Ligands designed to impose Tetrahedral Co-ordination: a Convenient Route to Aminoethyl and Aminopropyl Pendant Arm Derivatives of 1,5,9-Triazacyclododecane

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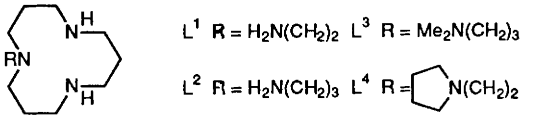
The macrocyclic ligands 1-(2-aminoethyl)- (L^1) and 1-(3-aminopropyl)-1,5,9-triazacyclododecane (L^2) have been synthesised from 2,4-dioxo-1,5,9-triazacyclododecane, and the complexes $[ZnL^1(OClO_3)]ClO_4$ (trigonal bipyramidal) and $[NiL^2(NCS)_2]$ (octahedral) characterised by X-ray crystallography; L^1 and L^2 form more stable complexes than do analogues bearing tertiary amino groups on the pendant arms, but allow higher co-ordination numbers.

We reported recently[1] that the pendant arm macrocycle 1-(3-dimethylaminopropyl)-1,5,9-triazacyclododecane (L^3) forms a tetrahedral complex with Zn^{II}, whilst the pyrrolidinylethyl pendant arm in 1-[2-(pyrrolidin-1-yl)ethyl]-1,5,9-triazacyclododecane (L^4) yields a trigonal-bipyramidal complex containing a co-ordinated perchlorate ion. However, these complexes, in which the pendant arms terminate in tertiary amine groups, are very unstable, being decomposed rapidly by traces of water. The particular instability of $[ZnL^3]^{2+}$ results from the low-coordination number of the central zinc(II) ion and steric crowding within the complexed ligand. To answer the question of whether a pendant *primary* amine might facilitate tetrahedral co-ordination, we synthesised the ligands 1-(2-aminoethyl)-1,5,9-triazacyclododecane (L^1) and 1-(3-aminopropyl)-1,5,9-triazacyclododecane (L^2) by a new route starting from the recently reported compound 2,4-dioxo-1,5,9-triazacyclododecane (**I**, Scheme 1).[2] Primary amines typically bind transition-metal cations more strongly than tertiary amines, so L^1 and L^2 can be expected to form more stable complexes than L^3 and L^4. We were interested, however, to see if the reduced steric hindrance allows further ligands to enter the co-ordination sphere, reducing the tendency toward tetrahedral co-ordination.

Since L^1 and L^2 contain *primary* amino groups they cannot be made by a modified Richman–Atkins method. Instead, they were synthesised in two steps (overall 25% yield in both cases) from compound **I** (Scheme 1).† This diamide behaves as a doubly protected macrocycle, the secondary amino group being readily functionalised with $NCCH_2$ or $NCCH_2CH_2$ groups to give **II** and **III** respectively (Scheme 1). In both cases BH_3·thf simultaneously reduced both the pendant cyano group and the amide protecting groups (Scheme 1).



L^1 $R = H_2N(CH_2)_2$ L^3 $R = Me_2N(CH_2)_3$

L^2 $R = H_2N(CH_2)_3$ L^4 R = N(CH₂)₂

The zinc(II) complexes were prepared from equimolar amounts of the ligands and $[Zn(Me_2SO)_4][ClO_4]_2$[3] in nitromethane. The ^1H and ^{13}C NMR spectra‡ reveal that they remain intact in acetonitrile solution, and in both cases indicate the presence of only one symmetrical isomer at room temperature. The complexes crystallise unchanged from water (no evidence of water or hydroxide co-ordination),[5] this robustness

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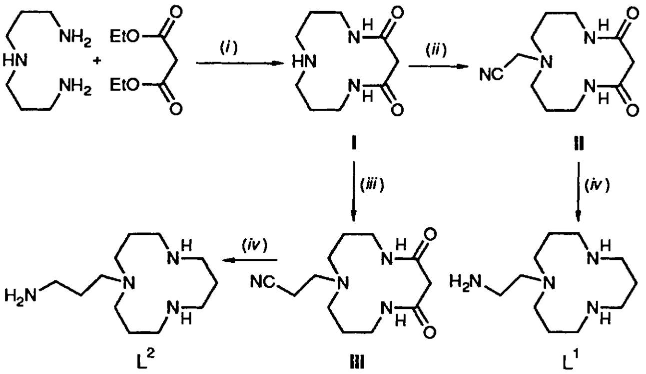
† Compound **I** was prepared by refluxing a solution of iminobis(propylamine) (13.12 g, 0.10 mol) and diethyl malonate (16.02 g, 0.10 mmol) in dry ethanol (1.2 dm^3) for 5 d (CaO guard tube).[3] The solvent was then removed by rotary evaporation, and the residue chromatographed (1–5% NH_3, 59–55% MeOH, 40% CH_2Cl_2 on SiO_2). The product was obtained as a colourless oil which rapidly crystallised, and which was recrystallised from tetrahydrofuran (thf). Yield 2.50 g, 12.5%. NMR ($CDCl_3$ *vs.* $SiMe_4$): ^1H, δ 8.50 (br, 2 H), 3.41 (q, 4 H), 3.15 (s, 2 H), 2.78 (m, 4 H), 1.69 (m, 4 H) and 1.57 (br, 1 H); ^{13}C, δ 167.40 (2 C), 48.78 (2 C), 46.22 (1 C), 40.44 (2 C) and 26.98 (2 C). *m/z* [electron-impact (EI)]: 199 ([**I**]$^+$).

The salt $Na_2S_2O_5$ (1.90 g, 10 mmol) in water (5 cm^3) was boiled for 10 min with 38% aqueous formaldehyde. After cooling, **I** (2.00 g, 10 mmol) was added with vigorous stirring. After 4 h aqueous sodium cyanide (0.49 g, 10 mmol) in water (5 cm^3) was added and the reaction mixture left stirring overnight. Extraction with dichloromethane, drying ($MgSO_4$) and evaporation yielded compound **II** as a white crystalline solid (1.20 g, 50%). NMR ($CDCl_3$ *vs.* $SiMe_4$): ^1H, δ 6.96 (br, 2 H), 3.45 (q, 4 H), 3.18 (s, 2 H), 2.70 (t, 6 H) and 1.81 (m, 4 H); ^{13}C, δ 167.67 (2 C), 113.8 (1 C), 53.16 (2 C), 46.49 (1 C), 41.16 (1 C), 39.19 (2 C) and 24.33 (2 C). *m/z* (EI): 239 ([**II**]$^+$) and 199 ([**II** − CH_2CN]$^+$).

Compound **I** (2.00 g, 10 mmol) was refluxed for 48 h with acrylonitrile (20 cm^3). On cooling a white solid precipitated which was filtered off and recrystallised from acetone (*ca.* 200 cm^3). Yield of compound **III** 1.76 g, 70%. NMR (^1H, $CDCl_3$ *vs.* $SiMe_4$), δ 7.46 (br, 2 H), 3.45 (q, 4 H), 3.21 (s, 2 H), 2.78 (t, 2 H), 2.63 (m, 6 H) and 1.81 (m, 4 H); (D_2O) 4.75 (s, 2 H), 3.23 (t, 4 H), 3.16 (s 2, H), 2.73 (t, 2 H), 2.61 (t, 2 H), 2.52 (t, 4 H) and 1.69 (p, 4 H); ^{13}C (D_2O), δ 170.42 (2 C), 121.57 (1 C), 51.47 (2 C), 48.60 (1 C), 46.14 (1 C), 39.71 (2 C), 24.06 (2 C) and 15.61 (1 C). *m/z* (EI): 252 ([**III**]$^+$) and 212 ([**III** − CH_2CN]$^+$).

Compound **II** (1.17 g, 5 mmol) was refluxed with BH_3·thf (1.0 mol dm^{-3} solution in thf; 15 cm^3, 15 mmol) for 24 h under nitrogen. After cooling, the reaction mixture was treated cautiously with water (2 cm^3), then sodium hydroxide solution (8 mol dm^{-3}, 5 cm^3), and stirred until all solids had dissolved. The organic phase was separated, and the aqueous phase extracted with thf (10 cm^3). The combined organic phases were dried ($MgSO_4$), evaporated, and the residue distilled *in vacuo* (Kugelrohr apparatus) to yield, after a short forerun of a white sublimate (1,5,9-triaza-13-boratricyclo[$7.3.1^{5,13}$]tridecane),[2,4] compound L^1 as a viscous oil. NMR ($CDCl_3$ *vs.* $SiMe_4$): ^1H, δ 3.00–2.40 (complex m, 16 H) and 1.70–1.50 (m, 6 H); ^{13}C, δ 53.1 (2 C), 50.1 (1 C), 49.2 (2 C), 47.3 (2 C), 40.7 (1 C), 26.9 (1 C) and 26.1 (2 C). *m/z* [chemical ionization (CI)]. 215 ([L^1 + H]$^+$). An identical procedure starting from **III** (1.26 g) yielded L^2. NMR (CD_3OD *vs.* $SiMe_4$): ^1H, δ 2.85–2.40 (complex m, 16 H) and 1.68 (m, 8 H); ^{13}C, δ 54.2 (2 C), 50.9 (1 C), 49.9 (2 C), 48.2 (2 C), 41.2 (1 C), 29.7 (2 C), 26.6 (2 C) and 26.5 (1 C). *m/z* (CI, NH_3): 229 ([L^2 + H]$^+$).

‡ $[ZnL^1][ClO_4]_2$. NMR (CD_3NO_2 *vs.* $SiMe_4$): ^1H, δ 4.13 (m, 2 H), 3.61 (m, 2 H), 3.49–3.20 (m, 4 H), 3.06 (p, 2 H), 2.98–2.75 (m, 10 H), 2.14–1.96 (m, 2 H) and 1.94–1.71 (m, 4 H); ^{13}C, δ 59.8 (2 C), 57.6 (1 C), 53.5 (2 C), 52.9 (2 C), 39.0 (1 C), 26.35 (2 C) and 25.6 (1 C). *m/z* [fast atom bombardment (FAB), 3-nitrobenzyl alcohol matrix]: *m/z* 379 {$[ZnL^1(ClO_4)]^+$ and 279 $[Zn(L^1 - H)]^+$} (Found: C, 27.4; H, 5.5; N, 11.5. Calc. for $C_{11}H_{26}Cl_2N_4O_8Zn$: C, 27.6; H, 5.5; N, 11.7%).



Scheme 1 (*i*) reflux, EtOH, 5 d; (*ii*) $Na_2S_2O_5$, formaldehyde, 4 h, then sodium cyanide, stirring overnight; (*iii*) reflux, acrylonitrile, 2 d; (*iv*) reflux, BH_3·thf (1.0 mol dm^{-3} solution in thf, 3 equivalents), 24 h, then water (**CAUTION**), NaOH(aq) (8 mol dm^{-3})

indicating the superiority of pendant primary amino groups as ligands for transition-metal ions.

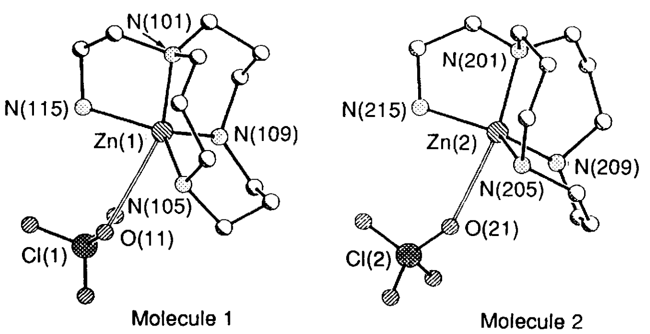


Fig. 1 Structures of the two crystallographically distinct molecules of $[ZnL^1(OClO_3)]ClO_4$. Ligand atoms are numbered sequentially around the ring [N(101), C(102), C(103), *etc*., and N(201), C(202), C(203), *etc*.], according to IUPAC recommendations. Hydrogen atoms are omitted for clarity. Bond distances: Zn(1)–N(101), 2.106(7), Zn(1)–N(105) 2.004(7), Zn(1)–N(109) 1.991(9), Zn(1)–N(115) 2.031(7), Zn(1)–O(11) 2.818(5); Zn(2)–N(201) 2.079(7), Zn(2)–N(205) 2.006(8), Zn(2)–N(209) 2.026(7), Zn(2)–N(215) 2.013(7) and Zn(2)–O(21) 2.528(5) Å

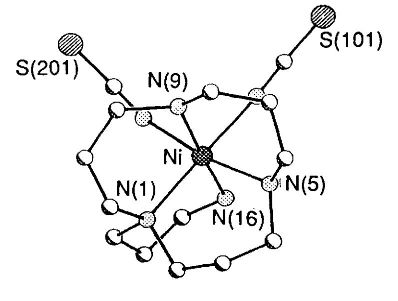


Fig. 2 Crystal structure of $[NiL^2(NCS)_2]$, viewed perpendicular to the plane of the macrocyclic ring. Bond distances: Ni–N(1) 2.179(8), Ni–N(5) 2.117(6), Ni–N(9) 2.088(12), Ni–N(16) 2.094(6), Ni–N(101), 2.134(7) and Ni–N(201) 2.054(8) Å

Infrared spectroscopy does not distinguish co-ordinated and unco-ordinated perchlorate in these complexes, but crystallography * shows that the L^1 complex, like its L^4 analogue,[1] binds one perchlorate to yield a five-co-ordinate cation (Fig. 1). In the two independent $[ZnL^1(OClO_3)]^+$ molecules the tertiary N atoms [N(101) and N(201)] and perchlorate anions O(11) and O(21) form the apices of a distorted trigonal bipyramid. The aminoethyl pendant arms afford chelate angles of 86.5(3) and 88.0(3)° whilst the propyl-linked chelates of the macrocyclic moiety maintain an average N–Zn–N angle of 104.8° (exactly the same as in $[ZnL^4][ClO_4]_2$). The non-chelating N–Zn–N angles increase to an average of 124.0° (*cf.* 118.2° in the L^4 complex) to permit the interaction with the counter ion. Because of the increased co-ordination number, Zn–N distances in $[ZnL^1(OClO_3)]^+$ (average 2.03 Å) somewhat exceed those in $[ZnL^3]^{2+}$ (2.00 Å), but correspond closely to those observed in $[ZnL^4(OClO_3)]^+$ (2.04 Å). The bonds to the tertiary N atoms are the longest in both crystallographically distinct molecules.

Due to severe twinning, the structure determination of $[ZnL^2][ClO_4]_2$ was not possible. However molecular mechanics calculations indicate that both $[ZnL^1]^{2+}$ and $[ZnL^2]^{2+}$ are significantly less hindered than their L^3 and L^4 analogues, and more readily interact with solvent molecules or perchlorate counter ions.

Because the d^{10} electronic configuration of Zn^{II} elicits no ligand-field stabilisation energy in *any* co-ordination geometry, the structures of its complexes of L^1–L^4 are largely determined by the conformational and steric properties of the ligands. In contrast, the structures of the nickel(II) complexes reflect the stability of this d^8 metal ion in octahedral co-ordination (*e.g.*, L^3 forms a μ-carbonato complex in which the pendant arm is not co-ordinated to the Ni^{II}).[7] Addition of L^2 to $[Ni(MeCN)_6][ClO_4]_2$ in acetonitrile followed by NaNCS (2 equivalents) gave *cis*-$[NiL^2(NCS)_2]$ as purple crystals.† The crystal structure (Fig. 2) shows that the macrocyclic ring occupies one face of the co-ordination octahedron, whilst the pendant arm chelates to a fourth site. The remaining two *cis* positions are occupied by *N*-bonded thiocyanates to give a neutral complex. Interestingly, the Ni atom lies away from the axis of the more closely bound thiocyanate group [C(201)–N(201)–Ni 164.4°]. This displacement probably arises from close interactions between the thiocyanate and the hydrogen atoms, particularly H(15a) and H(11a) of the $(CH_2)_3$ groups. Within the macrocycle, the tertiary bridgehead nitrogen atom [N(1)] binds the least strongly [Ni–N(1) 2.179(8) Å]. Of the remaining N atoms, those which are *trans* to each other form the shortest bonds to Ni, while N(5) [which, like N(1), is *trans* to a thiocyanate] binds at an intermediate distance. Chelating angles within the macrocycle

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* Crystal data. $C_{11}H_{26}Cl_2N_4O_8Zn$, $M = 478.6$, colourless plates (0.2 × 0.5 × 0.7 mm) from nitromethane–ethanol, monoclinic, space group $P2_1/c$, $a = 12.412(6)$, $b = 23.364(11)$, $c = 12.961(6)$ Å, $\beta = 92.08(4)°$, $U = 3759$ Å^3, $Z = 8$, $D_c = 1.69$ g cm^{-3}, $F(000) = 1984$, μ(Mo-Kα) = 16.4 cm^{-1}, $R = 0.0945$, $R' = 0.102$ for 5427 unique reflections [$I > 3\sigma(I)$]. $C_{14}H_{28}N_6NiS_2$, $M = 403.2$, purple blocks (0.1 × 0.2 × 0.1 mm) from acetonitrile, monoclinic, space group Pn, $a = 8.116(9)$, $b = 8.367(8)$, $c = 13.521(9)$ Å, $\beta = 99.25(7)°$, $U = 906.2$ Å^3, $Z = 2$, $D_c = 1.48$ g cm^{-3}, $F(000) = 428$, μ(Mo-Kα) = 13.0 cm^{-1}, $R = 0.038$, $R' = 0.042$ for 2213 unique reflections [$I > 2\sigma(I)$]. In each case the crystal was centred on a Syntex $P2_1$ four-circle diffractometer equipped with Mo-Kα radiation (graphite monochromator, $\lambda = 0.710\,73$ Å) operating in ω–2θ mode. Standard reflections showed no significant decrease in either case. Reflections were processed using a profile analysis; unique reflections considered observed were used in refinement. They were corrected for Lorentz, polarisation and absorption effects, the last by a Gaussian method. The structures were solved by direct methods using the SHELXTL PLUS[6] suite of crystallographic programs. Anisotropic thermal parameters were used for all non-hydrogen atoms. Hydrogen atoms were inserted at calculated positions and given fixed isotropic thermal parameters, $U = 0.08$ Å^2 for $[ZnL^1][ClO_4]_2$, 0.07 Å^2 for $[NiL^2(NCS)_2]$. Final refinement was on F by least-squares methods using a weighting scheme of the form $w = [1/\sigma^2(F) + gF^2]$ ($g = 0.0050$ and 0.0007 respectively), which was shown to be satisfactory by weight analyses. In $[ZnL^1(OClO_3)]ClO_4$ the O atoms displayed uniformly high thermal parameters, but there was no evidence for disorder. In addition the ligand atoms C(110), C(111), C(204), C(206) and C(207) displayed particularly large and anisotropic thermal motions, suggesting partial disorder, but this was not, however, modelled further. All crystals examined showed clear signs of twinning under polarised light; although this was relatively slight for the crystal used for data collection, the partial twinning probably contributed to the high final R factors. For $[NiL^2(NCS)_2]$ the non-centrosymmetric space group Pn (rather than $P2/n$) was selected on the basis of the value of Z and the probable lack of molecular symmetry. The x and z coordinates of the Ni atom were fixed to define the origin. The absolute structure was checked by refinement of a $\delta f''$ multiplier. Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1992, Issue 1, pp. xx–xxv.

† $[NiL^2(NCS)_2]$. UV/VIS [MeCN, λ/nm (ε/dm^3 mol^{-1} cm^{-1})]: 365 (sh), 580 (13.2) and 964 (7.4). m/z (FAB, negative ion): 461 $\{[NiL^2(NCS)_3]^-\}$, (positive ion) 344 $\{[NiL^2(NCS)_2]^+\}$ and 285 $\{[Ni(L^2 - H)]^+\}$. IR (Nujol mull, NaCl plates, cm^{-1}): 2088s, 2082s, 2076s and 2070s (Found: C, 41.2; H, 6.9; N, 20.5. Calc. for $C_{14}H_{28}N_6NiS_2$: C, 41.7; H, 7.0; N, 20.8%).

uniformly exceed 90° [94.8(2)–91.0(3)°]. Since the chelating angle in the pendant arm is only 88.5(2)°, these expansions can be ascribed to intra-annular repulsions. The strained conformation of the 12-membered macrocyclic ring also reflects this.

Because their pendant arms bind the central metal ion more readily, L^1 and L^2 form more stable complexes than do L^3 and L^4. However these less-hindered ligands permit increased co-ordination numbers for Zn^{II} and Ni^{II}, and do not promote tetrahedral co-ordination. We are currently investigating ligands with donor sets more suited to the electronic demands of this co-ordination geometry.

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