

Synthesis and co-ordination chemistry of 1,7-bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane

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The potentially octadentate ligand 1,7-bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane (H_2L), which contains two oxygen and two nitrogen donors on the groups attached to the macrocycle, has been isolated and characterized as the pentahydro-bromide or -perchlorate, $H_2L \cdot 5HY$ ($Y = Br$ or ClO_4). Its co-ordination chemistry towards nickel(II) and zinc(II) ions has been investigated and the structures of the complexes which have been obtained, $[NiL] \cdot 6.5H_2O$ **1**, $[Ni(H_{1.5}L)][ClO_4]_{1.5} \cdot 2H_2O$ **2** and $[Zn_3L_2][ClO_4]_2 \cdot 5H_2O$ **3**, have been determined by single-crystal X-ray analyses. The metal ion in **1** and **2** is in an approximately octahedral environment formed by the four nitrogen donors of the macrocycle and two donors from the dangling groups, either carboxyl oxygens **1** or methylimidazole nitrogens **2**. In the trimetallic zinc complex two metal ions, in peripheral positions, are seven-co-ordinated, whereas the third is tetrahedrally four-co-ordinated.

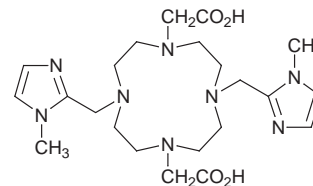
In recent years considerable attention has been addressed to metal complexes of 1,4,7,10-tetraazacyclododecane (cyclen) bearing pendant arms.¹ Depending on the number and the nature of substituent groups on the macrocycle framework, as well as on the requirements of the metal ions employed, such molecules appear to be suitable to co-ordinate both transition and rare-earth metal ions.^{2,3} The complexes with these ligands exhibit notable thermodynamic and kinetic stability and are therefore regarded as being potentially useful for applications in diagnostic⁴ and therapeutic medicine.⁵ In this context the rare-earth metal complexes with the ligand H_4dota [$H_4dota = 1,4,7,10$ -tetra(carboxymethyl)-1,4,7,10-tetraazacyclododecane] provide the most representative examples. The compound $Na[Gd(dota)(H_2O)]$, in particular, has been exploited as a magnetic resonance imaging (MRI) contrast agent in clinical practice.⁶ Moreover, all the rare-earth metal complexes with dota have been widely investigated for their peculiar behaviour in solution.⁷ Following the above points of interest, notable efforts have been focused on the development of cyclen-based ligands with donors of different nature on the dangling groups,⁸ mostly to (1) tune the co-ordinating properties of the ligand molecules toward the formation of metal complexes which may satisfy the requirements for biomedical applications and (2) investigate the factors which affect the stability of such complexes.

Most of the ligands which have been synthesized and used up to now contained four identical groups attached to the nitrogen atoms of the macrocycle, bearing either anionic or neutral donors. As anionic donors the oxygens of acetate⁹ or phosphinate¹⁰ groups have been employed, whereas amide,¹¹ alcohol¹² or ether¹³ oxygens have been used as neutral donors.

The kinetic inertness of the complexes formed by substituted cyclen ligands has been investigated with respect to the proton- or cation-mediated dissociation pathways.^{9b,14,15} It has been found that the kinetic stability is significantly affected by the overall charge on the metal complexes. Hence it would be of interest to study the effects of changes in the overall charge of the complexes formed by specific metal ions by varying the ratio of the charged to neutral donors on the dangling groups.

In recent years we have investigated the co-ordination of tri-¹⁶ and tetra-azamacrocycles¹⁷ functionalized with such residues as imidazole and pyrazole. In the course of these studies we have described the good-yield synthesis of cyclen disubstituted with methylimidazole.¹⁸ This molecule has been further derivatized to form 1,7-bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane,

H_2L , which contains two pairs of different donors, two oxygen and two nitrogen atoms, on the dangling groups. Its co-ordinating properties toward nickel(II) and zinc(II) have been investigated. The structures of the compounds $[NiL] \cdot 6.5H_2O$ **1**, where the L^{2-} anion is formed by complete deprotonation of the H_2L molecule, $[Ni(H_{1.5}L)][ClO_4]_{1.5} \cdot 2H_2O$ **2**, where $H_{1.5}L^{0.5-}$ is the partly deprotonated H_2L molecule, and of $[Zn_3L_2][ClO_4]_2 \cdot 5H_2O$ **3** have been determined by X-ray diffraction methods.



Experimental

Commercial solvents were dried from an appropriate drying agent just before use according to standard procedures. The NMR spectra were obtained with a Varian FT80 spectrometer operating at 20 MHz (¹³C). Positive chemical shifts are to high frequency relative to SiMe₄ as internal standard. Room-temperature electronic spectra were recorded in the range 250–1500 nm with a Perkin-Elmer Lambda 9 spectrophotometer, infrared spectra with a Perkin-Elmer 283 grating spectrophotometer. Elemental analyses were performed by the Micro-analytical Laboratory of the Department of Chemistry of the University of Florence. The compound 1,7-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane was prepared according to the published procedure.¹⁸ Hydrated nickel(II) and zinc(II) perchlorates were prepared by standard methods.

Syntheses

1,7-Bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane H_2L . Sodium bromoacetate (7.08 g, 0.044 mol) in water (10 cm³) was added to a solution of 1,7-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane (7.9 g, 0.010 mol) in water (50 cm³); the resulting solution was adjusted to pH 10 by adding a 5 M NaOH solution and warmed to 35 °C. Sodium hydroxide solution (5 M) was then added dropwise over 24 h while the pH, monitored

continuously by means of a combined pH electrode (Crison), was maintained between 10 and 11. Afterwards the water was eliminated from the reaction mixture at reduced pressure. The remaining solid was dissolved in ethanol and a crude product precipitated by acidification with HBr. The crude product was dissolved in diluted NaOH ethanol solution and acidification with HBr resulted in precipitation of a white solid which was collected, washed with diethyl ether and dried. Yield 64%. The compound crystallizes as $\text{H}_2\text{L}\cdot 5\text{HBr}\cdot \text{EtOH}$ with one molecule of ethanol as found from the ^{13}C NMR spectra (δ 16.9, 57.5) and elemental analysis (Found: C, 31.3; H, 5.2; N, 12.2. Calc. for $\text{C}_{24}\text{H}_{47}\text{Br}_5\text{N}_8\text{O}_5$: C, 31.1; H, 5.1; N, 12.1%). Addition of HClO_4 to the alkaline ethanol solution of the crude product yielded a white solid which was collected as described for the bromide derivative; also this compound crystallizes with ethanol and was characterized as $\text{H}_2\text{L}\cdot 5\text{HClO}_4\cdot \text{EtOH}$ (Found: C, 27.6; H, 4.5; Cl, 17.0; N, 10.7. Calc. for $\text{C}_{24}\text{H}_{47}\text{Cl}_5\text{N}_8\text{O}_{25}$: C, 28.1; H, 4.6; Cl, 17.3; N, 10.9%). ^{13}C NMR (D_2O , pD 1): δ 168.8 (CO_2H), 141.8 (C^2), 124.2 (C^4 , C^5), 119.6 (C^5 , C^4), 55.8 ($\text{CH}_2\text{CO}_2\text{H}$), 51.6 (CH_2 of macrocycle), 47.4 (CH_2 of macrocycle), 45.7 (CH_2 of imidazolomethyl) and 35.0 (CH_3 of imidazole).

[NiL]·6.5H₂O 1. CAUTION: perchlorate salts of metal complexes are potentially explosive. Although no accident occurred in the course of the operations described hereafter, when perchlorate salts are employed suitable precautions should be taken. The compound $\text{H}_2\text{L}\cdot 5\text{HBr}$ (0.44 g, 0.50 mmol) was dissolved in water (5 cm³) and adjusted to pH 8 by addition of 5 M NaOH; then methanol (30 cm³) was added. The compound $\text{Ni}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}$ (0.18 g, 0.50 mmol) in ethanol (20 cm³) was slowly added to the above warm solution. The resulting solution was slowly concentrated until a crystalline product was obtained. The violet solid was recrystallized from a water–dimethylformamide–butanol mixture. Yield 75% of $[\text{NiL}]\cdot 6.5\text{H}_2\text{O}$ (Found: C, 40.6; H, 7.2; N, 17.3. Calc. for $\text{C}_{22}\text{H}_{47}\text{N}_8\text{NiO}_{10.5}$: C, 40.6; H, 7.3; N, 17.2%). $\nu_{\text{asym}}(\text{CO}_2^-)$ 1590 cm⁻¹.

[Ni(H_{1.5}L)]][ClO₄]_{1.5}·2H₂O 2. The compound $\text{Ni}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}$ (0.12 g, 0.30 mmol) in ethanol (15 cm³) was slowly added to a water solution of the ligand pentahydrobromide (0.29 g, 0.30 mmol) adjusted to pH 6. Violet crystals of the complex were obtained on leaving the resulting solution at 40–50 °C. Yield 75%. The complex $[\text{Ni}(\text{H}_{1.5}\text{L})][\text{ClO}_4]_{1.5}\cdot 2\text{H}_2\text{O}$, which is soluble in water and warm methanol, may be recrystallized from a methanol–ethanol mixture (Found: C, 36.8; H, 5.4; N, 15.6. Calc. for $\text{C}_{22}\text{H}_{39.5}\text{Cl}_{1.5}\text{N}_8\text{NiO}_{12}$: C, 36.7; H, 5.5; N, 15.6%). $\nu_{\text{stretch}}(\text{CO}_2\text{H})$ 1730, $\nu_{\text{asym}}(\text{CO}_2^-)$ 1590, $\nu_{\text{stretch}}(\text{ClO})$ 1080 cm⁻¹.

Significant absorptions in the UV/VIS spectra of the nickel complexes [$\lambda_{\text{max}}/\text{nm}$ ($\epsilon/\text{cm}^2 \text{mmol}^{-1}$), ca. 10⁻³ mol dm⁻³]: **1**, diffuse reflectance, 525, 630 (sh), 1035; aqueous solution, 525 (55), 630 (sh), 1040 (30); **2**, diffuse reflectance, 375, 535, 630 (sh), 1015; aqueous solution, 375 (30), 535 (45), 630 (sh), 1020 (27).

[Zn₃L₂][ClO₄]₂·5H₂O 3. The solution of $\text{H}_2\text{L}\cdot 5\text{HBr}$ (0.27 g, 0.30 mmol) in water (5 cm³) was adjusted to pH 7 by addition of a 5 M NaOH solution; methanol (30 cm³) was then added. The compound $\text{Zn}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}$ (0.17 g, 0.45 mmol) in ethanol (20 cm³) was slowly added to the warm solution. White crystals of the complex precipitated on leaving the resulting solution at 40–50 °C. They were washed with ethanol, then light petroleum (b.p. 40–60 °C), and dried. The complex $[\text{Zn}_3\text{L}_2][\text{ClO}_4]_2\cdot 5\text{H}_2\text{O}$ was recrystallized from a methanol–ethanol mixture. Yield 80% (Found: C, 36.9; H, 5.5; N, 15.5; Zn, 13.6. Calc. for $\text{C}_{44}\text{H}_{78}\text{Cl}_2\text{N}_{16}\text{O}_{21}\text{Zn}_3$: C, 36.8; H, 5.5; N, 15.6; Zn, 13.7%). ^{13}C NMR (D_2O): δ 171.1 (CO_2^-), 147.2 (C^2), 126.6 (C^4 , C^5), 123.9 (C^5 , C^4), 59.7 (CH_2CO_2^-), 52.7 (CH_2 of macrocycle), 51.0 (CH_2 of macrocycle), 50.2 (CH_2 of imidazolomethyl) and 33.2 (CH_3 of imidazole). $\nu_{\text{asym}}(\text{CO}_2^-)$ 1585, $\nu_{\text{stretch}}(\text{ClO})$ 1090 cm⁻¹.

Crystallography

Crystal data and refinement parameters for the compounds $[\text{NiL}]\cdot 6.5\text{H}_2\text{O}$ **1**, $[\text{Ni}(\text{H}_{1.5}\text{L})][\text{ClO}_4]_{1.5}\cdot 2\text{H}_2\text{O}$ **2** and $[\text{Zn}_3\text{L}_2][\text{ClO}_4]_2\cdot 5\text{H}_2\text{O}$ **3** are given in Table 1. All operations were performed at 295 K using an Enraf-Nonius CAD4 diffractometer and graphite-monochromated Cu-K α radiation ($\lambda = 1.5418 \text{ \AA}$). Unit-cell parameters were obtained from the settings of 24 reflections in each case, with $33 < \theta < 40$ **1**, $27 < \theta < 43$ **2** and $27 < \theta < 41^\circ$ **3**. The ω – 2θ scan mode was used. The crystal of **1** used for the final data collection was an elongated plate, that of **2** was a needle, and that of **3** had approximately the shape of a prism with ill defined faces. The intensities of two standard reflections monitored periodically during the data collections did not reveal any effects of systematic decay. An empirical absorption correction was applied in each case to the data after structure solution at isotropic convergence.¹⁹ The principal computer programs used in the crystallographic calculations are listed in refs. 19–23. The atomic scattering factors were from ref. 21.

The structures were solved by direct methods with SIR²⁰ and by heavy-atom methods. The asymmetric unit of compound **1** contains two (symmetry-independent) $[\text{NiL}]$ units and 13 H₂O molecules. That of **2** contains one $[\text{Ni}(\text{H}_{1.5}\text{L})]^{1.5+}$ cation, two H₂O molecules and 1.5 ClO₄⁻ anions. One ClO₄⁻ anion lies at a general position and one on an inversion centre; the latter is therefore shared by two asymmetric units. Each $[\text{Ni}(\text{H}_{1.5}\text{L})]^{1.5+}$ cation of **2** shares one carboxylic hydrogen of a hydrogen bond with a complex cation related to the former by an inversion centre. The asymmetric unit of **3** contains the trimetal $[\text{Zn}_3\text{L}_2]^{2+}$ cation, two ClO₄⁻ anions and five water molecules.

All refinements were performed on F^2 . In the final model for compound **1** all non-hydrogen atoms were assigned anisotropic thermal parameters. The hydrogen atoms of the complex molecule were in calculated positions, riding on the respective C atoms, with $U_{\text{H}} = 1.2 U_{\text{C}}^{\text{eq}}$ ($U_{\text{H}} = 1.5 U_{\text{C}}^{\text{eq}}$ for the hydrogens of methyl groups, the orientations of which were refined), where U_{C}^{eq} is the equivalent isotropic thermal parameter of the carrier atom. Of the 26 H atoms of the water molecules 23 were located from ΔF maps; their positions were refined, with $U_{\text{H}} = 1.5 U_{\text{O}}^{\text{eq}}$, subject to a common geometrical restraint on the O–H bond lengths and the bond angle. Since the space group is acentric, the absolute configuration was assigned, within 2σ of the expected value of the Flack parameter.²⁴

In the model for compound **2** all non-hydrogen atoms were anisotropic and the non-carboxylic H atoms of the ligand were introduced as described for **1**. The H atoms of the two water molecules and of the carboxylic group involved in hydrogen bonding to the symmetry-related cation were not introduced, because of insufficient evidence from ΔF maps, whereas that of the second carboxylic group of the ligand was located and introduced in the calculations, the orientation of its O–H bond being refined. The ClO₄⁻ anion in general position was found to be predominantly distributed over two orientations and was refined as two tetrahedral images with a common Cl atom position but two distinct sets of Cl–O distances. The two tetrahedra of fractional O atoms were assigned complementary population parameters. A damping factor had to be applied in the course of the refinement, however not in the final cycle, to prevent oscillations in the anisotropic thermal parameters of the fractional O atoms forming the lower-weight image of the anion. Tetrahedral geometry was also imposed on the symmetry-independent fraction of the second anion, the Cl atom of which lay on an inversion centre.

Also the model for compound **3** was anisotropic with the ligand H atoms in calculated positions as for the other structures. The H atoms of the water molecules were not located and not introduced. One of the two ClO₄⁻ anions, affected by disorder, was modelled by two tetrahedral fractions, as described for **2**. A soft restraint imposing tetrahedral geometry was also

Table 1 Crystallographic data for [NiL]·6.5H₂O **1**, [Ni(H_{1.5}L)](ClO₄)_{1.5}·2H₂O **2** and [Zn₃L₂](ClO₄)₂·5H₂O **3**^a

	1	2	3
Formula	C ₂₂ H ₄₇ N ₈ NiO _{10.5}	C ₂₂ H _{39.5} Cl _{1.5} N ₈ NiO ₁₂	C ₄₄ H ₇₈ Cl ₂ N ₁₆ O ₂₁ Zn ₃
<i>M</i>	650.38	720.00	1434.22
Crystal system	Orthorhombic	Monoclinic	Monoclinic
Space group	<i>Pbc</i> 2 ₁ (no. 29)	<i>P2</i> ₁ / <i>c</i> (no. 14)	<i>P2</i> ₁ / <i>a</i> (no. 14)
<i>a</i> /Å	9.147(1)	8.951(3)	12.779(2)
<i>b</i> /Å	17.708(7)	21.214(5)	31.417(4)
<i>c</i> /Å	37.317(3)	16.745(3)	15.900(2)
β /° ^b		91.16(2)	105.65(1)
<i>U</i> /Å ³	6044(2)	3179(1)	6147(1)
<i>Z</i>	8	4	4
<i>D</i> _c /g cm ⁻³	1.429	1.504	1.550
<i>F</i> (000)	2776	1508	2984
Crystal size/mm	0.17 × 0.40 × 0.90	0.08 × 0.20 × 1.00	0.15 × 0.20 × 0.50
μ /mm ⁻¹	1.50	2.66	2.90
Collection range/°	5 ≤ 2θ ≤ 130	6 ≤ 2θ ≤ 120	5 ≤ 2θ ≤ 130
Data collected	+ <i>h</i> , + <i>k</i> , + <i>l</i>	± <i>h</i> , + <i>k</i> , + <i>l</i>	± <i>h</i> , + <i>k</i> , + <i>l</i>
No. measured reflections	5774	5005	9842
No. unique data	5219	4685	9251
Absorption correction factors ^c	0.71–1.28	0.85–1.10	0.88–1.11
No. parameters	822	464	838
Weights (<i>a</i> , <i>b</i> , <i>f</i>) ^d	0.1014, 1.288, 1/3	0.1159, 4.410, 1/3	0.0829, 5.916, 1/3
Goodness of fit	1.045	1.040	1.072
$R1 = \sum F_o - F_c / \sum F_o $ ^e	0.045	0.069	0.052
$wR2 = [\sum w(F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2]$ ¹	0.121	0.202	0.161
Largest features in final difference map/e Å ⁻³	0.38, -0.65	0.51, -0.39	0.56, -0.42

^a Details in common: scan width (1.20 + 0.35 tan θ)°; scan speed 1–5° min⁻¹. ^b For compound **1**, α = β = γ = 90°; for **2** and **3**, α = γ = 90°. ^c Range of absorption correction factors from DIFABS. ^d Weighting scheme according to the formula $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$, where $P = [\max(0, F_o^2) + (1 - f)F_c^2]$. ^e Based on the 5088 **1**, 3767 **2** and 7307 **3** reflections with $F_o > 4\sigma F_o$. $R1 = 0.046$ **1**, 0.086 **2** and 0.069 **3** for all unique reflections.

applied to the other anion. Of the five water molecules two were disordered, each of these being distributed over two positions. The pairs of sites were assigned complementary population parameters, which were refined.

CCDC reference number 186/966.

Results and Discussion

Synthesis of the ligand and metal complexes

1,7-Bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane (H₂L) was synthesized by alkylation of 1,7-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane with sodium bromoacetate in alkaline solution at ca. 35 °C. In the course of the reaction the pH of the solution was maintained constant by addition of NaOH. The alkylation was accomplished by the general procedure described for the synthesis of tetra-, tri- or mono-*N*-substituted cyclen molecules.^{8,9a,25} Care was taken that the temperature of the solution did not exceed 35 °C to avoid undesirable reactions at the imidazole groups. The ligand was characterized in its protonated form H₂L·5HY·EtOH (Y = Br or ClO₄). The bromide derivative is soluble in water and in polar organic solvents like methanol and ethanol; the perchlorate dissolves poorly in water and is substantially insoluble in polar organic solvents.

The reaction of hydrated Ni(ClO₄)₂ with an aqueous solution of H₂L at pH 8 yields a neutral complex which analyses as [NiL]·6.5H₂O **1**. This complex is soluble in methanol and ethanol. Its reflectance and solution electronic spectra exhibit three maxima at 1050, 630 and 525 nm and an intense charge transfer absorption at higher frequencies. This pattern is typical of octahedral high-spin chromophores of nickel(II). The infrared spectrum presents the $\nu_{\text{asym}}(\text{CO}_2^-)$ band at 1590 cm⁻¹, which suggests that the carboxymethyl groups are deprotonated. Therefore, it would be expected that the nickel atom attains six-co-ordination by binding to two oxygen atoms of the deprotonated carboxymethyl groups in addition to the four

nitrogen donors of the macrocycle; this is confirmed by the X-ray analysis (see below).

The reaction of hydrated Ni(ClO₄)₂ with a water solution of H₂L at pH 6 yields a complex which analyses as [Ni(H_{1.5}L)](ClO₄)_{1.5}·2H₂O **2**. This compound, which is poorly soluble in hot methanol, dissolves in water. Its reflectance spectrum and the solution electronic spectrum at pH < 7 exhibit three absorptions at maxima slightly shifted to lower frequencies with respect to those found for **1**; also the charge transfer absorption is significantly shifted to lower energies. The infrared spectrum of the solid exhibits, besides the ClO stretching band, two intense and well separated bands at 1730 and 1590 cm⁻¹ which are assigned to the $\nu_{\text{stretch}}(\text{CO}_2\text{H})$ and $\nu_{\text{asym}}(\text{CO}_2^-)$ modes. Such absorptions suggest that the compound contains both protonated and deprotonated carboxymethyl groups. This is consistent with the results of the X-ray investigation (see below). Compound **2** in aqueous solution at pH 8 yields an electronic spectrum superimposable on that of **1**, but the spectrum of **2** is recovered reversibly if the pH of the solution is lowered to 6. Such behaviour is indicative of rearrangements undergone by the chromophore in solution, consisting of mutual and reversible displacements of the imidazole and carboxymethyl groups from the immediate metal ion environment.

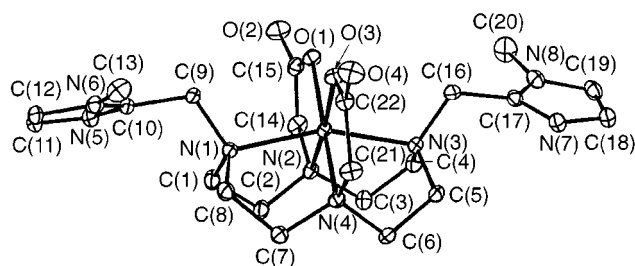
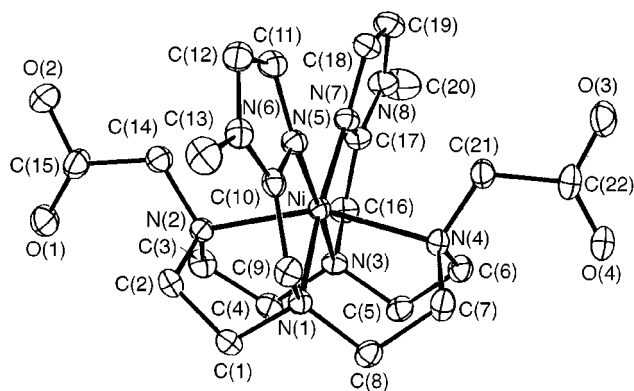
Zinc perchlorate yields the trimetallic species [Zn₃L₂](ClO₄)₂·5H₂O **3** irrespective of the pH value (in the range 5–8) of the solution containing H₂L. The ¹³C NMR spectrum of the complex exhibits one signal for each group of chemically equivalent carbon atoms of the ligand. This is not consistent with the notable lack of symmetry observed for the co-ordination in the solid state (see below) and is suggestive of dynamic behaviour of the complex cation in solution.

The X-ray structural investigation on compound **1** has revealed that the metal atom is six-co-ordinated by the four macrocycle nitrogen atoms and two oxygens of the carboxylate groups, in an approximately octahedral environment in which the macrocycle spans two contiguous faces of the octahedron (Fig. 1). The two symmetry-independent molecules in the structure have closely similar geometries (Table 2). The methyl-

Table 2 Selected bond distances (Å) and angles (°) for [NiL]·6.5H₂O **1***

Ni(1)–O(1)	2.041(3)	Ni(2)–O(5)	2.036(3)
Ni(1)–O(3)	2.020(3)	Ni(2)–O(7)	2.026(3)
Ni(1)–N(1)	2.201(4)	Ni(2)–N(9)	2.161(3)
Ni(1)–N(2)	2.126(3)	Ni(2)–N(10)	2.111(3)
Ni(1)–N(3)	2.172(3)	Ni(2)–N(11)	2.174(3)
Ni(1)–N(4)	2.112(3)	Ni(2)–N(12)	2.118(3)
O(1)–Ni(1)–O(3)	87.83(12)	O(5)–Ni(2)–O(7)	87.10(12)
O(1)–Ni(1)–N(1)	96.38(12)	O(5)–Ni(2)–N(9)	97.68(12)
O(1)–Ni(1)–N(2)	82.65(12)	O(5)–Ni(2)–N(10)	83.05(12)
O(1)–Ni(1)–N(3)	99.06(12)	O(5)–Ni(2)–N(11)	97.69(13)
O(1)–Ni(1)–N(4)	170.22(13)	O(5)–Ni(2)–N(12)	169.50(13)
O(3)–Ni(1)–N(1)	97.46(13)	O(7)–Ni(2)–N(9)	100.58(13)
O(3)–Ni(1)–N(2)	170.44(13)	O(7)–Ni(2)–N(10)	169.81(13)
O(3)–Ni(1)–N(3)	98.91(13)	O(7)–Ni(2)–N(11)	95.77(13)
O(3)–Ni(1)–N(4)	82.51(13)	O(7)–Ni(2)–N(12)	82.41(13)
N(1)–Ni(1)–N(2)	82.77(13)	N(9)–Ni(2)–N(10)	83.39(13)
N(1)–Ni(1)–N(3)	157.85(12)	N(9)–Ni(2)–N(11)	158.04(13)
N(1)–Ni(1)–N(4)	83.39(13)	N(9)–Ni(2)–N(12)	83.74(13)
N(2)–Ni(1)–N(3)	83.55(13)	N(10)–Ni(2)–N(11)	83.02(13)
N(2)–Ni(1)–N(4)	106.98(13)	N(10)–Ni(2)–N(12)	107.45(13)
N(3)–Ni(1)–N(4)	84.04(13)	N(11)–Ni(2)–N(12)	84.00(13)

* Values for the two independent molecules in the asymmetric unit are in separate columns.

**Fig. 1** View of one of the two symmetry-independent [NiL] molecules in the structure of compound **1**. The other molecule has a substantially identical structure**Fig. 2** View of the [Ni(H_{1.5}L)]^{1.5+} cation in the structure of compound **2**

imidazole groups in the pendent arms of the L²⁻ ligand are unco-ordinated. The Ni–N distances are grouped into two sets, with 2.117(7) Å and 2.177(17) Å mean values, the shorter distances being formed by the macrocycle nitrogens bearing the carboxylate groups. Overall smaller and well grouped values of the Ni–N distances [2.132(12) Å mean] have been found for the two molecules of the [Ni(doda)] compound,²⁶ formed by a ligand which differs from L²⁻ in the absence of methylimidazole substituents on two *trans* nitrogens of the macrocycle. The 13 water molecules which are present in the asymmetric unit of **1** form an extensive net of hydrogen bonds among themselves and with the oxygen or nitrogen atoms of the ligands. About 50% of these interactions (below 3.00 Å) involve exclusively

Table 3 Selected bond distances (Å) and angles (°) for [Ni(H_{1.5}L)]·[ClO₄]_{1.5}·2H₂O **2**

Ni–N(1)	2.183(2)	Ni–N(4)	2.193(2)
Ni–N(2)	2.190(2)	Ni–N(5)	2.062(2)
Ni–N(3)	2.187(2)	Ni–N(7)	2.063(2)
N(1)–Ni–N(2)	82.79(8)	N(2)–Ni–N(7)	103.80(9)
N(1)–Ni–N(3)	105.71(9)	N(3)–Ni–N(4)	83.39(9)
N(1)–Ni–N(4)	81.41(8)	N(3)–Ni–N(5)	172.21(8)
N(1)–Ni–N(5)	79.95(9)	N(3)–Ni–N(7)	79.78(9)
N(1)–Ni–N(7)	172.13(8)	N(4)–Ni–N(5)	102.97(9)
N(2)–Ni–N(3)	81.71(9)	N(4)–Ni–N(7)	93.80(9)
N(2)–Ni–N(4)	154.44(8)	N(5)–Ni–N(7)	95.15(9)
N(2)–Ni–N(5)	93.87(9)		

water oxygens and the remaining 50% involve such oxygens and the ligand donor atoms.

The co-ordination geometry about the nickel(II) ion in compound **2** is grossly similar to that of **1** (Fig. 2 and Table 3), although in compound **2** the methylimidazole nitrogens, rather than the carboxyl oxygens, are co-ordinated in addition to the macrocycle nitrogens. At variance with **1**, the Ni–N distances formed by the macrocycle nitrogens (hereafter N_m atoms) in **2** are similar to each other and their mean, 2.188(4) Å, is larger than the values found for **1**. This has to be ascribed to small differences in the mode of binding to the metal by the methylimidazole-bearing arms in **2**, compared to those bearing carboxylate groups in **1**. In particular, a significant role appears to be played by the existence or absence of close contacts between atoms of the chelating arms. Close contacts are detected for **2** [there is a 2.18 Å distance between the H atoms on N(5) and N(7)] but not for **1** and produce the considerably larger (by *ca.* 8°) N(5)–Ni–N(7) angle in **2** than the corresponding O–Ni–O angle in the two molecules of **1** (Tables 2 and 3). The consequent shift (by 0.10 Å) of the metal atom away from the best plane through the N_m atoms on going from **1** to **2** is at the origin of the overall lengthening of Ni–N_m distances noted above. In addition to this overall effect, the above contacts between two co-ordinating arms in **2** may cause a larger lengthening of the Ni–N_m bonds formed by the N_m atoms carrying those arms, compared to the other two Ni–N_m bonds in **2**, yielding the overall similarity of Ni–N_m distances in that compound. The effects of crowding about the metal atom in related nickel(II) complexes with methylimidazole or pyrazole substituents on the macrocycle have been considered.¹⁸ The present compound **2**, with an 11.1(1)° angle between the (normals to the) planes through the chelate rings formed by the pendant arms and a 27.9(1)° angle between the planes through the methylimidazole groups, may be ranked among the complexes where significant repulsions exist between the dangling groups.¹⁸ In other cases,^{17a} particularly where four identical substituents are present on the macrocycle, the repulsions between dangling groups are released by co-operative rotations about bonds in the pendant arms.

The formula of compound **2** has been assigned by taking into account the fraction of deprotonated carboxyl groups as well as the anion:metal ratio. The carboxyl group of C(15) is undissociated: the H atom on O(2) has been located and its position refined. Moreover, the C(15)–O(1) and C(15)–O(2) distances, 1.205(4) and 1.301(4) Å respectively, are consistent with the assumption of an undissociated carboxyl group. The other carboxyl group, on the other hand, is involved in the formation of a hydrogen bond with a symmetry-related group [O(3)···O(3)ⁱ 2.53 Å; I 2 – x, –y, –z]. Its C–O distances, C(22)–O(3) 1.254(4) and C(22)–O(4) 1.215(4) Å, suggest that one bond, C(22)–O(4), is fully carbonylic whereas the other one may have intermediate character. Combined with the geometry of the (linear) hydrogen bond, this suggests that only one hydrogen atom is shared by O(3) and its symmetric counterpart. A similar

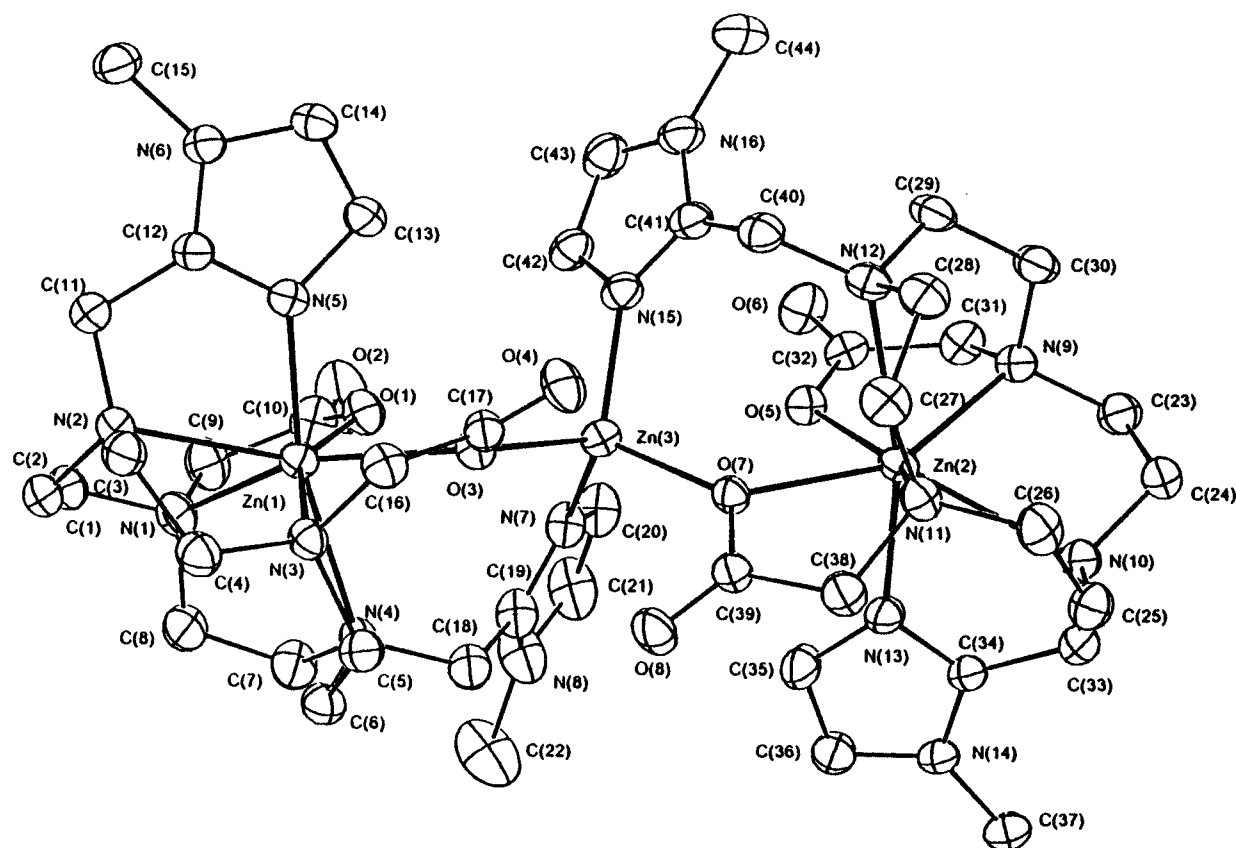


Fig. 3 View of the $[Zn_3L_2]^{2+}$ cation in the structure of compound 3

type of interaction has been reported for the $[Ni(doda)]$ compound.²⁶ The ΔF map of **2** exhibits a $0.36 \text{ e } \text{\AA}^{-3}$ peak corresponding to the inversion centre relating the two oxygen atoms; however, this is at too long a distance from such atoms to provide direct evidence of electron density and should probably be attributed to symmetry-averaging effects. However, the strongest support to the formula proposed for **2** is provided by the non-integral number (1.5) of ClO_4^- anions in the asymmetric unit, one of these being in a general position whereas the other one lies on a symmetry element (see Experimental section). The two water molecules form hydrogen bonds between themselves and with the carboxyl oxygens yielding an extensive net of such bonds.

In the trimetallic $[Zn_3L_2]^{2+}$ cation of compound **3** (Fig. 3) each of the two peripheral zinc(II) ions is seven-co-ordinated by the four macrocycle donors, one methylimidazole nitrogen and two carboxylate oxygens, one of these being bridging the central zinc(II) ion. The co-ordination geometry, closely similar for the two peripheral ions, may be approximately described in terms of a pentagonal bipyramid with the axial direction (defined by the co-ordinated methylimidazole nitrogen and a macrocycle nitrogen almost in *trans* positions) forming an angle of *ca.* 8° with the normal to the best plane through the other five donors. The bond distances about the peripheral metal atoms (Table 4) are scattered over a rather wide range, but their mean, 2.287 \AA , is only slightly smaller than that (2.305 \AA) found for a seven-co-ordinate zinc(II) complex formed by a related (but neutral) ligand, with three co-ordinated dangling pyrazole groups,^{17a} in a rather different geometry from that of **3**. The zinc(II) ion in the central position in the cation of **3** is four-co-ordinated by two methylimidazole nitrogens, provided by the dangling groups of the L^{2-} ligands not involved in the co-ordination to the peripheral metal ions, and by the two bridging oxygen atoms, in a substantially tetrahedral geometry. The (fractional) water molecules in the structure form hydrogen bonds among themselves and with carboxylate oxygen atoms but, due to the large size of the complex cation, they do not

Table 4 Selected bond distances (\AA) and angles ($^\circ$) for $[Zn_3L_2][ClO_4]_2 \cdot 5H_2O$ **3**

Zn(1)–O(1)	2.036(4)	Zn(2)–N(9)	2.247(4)
Zn(1)–O(3)	2.310(3)	Zn(2)–N(10)	2.547(4)
Zn(1)–N(1)	2.303(4)	Zn(2)–N(11)	2.224(4)
Zn(1)–N(2)	2.522(4)	Zn(2)–N(12)	2.540(4)
Zn(1)–N(3)	2.229(4)	Zn(2)–N(13)	2.108(4)
Zn(1)–N(4)	2.463(4)	Zn(3)–O(3)	1.979(3)
Zn(1)–N(5)	2.141(4)	Zn(3)–O(7)	1.964(3)
Zn(2)–O(5)	2.039(3)	Zn(3)–N(7)	1.990(4)
Zn(2)–O(7)	2.313(3)	Zn(3)–N(15)	1.966(4)
O(1)–Zn(1)–O(3)	82.55(13)	O(5)–Zn(2)–N(11)	146.9(2)
O(1)–Zn(1)–N(1)	79.2(2)	O(5)–Zn(2)–N(12)	82.55(13)
O(1)–Zn(1)–N(2)	132.0(2)	O(5)–Zn(2)–N(13)	91.28(14)
O(1)–Zn(1)–N(3)	152.4(2)	O(7)–Zn(2)–N(9)	152.27(13)
O(1)–Zn(1)–N(4)	88.0(2)	O(7)–Zn(2)–N(10)	132.65(12)
O(1)–Zn(1)–N(5)	89.9(2)	O(7)–Zn(2)–N(11)	71.05(13)
O(3)–Zn(1)–N(1)	151.6(2)	O(7)–Zn(2)–N(12)	81.31(12)
O(3)–Zn(1)–N(2)	134.85(13)	O(7)–Zn(2)–N(13)	86.10(14)
O(3)–Zn(1)–N(3)	71.86(13)	N(9)–Zn(2)–N(10)	74.19(14)
O(3)–Zn(1)–N(4)	80.58(12)	N(9)–Zn(2)–N(11)	119.2(2)
O(3)–Zn(1)–N(5)	84.44(14)	N(9)–Zn(2)–N(12)	76.71(13)
N(1)–Zn(1)–N(2)	72.9(2)	N(9)–Zn(2)–N(13)	113.9(2)
N(1)–Zn(1)–N(3)	119.7(2)	N(10)–Zn(2)–N(11)	74.7(2)
N(1)–Zn(1)–N(4)	77.2(2)	N(10)–Zn(2)–N(12)	121.46(13)
N(1)–Zn(1)–N(5)	116.9(2)	N(10)–Zn(2)–N(13)	70.56(14)
N(2)–Zn(1)–N(3)	75.2(2)	N(11)–Zn(2)–N(12)	77.25(14)
N(2)–Zn(1)–N(4)	121.44(13)	N(11)–Zn(2)–N(13)	102.6(2)
N(2)–Zn(1)–N(5)	70.16(14)	N(12)–Zn(2)–N(13)	166.8(2)
N(3)–Zn(1)–N(4)	78.00(14)	O(3)–Zn(3)–O(7)	110.97(12)
N(3)–Zn(1)–N(5)	97.6(2)	O(3)–Zn(3)–N(7)	104.9(2)
N(4)–Zn(1)–N(5)	165.0(2)	O(3)–Zn(3)–N(15)	108.5(2)
O(5)–Zn(2)–O(7)	80.22(12)	O(7)–Zn(3)–N(7)	108.7(2)
O(5)–Zn(2)–N(9)	80.4(2)	O(7)–Zn(3)–N(15)	109.8(2)
O(5)–Zn(2)–N(10)	138.44(14)	N(7)–Zn(3)–N(15)	113.9(2)

form a net of bonds extended to the whole structure, as occurs instead for the other two compounds. It should be recalled in this context that the possibility of strong interactions between

molecules of the polar solvent and the immediate metal environment on complexes formed by ligands of this type with suitable metal ions is at the basis of the use of such compounds as contrast agents.⁶

Finally, it may be worth noting some aspects of the co-ordination behaviour of the potentially octadentate H₂L ligand with respect to a small cation, like nickel(II), having preference for six-co-ordination. Although the co-ordination geometry appears to be grossly unaffected by substantial pH changes, the nature of the donor set varies with pH as a consequence of the competition between the proton and the metal ion (encapsulated by the macrocycle) for the basic sites provided by the carboxylate oxygens and the methylimidazole nitrogens. The availability of such sites for the metal varies with the nature of the medium, yielding either neutral or charged species with different physical properties.

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