel(II) generally led to the formation of high-spin five-co-ordinate complexes. All of the complexes of L$^1$ detailed in Tables 1 and 2, with the exception of the bis(isothiocyanate), exhibit electronic spectral, magnetic, and conductance data which are consistent with this formulation. This is not unexpected, since Barefield and co-workers and Moore and co-workers[6,7] have both independently shown that complexes of the structurally related ligand 1,4,8,11-tetramethyl-1,4,8,11-tetra-azacyclotetradecane (tetramethylcyclam) are normally five-co-ordinate, having either square-planar or trigonal-bipyramidal geometries, depending upon the nature of their environment. Apparently this arises for steric reasons. It is observed crystallographically that the ligand co-ordinates with the four methyl groups projecting from the same face of the macrocycle, which itself adopts a partially folded configuration, away from that face, in order to minimise the steric interactions between the methyl groups. Besides obstructing ligation at the axial co-ordination site opposite to the methyl groups, and thus frequently rendering the complexes five-co-ordinate, this partially folded configuration also causes the macrocycle to be unusually labile.[8]

As well as being mostly five-co-ordinate, nickel(II) complexes of L$^1$ show this high lability, strongly suggesting that the manner in which the ligand binds is the same as that adopted by tetramethylcyclam. Complexes (1)—(7) all rapidly decompose upon being heated in water to *ca.* 40 °C. The ligand is insoluble in water at this temperature thus allowing the equilibrium to move completely towards the hexa-aquanickel(II) species. Further evidence for the suggestion that tetracyanoethylcyclam is binding to nickel(II) in the same manner as tetramethylcyclam derives from the formation of the single six-co-ordinate complex, (5). As is the case with tetramethylcyclam, where the analogous compound alone has been made,[8] it appears that it is only in the presence of NCS$^-$ that such species can be isolated. The i.r. spectrum of each compound shows two isothiocyanate (C≡N) absorptions as is to be expected either for *cis* or *trans* isothiocyanates when the two faces of the macrocycle are inequivalent.

Assuming, then, that tetracyanoethylcyclam is co-ordinating in a partially or fully folded configuration

TABLE 1

Analytical, infrared, and conductance data

| Compound | Analysis (%) Found C | Found H | Found N | Calc. C | Calc. H | Calc. N | $\nu(C\equiv N)$/[a] cm$^{-1}$ | $\Lambda$/[b] S cm$^2$ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| $L^1$ Tetracyanoethylcyclam | 64.0 | 8.65 | 27.6 | 64.0 | 8.80 | 27.2 | 2 248 | |
| (1) $[NiL^1]_n[ClO_4]_{2n}$ | 39.9 | 5.75 | 16.5 | 39.4 | 5.40 | 16.7 | 2 282, 2 250 | [c] |
| (2) $[NiL^1(NCS)][ClO_4]$ | 43.6 | 5.80 | 19.8 | 43.9 | 5.75 | 20.1 | 2 258, 2 085 | 79 |
| (3) $[NiL^1Cl][ClO_4]$ | 43.8 | 5.85 | 18.5 | 43.6 | 6.00 | 18.5 | 2 255 | 91 |
| (4) $[NiL^1Br][ClO_4]$ | 40.3 | 5.40 | 17.2 | 40.6 | 5.60 | 17.2 | 2 255 | 91 |
| (5) $[NiL^1(NCS)_2]$ | 48.6 | 6.05 | 23.4 | 49.1 | 6.20 | 23.8 | 2 248, 2 120, 2 100 | Non-electrolyte |
| (6) $[NiL^1Cl]Cl$ | 48.5 | 6.55 | 21.0 | 48.7 | 6.70 | 20.7 | 2 255 | 81 |
| (7) $[NiL^1Br]Br$ | 41.7 | 5.55 | 17.5 | 41.9 | 5.75 | 17.8 | 2 252 | 83 |
| (8) $[NiL^2][ClO_4]_2$ | 35.4 | 5.80 | 15.1 | 35.6 | 6.00 | 15.1 | | 173 |

[a] Nujol mulls. [b] $10^{-3}$ mol dm$^{-3}$ in nitromethane at 20 °C. [c] No value is obtainable in nitromethane since the molecular weight of the polymer is unknown. In $H_2O$ and $CH_3CN$, where the complex is monomeric, values of 262 and 267, respectively [both indicative of a 2 : 1 electrolyte (W. J. Geary, *Co-ordination Chem. Rev.*, 1971, **7**, 81)] were obtained.

TABLE 2

Electronic spectral and magnetic data

| | Compound | Colour | $\mu_{eff.}$[a] | Electronic spectral data [b]/cm$^{-1}$ ($\varepsilon$/dm$^3$ mol$^{-1}$ cm$^{-1}$) |
|---|---|---|---|---|
| (1) | $[NiL^1]_n[ClO_4]_{2n}$ | Dark green | 2.94 | 25 200, 20 600, 15 400, 10 000, 7 900 [c]<br>25 800 (25), 16 000 (11), 9 900 (8) [d] |
| (2) | $[NiL^1(NCS)][ClO_4]$ | Yellowish green | 3.32 | 25 700 (148), 22 900 (sh) (53), 15 350 (30), 9 200 (13), 8 000 (12), 7 700 (11) |
| (3) | $[NiL^1Cl][ClO_4]$ | Yellowish green | 3.35 | 22 730 (114), 19 160 (sh) (18), 16 720 (15), 13 400 (43), 12 450 (sh) (30), 7 100 (12) |
| (4) | $[NiL^1Br][ClO_4]$ | Yellowish green | 3.34 | 22 370 (166), 19 160 (sh) (43), 16 080 (43), 13 620 (62), 12 470 (sh) (48), 7 000 (10) |
| (5) | $[NiL^1(NCS)_2]$ | Pale blue | 2.96 | 26 050 (62), 16 720 (17), 10 200 (16) |
| (6) | $[NiL^1Cl]Cl$ | Yellowish green | 3.32 | 22 830 (119), 19 450 (sh) (21), 16 610 (16), 13 420 (44), 12 440 (sh) (28), 9 100 (16), 5 800 (18) |
| (7) | $[NiL^1Br]Br$ | Yellowish green | 3.31 | 22 370 (150), 18 650 (sh) (15), 16 130 (20), 13 210 (49), 12 440 (sh) (39), 8 400 (7), 5 200 (12) |
| (8) | $[NiL^2][ClO_4]_2$ | Mauve | 3.28 | 28 400 (13), 17 400 (8), 10 400 (5) [d] |

[a] B.M. at 20 °C; 1 B.M. = $9.27 \times 10^{-24}$ A m$^2$. [b] $CH_3NO_2$ solutions unless otherwise specified. [c] Solid-state. [d] $H_2O$ solution.

with all the pendant nitriles projecting towards the fifth co-ordination site, but not capable of bonding to it, there exists the further consideration of whether or not any of the pendant nitriles are co-ordinating, in an intermolecular sense, to another metal ion. The frequency of the nitrile $\nu(C\equiv N)$ stretch, which is present at 2 248 cm$^{-1}$ in the i.r. spectrum of $L^1$, provides a convenient probe for this, since it is well established[9] that co-ordination of a nitrile group is accompanied by a significant change in the frequency of this absorption. Reference to Table 1, in which the relevant i.r. absorptions for each complex are tabulated, shows that in only one case amongst the compounds studied was co-ordination of a nitrile observed and that this occurs for complex (1) where the relatively weakly co-ordinating perchlorate anion has been used. For this compound two $\nu(C\equiv N)$ bands are seen; one strong band at approximately the same frequency as that in the free ligand and another weaker band 32 cm$^{-1}$ to higher frequency. This is taken as being indicative of the presence of both free and 'end on'[9] co-ordinated nitriles, and is consistent with the complex being five-co-ordinate in the solid state and hence only capable of co-ordinating one of the four available nitriles. For the other complexes, where more strongly co-ordinating anions are present, it is these which occupy the fifth co-ordination site to the exclusion of the nitrile.

Since co-ordination of the nitrile in compound (1) can only arise through an intermolecular bridging process the complex must be polymeric. This was confirmed by a molecular-weight determination in nitromethane, which gives a number average molecular weight of 342, within experimental error of the number average value of 336 which one would expect should complete polymerisation of the cationic species in this particular $MX_2$ system have occurred. Examination of molecular models confirms that extensive polymerisation can take place with the ligand bound in the manner proposed.

In a manner which is in accordance with the well known ease with which co-ordinated nitriles may be displaced by other ligands,[9] the polymeric structure of (1) can readily be broken. Thus the monomeric compounds (2)—(4) were all prepared from the polymer by addition of the appropriate anion. Dissolution in water also breaks the nitrile linkage. A molecular-weight determination of (1) in cold aqueous solution gave a value of 701 which is consistent with that expected for the diaquated monomer ($M$ = 706). That the species is diaquated, and hence octahedral, is substantiated by the electronic spectrum of (1) in aqueous solution (Table

2) which is markedly different to that shown by (1) in the solid state or in nitromethane solution and is indicative of octahedral nickel(II).

When an aqueous solution of (1) is heated above 40 °C the free ligand, which at this temperature has precipitated, begins to redissolve, regenerating the original deep green colour of the solution. On reaching 100 °C the solution starts to adopt a purplish colouration. This colour has fully developed after *ca.* 48 h, and at this stage a mauve crystalline material, (8), may be isolated in 28% yield (the remainder of the product could not be induced to crystallise). Electronic spectral and magnetic data (Table 2) show that this is an octahedral nickel(II) species. It is a 2 : 1 electrolyte in nitromethane and its molecular weight in aqueous solution (calc. 742; found 729) and elemental analysis are consistent with its formulation as the monomeric hydrolysis product $[NiL^2][ClO_4]_2$. The i.r. spectrum gives no indication of co-ordinated perchlorate groups and this implies that the co-ordination sphere is completed by two intramolecularly co-ordinating amide groups. It was verified that the ligand is in fact the tetra-amide, $L^2$, by removing it from the metal with cyanide in the usual way.[10] The product obtained is a colourless sticky oil whose $^{13}C$ n.m.r., i.r., and mass spectral data (detailed in the Experimental section) are consistent with this formulation.

This hydrolysis process is clearly metal dependent, since refluxing $L^1$ either with water or water containing one mole equivalent of sodium perchlorate only brings about decomposition. This is evident from the $^{13}C$ n.m.r. of the products. Refluxing any of the other complexes, (2)—(7), in water also leads to formation of the co-ordinated tetra-amide, but at a markedly slower rate than that shown by (1).

The fact that (8) is octahedral containing two co-ordinated pendant donors is interesting for, if the two amides are ***trans***, it necessitates that at least one of the tertiary nitrogens (and more likely two, to give the stable ***trans*** III configuration [6]) has undergone inversion during the course of the reaction. This is necessary so as to allow the pendant donors, which were all positioned over one face of the macrocycle in the precursor, access to both of the axial co-ordination sites. Such an inversion at a tertiary nitrogen can only occur if accompanied by metal–nitrogen bond fission. This is a relatively high-energy process and has not been hitherto observed with compounds of this type. If the two co-ordinated amides are *cis* then the macrocyclic framework must have been forced into an extremely crowded *cis*-octahedral conformation, again for which there is no clear precedent although the bis(isothiocyanate) complexes referred to above may be of this type. Work is in progress on the chemistry of the tetra-amide ligand to clarify this situation.

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