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Nitrogen- and carbon-based isomerism in the copper(II) complexes of 6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane-6,13-diamine

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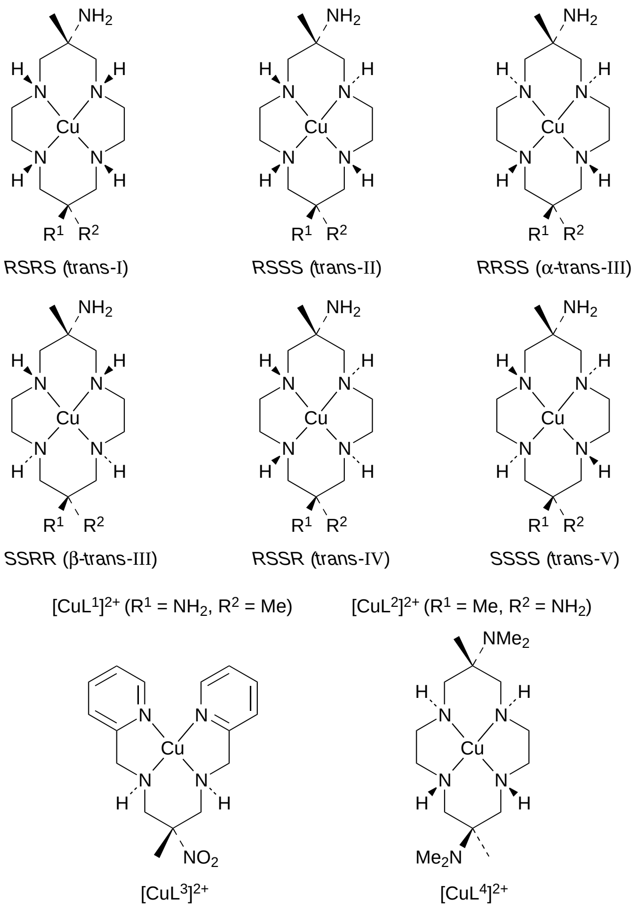
A number of N- and C-based diastereomeric copper(II) complexes of the pendant-arm macrocyclic hexaamines *trans*- and *cis*-6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane-6,13-diamine (L^1 and L^2) have been isolated and characterised. The crystal structures of the complexes *RRSS*-$[CuL^1(OH_2)_2][ClO_4]_2$, *SSRR*-$[Cu(H_2L^1)(OClO_3)_2][ClO_4]_2 \cdot 2H_2O$, *RSRS*-$[CuL^1(OClO_3)]ClO_4$, *RSRS*-$[CuL^2(OClO_3)]ClO_4$ and *RRSS*-$[Cu(H_2L^2)(OClO_3)_2][ClO_4]_2$ have been determined. Some unusual structural and spectroscopic variations are found across this series of diastereomers. The protonation constants of the pendant primary amines are dependent on the relative dispositions of the adjacent macrocyclic secondary amine H atoms, which is indicative of intramolecular hydrogen-bonding interactions.

A number of reports now exist describing the co-ordination chemistry of the isomeric hexaamine macrocycles *trans*- and *cis*-6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane-6,13-diamine, L^1 and L^2 respectively.[1,2] Depending on the metal ion and reaction conditions, hexa-, penta- or tetra-dentate co-ordination of either compound can occur, where both, one or neither pendant amine is co-ordinated in addition to the tetradentate macrocyclic (cyclam) core. At this time only one example is known where either ligand is not bound through its macrocyclic N-donors.[3]

Some time ago it was recognised that there are five possible non-degenerate N-based isomers of cyclam (1,4,8,11-tetraazacyclotetradecane) co-ordinated in a tetradentate manner.[4] In addition to these five diastereomers, other N-based isomers become possible when substituents are attached to the macrocyclic ring, some of which are shown in Scheme 1 for the copper(II) complexes of L^1 and L^2. In particular, it is notable that two centrosymmetric N-based diastereomers of $[CuL^1]^{2+}$, commonly referred to as α (*RRSS*) and β (*SSRR*),[5] arise from the dispositions of the pendant amines with respect to their adjacent secondary amine H atoms.

The vast majority of structurally characterised complexes of cyclam and its derivatives exhibit this same centrosymmetric *RRSS/SSRR* (*trans*-III) configuration of N-donors. Less common is the *RSRS* (*trans*-I) form and even more scarce are examples of the *RSSS* (*trans*-II) and *RSSR* (*trans*-IV) configurations. The planar *SSSS* (*trans*-V) isomer has not been observed as such, but instead this N-based configurational isomer forces the macrocycle to fold into a *cis* conformation so that the four N-donors are no longer coplanar, and there exist many examples of this *cis*-co-ordinated structural form. It is pertinent that the less common configurations have generally been stabilised by N-alkylation, which dramatically slows the rate of N-based isomerisation. It is now generally accepted that the thermodynamically most stable configuration is indeed the *RRSS/SSRR* isomer for complexes of the majority of transition-metal ions.



Scheme 1 The N-based diastereomers of a $[CuL^1]^{2+}$ and $[CuL^2]^{2+}$

The compound L^1 was first reported as a by-product of the zinc–acid reduction of L^3. The crystal structure of the recomplexed *RRSS*-$[CuL^1(OClO_3)_2]$ confirmed the identity of this unexpected product.[6] Soon after a more conventional synthesis of the macrocycle was reported employing the now well worked metal-directed chemistry involving condensation of co-ordinated primary amines, nitroethane and formaldehyde,[7] and the crystal structure of the protonated, N-based isomer *SSRR*-$[Cu(H_2L^1)(OClO_3)_2][ClO_4]_2 \cdot 6H_2O$ was determined. In the course of our investigations of the co-ordination chemistry of L^1 and L^2 we have identified a number of N-based isomeric forms of these macrocycles when bound to Cu^{II}. In an earlier paper reporting the synthesis and chromatographic separation of the macrocycles L^1 and L^2 as their tetradentate co-ordinated copper(II) complexes, we found that $[Cu(H_2L^1)]^{4+}$ could be separated into a number of N-based isomeric forms in strongly acidic solution.[8] The complex $[Cu(H_2L^2)]^{4+}$ eluted as only a single band distinct from the N-based isomers of $[Cu(H_2L^1)]^{4+}$. Each C- and N-based isomer exhibited different visible electronic maxima, but none of the separated copper(II) complexes was isolated as a solid. In this work, we report the crystal structure analyses of three N-based isomeric forms of $[CuL^1]^{2+}$, and two N-based isomers of $[CuL^2]^{2+}$. The structural and spectroscopic variations of these C- and N-based isomers will be illustrated. In addition, the stability towards N-based isomerisation is demonstrated.

Experimental

Syntheses

The compounds *trans*- and *cis*-6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane-6,13-diamine hexahydrochloride (L^1·6HCl and L^2·6HCl respectively) were prepared as described.[8]

$[CuL^1]^{2+}$ Complexes. A solution of L^1·6HCl (3.0 g, 6 mmol), $CuCl_2·2H_2O$ (1.2 g, 7 mmol) and KOH (2.0 g) in methanol (50 cm^3) was stirred at room temperature until all of the reagents had dissolved. The mixture was evaporated to dryness then redissolved in water (500 cm^3), gravity filtered and charged onto a 1 m × 2 cm column of SP Sephadex C-25 cation-exchange resin (Na^+ form). The eluent was 0.1 mol dm^{-3} trisodium citrate (3-carboxy-3-hydroxypentane-1,5-dioate) (pH ≈ 8). A green-blue band of free Cu^{2+}(aq) eluted quickly and was discarded. The purple macrocyclic complexes were eluted in the following order.

Band 1 (λ_{max} 529 *nm*). This band eluted well before other complexes, but too little was present to isolate as a solid.

Band 2 (λ_{max} 522 *nm*), RRSS-$[CuL^1]^{2+}$. The eluate was diluted five-fold and charged onto a smaller Sephadex column (15 × 3 cm). Elution with 0.5 mol dm^{-3} $NaOCl_4$ afforded a single maroon band which precipitated as an orange powder of the monohydrate on concentration to *ca.* 30 cm^3. The solid was filtered off, washed with ethanol and diethyl ether then air dried (Found: C, 27.0; H, 5.9; N, 16.0. Calc. for $C_{12}H_{30}Cl_2CuN_6O_8$: C, 26.8; H, 6.0; N, 16.6%). Violet crystals of the diaqua complex suitable for X-ray analysis grew from the filtrate on standing. Electronic spectrum (water): λ_{max} 501 (82.5) and 252 nm (ε 7000 dm^3 mol^{-1} cm^{-1}).

Band 3 (λ_{max} 514 *nm*). Minor, discarded.

Band 4 (λ_{max} 513 *nm*). Minor, discarded.

Band 5 (λ_{max} 526 *nm*). Minor, discarded.

Band 6 (λ_{max} 523 *nm*), SSRR-$[CuL^1]^{2+}$/RSRS-$[CuL^1]^{2+}$. This band was diluted five-fold and charged onto a Sephadex column (15 × 3 cm). Elution with 0.5 mol dm^{-3} $NaClO_4$ afforded a purple band (*RSRS*-$[CuL^1]^{2+}$), which precipitated as crimson flakes of the monoprotonated complex upon concentration to *ca.* 30 cm^3. The solid *RSRS*-$[Cu(HL^1)][ClO_4]_3·H_2O$ was filtered off, washed with ethanol and diethyl ether then air dried (Found: C, 22.3; H, 5.3; N, 12.9. Calc. for $C_{12}H_{33}Cl_3CuN_6O_{13}$: C, 22.5; H, 5.2; N, 13.2%). Crystals of the non-protonated complex *RSRS*-$[CuL^1][ClO_4]_2$ suitable for X-ray work precipitated from the filtrate at pH ≈ 8. Electronic spectrum (water): λ_{max} 510 (90.8) and 254 nm (ε 6800 dm^3 mol^{-1} cm^{-1}).

A purple band precipitated at the top of the column, which redissolved and eluted upon changing the eluent to 0.5 mol dm^{-3} NaCl. The diprotonated complex *SSRR*-$[Cu(H_2L^1)]Cl_4·2H_2O$ precipitated as a purple powder upon concentration of the eluate to *ca.* 30 cm^3. It was filtered off, washed with ethanol and diethyl ether then air dried (Found: C, 28.9; H, 7.6; N, 17.5. Calc. for $C_{12}H_{36}Cl_4CuN_6O_2$: C, 28.7; H, 7.2; N, 16.8%). Recrystallisation of *SSRR*-$[Cu(H_2L^1)]Cl_4·2H_2O$ from weakly acidic $NaClO_4$ solution afforded ruby-red crystals of *SSRR*-$[Cu(H_2L^1)(OClO_3)_2][ClO_4]_2·2H_2O$ suitable for X-ray work. Electronic spectrum (water): λ_{max} 518 (63.4) and 252 nm (ε 6700 dm^3 mol^{-1} cm^{-1}).

$[CuL^2]^{2+}$ Complexes. A solution of L^2·6HCl (3.5 g, 7 mmol) and $Cu(NO_3)_2·2.5H_2O$ (1.7 g, 7 mmol) in water (1 dm^3) was neutralised with dilute NaOH solution. After gravity filtration the purple filtrate was charged onto a 1 m × 2 cm column of SP Sephadex C-25 cation-exchange resin (Na^+ form). The eluent was 0.05 mol dm^{-3} trisodium citrate (pH ≈ 8). A green-blue band of free Cu^{2+}(aq) eluted quickly and was discarded. The purple macrocyclic complexes eluted in the following order.

Band 1 (λ_{max} 531 *nm*). Minor, discarded.

Band 2 (λ_{max} 534 *nm*). Minor, discarded.

Band 3 (λ_{max} 543 *nm*). Minor, discarded.

Band 4 (λ_{max} 555 *nm*). Minor, discarded.

Band 5 (λ_{max} 533 *nm*). This band was broad with a noticeable variation in colour (indigo at front and violet at the rear). The eluate was diluted five-fold and charged onto a Sephadex column (15 × 3 cm). Elution with 0.5 mol dm^{-3} $NaClO_4$ gave two well separated bands. The first band {*RSRS*-$[CuL^2(OClO_3)]ClO_4·H_2O$} precipitated upon concentration of the eluate to *ca.* 30 cm^3. The solid was filtered off, washed with ethanol and diethyl ether then air dried (Found: C, 26.3; H, 5.8; N, 15.3. Calc. for $C_{12}H_{32}Cl_2CuN_6O_9$: C, 26.8; H, 6.0; N, 15.6%). The filtrate afforded purple hexagonal pyramidal prisms suitable for X-ray work. Electronic spectrum (water): λ_{max} 512 (81.1) and 252 nm (ε 5600 dm^3 mol^{-1} cm^{-1}).

The second band was concentrated to *ca.* 30 cm^3 and a purple powder of *RRSS*-$[Cu(H_2L^2)(OClO_3)_2][ClO_4]_2$ precipitated on standing. It was filtered off, washed with ethanol and diethyl ether then air dried (Found: C, 20.1; H, 4.6; N, 11.7. Calc. for $C_{12}H_{32}Cl_4CuN_6O_{16}$: C, 20.0; H, 4.5; N, 11.6%). The filtrate afforded purple crystals suitable for X-ray work. Electronic spectrum (water): λ_{max} 512 (75.1) and 251 nm (ε 6700 dm^3 mol^{-1} cm^{-1}).

The three solids obtained from the $Cu^{II} + L^1$ reaction were obtained in approximately equal proportions as were the two complexes isolated from the $Cu^{II} + L^2$ system. Quantitative yields were not possible due to coprecipitation of the eluent salt, *i.e.* $NaClO_4$ or NaCl, which limited the number of crops of each complex that could be obtained from successive filtrates. Performing either of the above complexation reactions in MeOH or in water had little effect on the isomeric distribution.

Physical methods

Solution UV/VIS spectra were measured on a Perkin-Elmer Lambda 12 spectrophotometer. Cyclic voltammetry was performed with a BAS 100B analyser employing a glassy carbon working electrode, an Ag–AgCl reference electrode and a platinum auxiliary electrode. Direct current polarography was performed with a Metrohm E 506 potentiostat with a E 505 dropping-mercury electrode, a calomel reference electrode and a platinum auxiliary electrode. All solutions for electrochemistry were *ca.* 5×10^{-3} mol dm^{-3} in analyte and 0.1 mol dm^{-3} in NaCl, and were purged with N_2 before measurement. Potentiometric titrations of acidified ($HClO_4$) aqueous solutions (0.1 mol dm^{-3} NEt_4ClO_4) of complex were carried out at 298 K with a Metrohm 665 Dosimat and an Orion model 720A pH meter, using NEt_4OH as the base. Data were analysed with the program TITFIT.[9]

Crystallography

Cell constants were determined by a least-squares fit to the setting parameters of 25 independent reflections measured on an Enraf-Nonius CAD4 four-circle diffractometer employing graphite-monochromated Mo-Kα radiation (0.710 73 Å) and operating in the ω–2θ scan mode. Data reduction and empirical absorption corrections (ψ scans) were performed with the XTAL[10] package, except for the structure of *RRSS*-$[Cu(H_2L^2)(OClO_3)_2][ClO_4]_2$ where absorption corrections were applied with the program DIFABS.[11]

Structure solutions. Structures were solved by heavy-atom methods with SHELXS 86[12] and refined by full-matrix least-squares analysis on F^2 with SHELXL 93.[13] All non-H atoms were refined with anisotropic thermal parameters except minor contributors to perchlorate O-atom disorder. Alkyl H atoms were included at estimated positions and their thermal parameters were restrained to be 1.3 times that of their attached C atom, whereas amine and aqua H atoms were first located from difference maps then restrained in a similar manner to that employed for all alkyl H atoms. Hydrogen atoms of non-co-ordinated water were not modelled. Selected bond lengths and angles are presented in Table 1, and the atomic nomenclature is defined in Figs. 1–4 and 6 drawn with PLATON.[14] The packing diagram (Fig. 5) was produced with the program PLUTON.[15]

Crystal data. *RRSS*-$[CuL^1(OH_2)_2][ClO_4]_2$, $C_{12}H_{34}Cl_2CuN_6O_{10}$, $M = 556.9$, triclinic, space group $P1$, $a = 7.6589(7)$, $b = 9.2616(7)$, $c = 9.594(1)$ Å, $\alpha = 115.168(8)$, $\beta = 113.926(8)$, $\gamma = 81.721(7)°$, $U = 562.67(9)$ Å^3, D_c $(Z = 1) = 1.643$ g cm^{-3}, μ(Mo-Kα) = 12.69 cm^{-1}, $F(000) = 291$, $T = 293$ K. Specimen: purple prism 0.8 × 0.33 × 0.30 mm, $A^*_{min,max}$ 1.004, 1.359; $N = 1965$, $N_o = 1903$ $[|F_o| > 2\sigma(|F_o|)$, $2 < \theta < 25°]$, *hkl* 0–9, −10 to 10, −10 to 10. Final $R1 = 0.036$, $wR2 = 0.097$, $w^{-1} = \sigma(F_o)^2 + (0.0603P)^2 + 0.38P$ where $P = (F_o^2 + 2F_c^2)/3$, number of parameters = 227, goodness of fit = 1.110. Residual extrema ±0.5 e Å^{-3}.

SSRR-$[Cu(H_2L^1)(OClO_3)_2][ClO_4]_2\cdot 2H_2O$, $C_{12}H_{36}Cl_4CuN_6O_{18}$, $M = 757.8$, orthorhombic, space group *Pbca*, $a = 14.954(4)$, $b = 12.128(3)$, $c = 15.816(4)$ Å, $U = 2868(1)$ Å^3, D_c $(Z = 4) = 1.755$ g cm^{-3}, μ(Mo-Kα) = 12.21 cm^{-1}, $F(000) = 1564$, $T = 293$ K. Specimen: red prism 0.23 × 0.23 × 0.23 mm, $A^*_{min,max}$ 1.000, 1.980; $N = 2523$, $N_o = 1607$ $[|F_o| > 2\sigma(|F_o|)$, $2 < \theta < 25°]$, *hkl* 0–10, 0–9, 0–10. Final $R1 = 0.060$, $wR2 = 0.161$, $w^{-1} = \sigma(F_o)^2 + (0.128P)^2$ where $P = (F_o^2 + 2F_c^2)/3$, number of parameters = 193, goodness of fit = 1.042. Residual extrema +0.9 and −1.0 e Å^{-3}.

RSRS-$[CuL^1(OClO_3)]ClO_4$, $C_{12}H_{30}Cl_2CuN_6O_8$, $M = 520.9$, triclinic, space group $P1$, $a = 9.088(2)$, $b = 9.8045(8)$, $c = 12.407(1)$ Å, $\alpha = 78.539(8)$, $\beta = 79.71(1)$, $\gamma = 83.44(1)°$, $U = 1062.5(3)$ Å^3, D_c $(Z = 2) = 1.628$ g cm^{-3}, μ(Mo-Kα) = 13.31 cm^{-1}, $F(000) = 542$, $T = 293$ K. Specimen: purple prism 0.5 × 0.5 × 0.5 mm, $A^*_{min,max}$ 1.013, 1.235; $N = 3730$, $N_o = 2726$ $[|F_o| > 2\sigma(|F_o|)$, $2 < \theta < 25°]$, *hkl* 0–10, −11 to 11, −14 to 14. Final $R1 = 0.042$, $wR2 = 0.112$, $w^{-1} = \sigma(F_o)^2 + (0.0741P)^2 + 0.51P$ where $P = (F_o^2 + 2F_c^2)/3$, number of parameters = 272, goodness of fit = 1.032. Residual extrema ±0.4 e Å^{-3}.

RSRS-$[CuL^2(OClO_3)]ClO_4$, $C_{12}H_{30}Cl_2CuN_6O_8$, $M = 520.9$, hexagonal, space group $P6_1$, $a = 8.8557(4)$, $c = 46.29(1)$ Å, $U = 3143.9(7)$ Å^3, D_c $(Z = 6) = 1.651$ g cm^{-3}, μ(Mo-Kα) = 13.49 cm^{-1}, $F(000) = 1626$, $T = 293$ K. Specimen: purple prism 0.7 × 0.7 × 0.3 mm, $A^*_{min,max}$ 1.000, 1.304; $N = 3700$, $N_o = 3227$ $[|F_o| > 2\sigma(|F_o|)$, $2 < \theta < 25°]$, *hkl* −9 to 9, 0–10, −55 to 55. Final $R1 = 0.038$, $wR2 = 0.094$, $w^{-1} = \sigma(F_o)^2 + (0.0549P)^2 + 1.43P$ where $P = (F_o^2 + 2F_c^2)/3$, number of parameters = 273, goodness of fit = 1.086. Residual extrema ±0.4 e Å^{-3}.

RRSS-$[Cu(H_2L^2)(OClO_3)_2][ClO_4]_2$, $C_{12}H_{32}Cl_4CuN_6O_{16}$, $M = 721.9$, orthorhombic, space group *Pbca*, $a = 11.670(4)$, $b = 14.492(2)$, $c = 15.167(6)$ Å, $U = 2565(1)$ Å^3, D_c $(Z = 4) = 1.869$ g cm^{-3}, μ(Mo-Kα) = 13.55 cm^{-1}, $F(000) = 1484$, $T = 293$ K. Specimen: purple prism 0.27 × 0.20 × 0.20 mm, $A^*_{min,max}$ 0.754, 1.503; $N = 2255$, $N_o = 897$ $[|F_o| > 2\sigma(|F_o|)$, $2 < \theta < 25°]$, *hkl* 0–13, 0–17, 0–18. Final $R1 = 0.088$, $wR2 = 0.223$, $w^{-1} = \sigma(F_o)^2 + (0.1312P)^2 + 10.8P$ where $P = (F_o^2 + 2F_c^2)/3$, number of parameters = 203, goodness of fit = 1.008. Residual extrema +0.5 and −0.4 e Å^{-3}.

Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 186/403.

Results and Discussion

The complexation reactions leading to isomeric mixtures of either $[CuL^1]^{2+}$ or $[CuL^2]^{2+}$ are rapid, with purple acid-stable solutions being produced upon mixing neutralised aqueous or methanolic solutions of the free macrocycle and a copper(II) salt. All complexes exhibit quite striking resistance to acid-catalysed dissociation, and remain co-ordinated in 5 mol dm^{-3} HCl for months without noticeable loss of colour. Moreover, the crystallised N-based isomeric forms do not appear to interconvert.

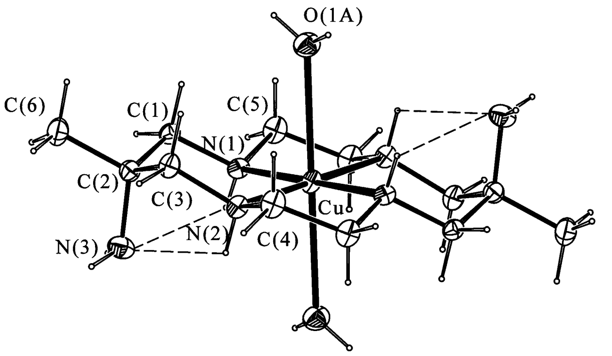


Fig. 1 View of the *RRSS*-$[CuL^1(OH_2)_2]^{2+}$ cation

Structural characterisation

The crystal structure of *RRSS*-$[CuL^1(OH_2)_2][ClO_4]_2$ revealed the complex cation on a centre of symmetry, with perchlorate anions on general sites (Fig. 1). The pairs of unique Cu−N bond lengths are the same within experimental error. The axial Cu−O bonds are considerably longer (*ca.* 25%) than the equatorial Cu−N bond lengths, so the co-ordination geometry may be considered to be tetragonally elongated octahedral. This geometry is the one most commonly observed in tetraazamacrocyclic complexes of Cu^{II}. The tetragonal distortion arises predominantly from the pseudo-Jahn–Teller effect[16] operative on the d^9 metal centre. The co-ordination geometry of *RRSS*-$[CuL^1(OH_2)_2]^{2+}$ is not significantly different from that found in the diperchlorato analogue *RRSS*-$[CuL^1(OClO_3)_2]$.[6] A notable feature of the structure of *RRSS*-$[CuL^1(OH_2)_2]^{2+}$ is the proximity of the pendant amine to the adjacent secondary amine H atoms. Significant hydrogen-bonding interactions [N(3)···H(1)−N(1) 2.54(3) Å, N(3)···H(2)−N(2) 2.47(2) Å] are found in this structure and also in the closely related complex *RRSS*-$[CuL^4(OH_2)_2]^{2+}$.[17]

The crystal structural analysis of *SSRR*-$[Cu(H_2L^1)(OClO_3)_2][ClO_4]_2\cdot 2H_2O$ defined the complex as polymorphic[18] with *SSRR*-$[Cu(H_2L^1)(OClO_3)_2][ClO_4]_2\cdot 6H_2O$.[7] The present structure revealed the complex on a centre of symmetry, with the anions and water molecules on general sites. The expected tetragonally elongated *trans*-CuN_4O_2 co-ordination geometry is apparent (Fig. 2), with perchlorate ligands occupying axial sites. The conformation and configuration of the complex cation is the same as that defined in the structure of *SSRR*-$[Cu(H_2L^1)(OClO_3)_2][ClO_4]_2\cdot 6H_2O$, yet the Cu−N bond lengths in the present structure [1.997(4) and 2.013(4) Å] are somewhat shorter than those previously reported[7] for the polymorph [2.021(5) and 2.027(6) Å]. The origin of these structural differences between essentially identical co-ordination environments is unclear.

In the crystal structure of *RSRS*-$[CuL^1(OClO_3)]ClO_4$ all the ions are on general sites. A remarkable feature of this structure is the pentadentate co-ordination mode of the ligand (Fig. 3), with a significantly longer axial Cu−N bond length [2.333(3) Å] being identified relative to the macrocyclic Cu−N bonds (average 2.00 Å). Pentadentate co-ordination of L^1 to Cu^{II} has not been found before. There is a weak co-ordinate bond with a perchlorate ligand *trans* to the co-ordinated pendant amine [Cu−O(1A) 2.668(3) Å]. Interestingly, this Cu−O bond length is considerably longer than those in *RRSS*-$[CuL^1(OH_2)_2]^{2+}$

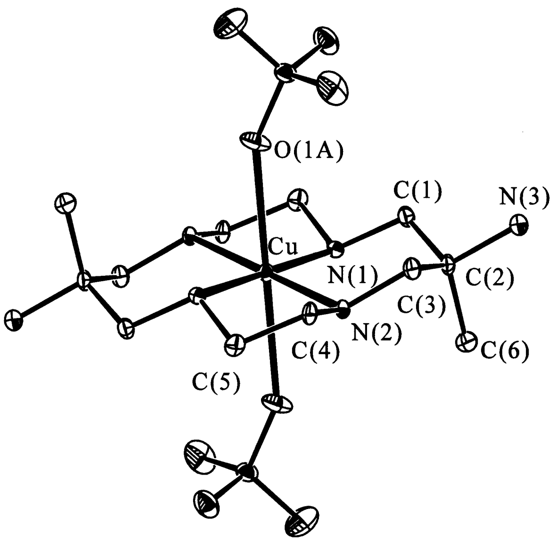


Fig. 2 View of the *SSRR*-[Cu(H$_2$L^1)(OClO$_3$)$_2$]$^{4+}$ cation (H atoms omitted for clarity)

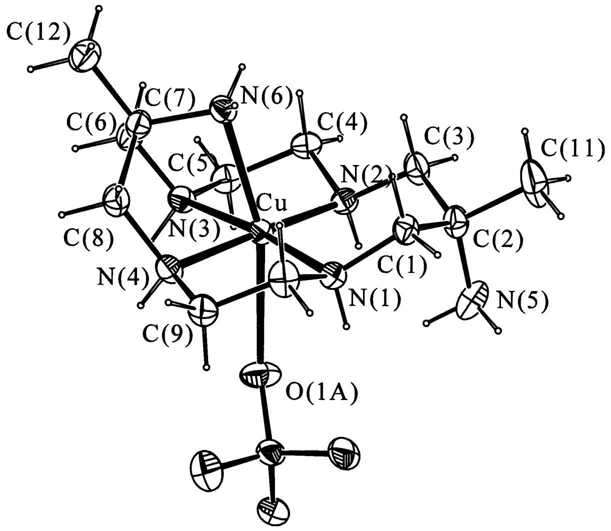


Fig. 3 View of the *RSRS*-[CuL^1(OClO$_3$)]$^+$ cation

[2.569(2) Å] and *SSRR*-[Cu(H$_2$L^1)(OClO$_3$)$_2$]$^{2+}$ [2.543(4) Å] yet the average of the axial Cu−N/Cu−O bond lengths is similar to the Cu−O bond lengths in the other structures. This reflects a balance between the axial bond lengths where a shortening of the Cu−N(6) bond length, resulting from steric demands of the chelating primary amine, causes a lengthening of the *trans* Cu−O bond length. It is notable that all structurally characterised complexes of L^1 in the *RSRS* configuration have pentadentate co-ordination; namely [Ni(HL^1)Cl]$^{2+}$,[5] [VO(L^1)]$^{2+}$,[19] [CoL^1(OH$_2$)]$^{3+}$ and [L^{1}Co(O$_2$)CoL^1]$^{4+}$.[20]

The six-membered chelate ring N−Cu−N angles are significantly different. The N(3)−Cu−N(4) angle (88.7°) is contracted from that found in the structures of the *RRSS* and *SSRR* isomers (≈94°). This reflects the influence of the co-ordinated pendant amine in tightening the five- and six-membered chelate rings comprising the rigid structural unit defined by the donor atoms N(3), N(4) and N(6). Interestingly, the *trans* N(1)−Cu−N(2) angle is widened (97.3°) relative to the expected value, presumably in order to relieve strain in the rigid fused five-membered chelate-ring structure.

The disposition of the non-co-ordinated pendant amine of *RSRS*-[CuL^1(OClO$_3$)]$^+$ is quite unusual. Unlike that found in the structure of *RRSS*-[CuL^1(OH$_2$)$_2$]$^{2+}$, the lone pair of this amine is not directed towards the adjacent secondary amine H atoms, but instead forms an intermolecular hydrogen bond to the secondary amine H atom of a neighbouring complex cation [N(5)···H(2)−N(2) 2.34(1) Å]. The co-ordinated perchlorate also forms an intermolecular hydrogen-bond to a secondary amine H atom [O(1C)···H(3)−N(3) 2.15(1) Å].

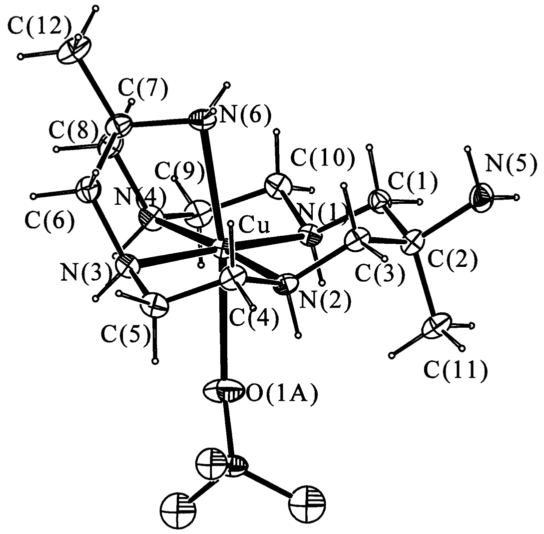


Fig. 4 View of the *RSRS*-[CuL^2(OClO$_3$)]$^+$ cation

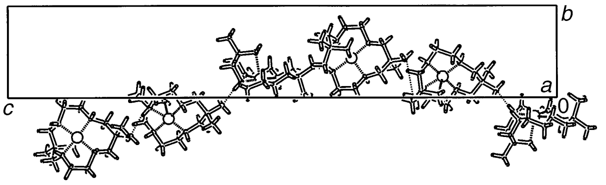


Fig. 5 Unit-cell diagram of *RSRS*-[CuL^2(OClO$_3$)]ClO$_4$

The *RSRS* configuration is unusual for complexes of the secondary amine cyclam family,[21,22] and is far more commonly observed when the macrocyclic amines have been N-alkylated.[23] It is generally believed that the *RSRS* configuration of fourteen-membered tetraaza macrocyclic complexes is favoured on kinetic grounds[24] where the metal enters the macrocycle from the side of the ring *anti* to the secondary amine H atoms (or alkyl groups for the tertiary amine analogues). For secondary amines, rapid inversion at N leads to the *RRSS* isomer in most cases, whereas inversion at N of co-ordinated tertiary amines is prevented, or at least retarded substantially, and the complex becomes trapped in the *RSRS* configuration.

The crystal structure of *RSRS*-[CuL^2(OClO$_3$)]ClO revealed all molecules on general sites. A view of the complex cation is given in Fig. 4, showing the pentadentate co-ordination of the macrocyclic ligand. The non-co-ordinated pendant amine forms an intermolecular hydrogen bond to a neighbouring secondary amine H atom [N(5)···H(3)−N(3) 2.13 Å]. This hydrogen-bonding interaction connects the complexes in a 'head-to-tail' fashion along the six-fold screw axis. It is interesting that the rotational disposition of the free pendant amine lone pair defines the observed chirality of the helical array (and hence the space group is $P6_1$ rather than $P6_5$). The packing diagram (Fig. 5) illustrates this quite unusual arrangement. Apart from the different intermolecular contacts, the co-ordination geometries of *RSRS*-[CuL^1(OClO$_3$)]$^+$ and *RSRS*-[CuL^2(OClO$_3$)]$^+$ are virtually the same.

The crystal structure analysis of *RRSS*-[Cu(H$_2$L^2)(OClO$_3$)$_2$][ClO$_4$]$_2$ found the complex cation disordered about a centre of symmetry (Fig. 6). That is, the positions of one pair of pendant ammonium and methyl groups were reversed by symmetry constraints. Of course this geometry would be consistent with a complex of the centrosymmetric isomeric ligand L^1. However, an isomerically pure sample of L^2·6HCl was used so there can be no doubt that the actual structure is a result of disorder. This was also reflected in the perchlorate anions which

Table 1 Selected bond lengths (Å) and angles (°)

	RRSS-$[CuL^1(OH_2)_2]^{2+}$	*SSRR*-$[Cu(H_2L^1)(OClO_3)_2]^{2+}$	*RSRS*-$[CuL^1(OClO_3)]^+$	*RSRS*-$[CuL^2(OClO_3)]^+$	*RRSS*-$[Cu(H_2L^2)(OClO_3)_2]^{2+}$
Cu–N(1)	2.016(2)	2.013(4)	1.996(3)	2.004(4)	2.00(1)
Cu–N(2)	2.011(2)	1.997(4)	1.984(3)	2.005(4)	2.004(9)
Cu–N(3)			2.012(3)	2.009(4)	
Cu–N(4)			2.024(3)	2.014(4)	
Cu–N(5)			2.333(3)	2.323(4)	
Cu–O(1A)	2.569(2)	2.543(4)	2.668(3)	2.732(4)	2.87(2)
N(1)–Cu–N(2)	93.65(8)	94.6(2)	97.3(1)	97.4(2)	93.9(4)
N(3)–Cu–N(4)			88.7(1)	87.9(2)	
N(1)–Cu–N(1A)	90.74(9)	97.2(2)	89.2(1)	79.2(2)	95.7(5)
N(1)–Cu–N(3)			173.7(1)	173.4(2)	
N(1)–Cu–N(6)			101.6(1)	100.6(1)	
O(1A)–Cu–N(6)			164.0(1)	167.4(2)	

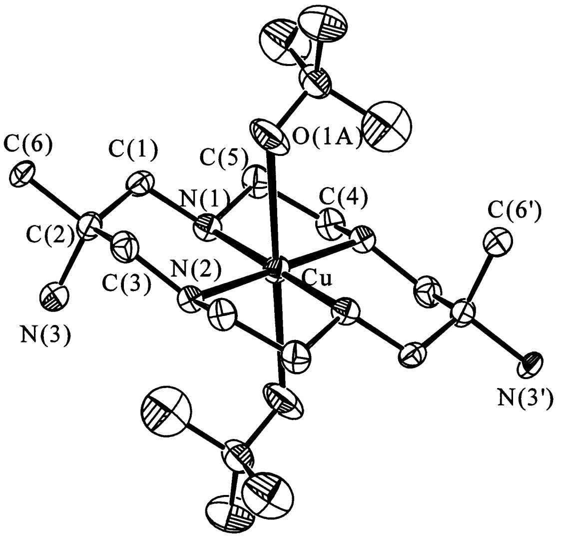


Fig. 6 View of the *RRSS*-$[Cu(H_2L^2)(OClO_3)_2]^{4+}$ cation (H atoms omitted for clarity). The position of the disordered atoms N(3′) and C(6′) have been interchanged (see text)

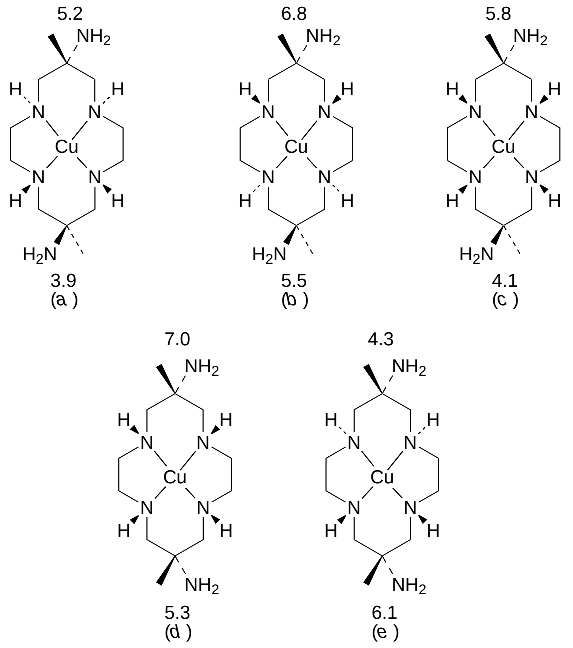
were much more severely disordered than found in the other structures reported in this work. Nevertheless, the co-ordination geometry was not significantly different from that in the other N- and C-based isomers. The axially bound perchlorate ligand lies further away from the metal centre than in the other structures of the L^1 and L^2 complexes. There does not appear to be an obvious reason for this, and it may be an artefact of the methyl/ammonium group disorder. Importantly, hydrogen-bonding interactions between perchlorate anions and amine H atoms are a general feature of all the structures in this work, so disorder in the position of the pendant amines should be correlated with disorder in the perchlorate anions.

Stereochemical considerations

In this work only complexes exhibiting the *RRSS, SSRR* or *RSRS* N-based configurational isomers were isolated. Indeed, the three isomeric, crystallised forms of $[CuL^1]^{2+}$ (*RRSS, SSRR* and *RSRS*) represent the only possible isomers of $[CuL^1]^{2+}$ in the *trans*-III or I forms. There are also three possible N-based isomers of $[CuL^2]^{2+}$ in either the *trans*-III or -I form; those being *RRSS, RSRS* and *SRSR*. However, only two N-based isomers, *RSRS*- and *RRSS*-$[CuL^2]^{2+}$, were isolated from the complexation reaction of L^2 with Cu^{II}. The unobserved *SRSR*-$[CuL^2]^{2+}$ isomer would find both amines *cis* to their adjacent secondary amine H atoms, and hence unable to co-ordinate. It appears that pentadentate co-ordination of both L^1 and L^2 is necessary to stabilise the copper(II) complexes in the uncommon *RSRS/SRSR* N-based configuration.

Table 2 Physical data

	λ_{max}/nm	$E_{\frac{1}{2}}$/V *vs.* SCE	pK_a
RRSS-$[CuL^1]^{2+}$	501	−0.74	5.2, 3.9
SSRR-$[CuL^1]^{2+}$	518	−0.77	6.8, 5.5
RSRS-$[CuL^1]^{2+}$	510	−0.75	5.8, 4.1
RSRS-$[CuL^2]^{2+}$	512	−0.74	7.0, 5.3
RRSS-$[CuL^2]^{2+}$	512	−0.75	6.1, 4.3



Scheme 2 Stepwise pK_a values for (*a*) *RRSS*-$[CuL^1]^{2+}$, (*b*) *SSRR*-$[CuL^1]^{2+}$, (*c*) *RSRS*-$[CuL^1]^{2+}$, (*d*) *RSRS*-$[CuL^2]^{2+}$ and (*e*) *RRSS*-$[CuL^2]^{2+}$

Solution properties

The pendant primary amine pK_a values of the five isolated copper(II) complexes were determined by potentiometric titration, and the data are summarised in Table 2. Remarkable differences across the series were found, which correlate with the disposition of the pendant amine relative to the secondary amine H atoms sharing the same six-membered chelate ring, *i.e.* either *cis* or *trans* (Scheme 2). It is quite apparent that the low pK_a values identified for *RRSS*-$[CuL^1]^{2+}$ (*cis/cis*) relative to *SSRR*-$[CuL^1]^{2+}$ (*trans/trans*) are a consequence of the influence of the secondary amine H atoms. That is, the hydrogen-bonding interactions identified in the crystal structure of *RRSS*-$[CuL^1(OH_2)_2]^{2+}$ are evidently maintained in solution, thus lowering the pK_a values of the pendant amines. In the case of *SSRR*-

$[CuL^1]^{2+}$ no intramolecular hydrogen-bonding interactions are possible, and the corresponding pK_a values are 1.6 units higher than for *RRSS*-$[CuL^1]^{2+}$. The intermediate values found for *RSRS*-$[CuL^1]^{2+}$ (*cis/trans*) are also consistent with this theme. It then follows that the higher pK_a value of *RSRS*-$[CuL^1]^{2+}$ corresponds to the (formerly) co-ordinated pendant amine. The potentiometric data for *RSRS*-$[CuL^2]^{2+}$ (*trans/trans*) do not differ significantly from those found for *SSRR*-$[CuL^1]^{2+}$ (*trans/trans*). Similarly the pK_a values for *RRSS*-$[CuL^2]^{2+}$ (*cis/trans*) are similar to those of *RSRS*-$[CuL^1]^{2+}$ (*cis/trans*). The pK_a values in Table 2 may be compared with the corresponding primary amine protonation constants of free $[H_2L^1]^{2+}$ (5.5, 6.3)[25] and $[H_2L^2]^{2+}$ (5.4, 6.3).[3] Similar electrostatic effects are operative on the dipositively charged free macrocycles and their $[CuL^1]^{2+}$ and $[CuL^2]^{2+}$ analogues, so the pK_a values are also comparable.

The five N- and C-based isomeric complexes each exhibit a two-electron $Cu^{II/0}$ polarographic wave around −0.74 V *vs.* saturated calomel electrode (SCE) (Table 2). Cyclic voltammetry on a glassy carbon working electrode yielded broad, ill defined irreversible waves for all complexes on the verge of the solvent-limited potential ($E \approx -1.1$ V *vs.* Ag–AgCl). There was no evidence of other waves at less negative potentials, and it is unlikely that the observed responses are related to metal-centred reductions. Reductions of pendant amine protons or axially co-ordinated aqua ligands are more likely to be associated with the observed voltammetric peaks. The intensity of these waves evidently masks the anticipated metal-centred responses of the complexes. It is generally found that secondary amine tetraazamacrocyclic complexes of Cu^{II} yield irreversible reduction waves, with dissociation of the reduced complex occurring rapidly on the voltammetric time-scale.

In neutral aqueous solution all five copper(II) complexes reported in this work display a single visible electronic maximum (Table 2) comprising an envelope of the four transitions $(d_{xy},d_{xz},d_{yz},d_{z^2}) \longleftarrow d_{x^2-y^2}$. The *RRSS*-$[CuL^1]^{2+}$ isomer displays the highest-energy electronic maximum (501 nm), whereas the *SSRR*-$[CuL^1]^{2+}$ complex exhibits the lowest-energy transition (518 nm). However, comparison of their crystal structures reveals very similar Cu−N and Cu−O bond lengths and valence angles. The electronic maximum of *RSRS*-$[CuL^1]^{2+}$ (510 nm) lies between those of the *RRSS* and *SSRR* N-based isomers, whereas the neutral aqueous solution electronic spectra of *RSRS*- and *RRSS*-$[CuL^2]^{2+}$ are almost identical (λ_{max} 512 nm). It is difficult to say whether primary amine co-ordination in the solid-state structures of *RSRS*-$[CuL^1(OClO_3)]^+$ and -$[CuL^2(OClO_3)]^+$ persists at pH 6 or higher, or whether substitution by an aqua ligand takes place. It is more likely that they are not co-ordinated, as the maxima exhibited in the five spectra exhibit quite similar absorption coefficients, which implies that the same centrosymmetric *trans*-$Cu^{II}N_4O_2$ chromophore is present in each case. The inherently poorly co-ordinating perchlorate ligands, identified in all but one of the structures in this work, are definitely displaced by water in aqueous solution. The differences between the electronic maxima of the five isomers are diminished when the spectra are measured in 3 mol dm^{-3} HCl solution: *RRSS*-$[Cu(H_2L^1)]^{4+}$ (λ_{max} 520), *SSRR*-$[CuL^1]^{2+}$ (528), *RSRS*-$[CuL^1]^{2+}$ (528), *RSRS*-$[CuL^2]^{2+}$ (528) and *RRSS*-$[CuL^2]^{2+}$ (528 nm). Under these conditions the pendant amines of all complexes are obviously protonated.

The observed variations in electronic maxima are difficult to explain in the absence of any major structural differences between the five isomers, remembering that all complexes would be expected to exist as *trans*-$Cu^{II}N_4O_2$ chromophores in solution. It is pertinent that the observed visible electronic maxima are weighted averages of four transitions of similar energy, and that some of these components may vary almost independently of one another. The energy of the $d_{z^2} \longleftarrow d_{x^2-y^2}$ transition is known to be sensitive to d–s mixing[26] and to variations in axial (z) ligand fields, whereas the $d_{xz} \longleftarrow d_{x^2-y^2}$, $d_{xy} \longleftarrow d_{x^2-y^2}$ and $d_{yz} \longleftarrow d_{x^2-y^2}$ transitions will be almost independent of these two effects. Therefore, it is clear that shifts in the overall observed visible electronic maxima in these systems may have their origins in subtle variations in the energies, or intensities, of one or more of the components of the envelope. Single-crystal polarised electronic spectra may clarify this issue, but further discussion of the observed spectral variations at this time can only be speculative.

Nevertheless, these spectroscopic results are relevant to earlier work[8] concerning the chromatographic separation of the N- and C-based isomeric mixture of $[Cu(H_2L^1)]^{4+}$ and $[Cu(H_2L^2)]^{4+}$ in 3 mol dm^{-3} HCl solution. Briefly, four bands were observed in the order: (*i*) $[Cu(H_2L^1)]^{4+}$, λ_{max} 528; (*ii*) $[Cu(H_2L^1)]^{4+}$, 538; (*iii*) $[Cu(H_2L^2)]^{4+}$, 528; (*iv*) $[Cu(H_2L^1)]^{4+}$, 518 nm. It now emerges that band (*i*) was a mixture of *RSRS*- and *SSRR*-$[Cu(H_2L^1)]^{4+}$, (*iii*) was a mixture of *RSRS*- and *RRSS*-$[Cu(H_2L^2)]^{4+}$ and (*iv*) was *RRSS*-$[Cu(H_2L^1)]^{4+}$. This leaves the identity of band (*ii*) uncertain. Its unusually low-energy maximum points to the formation of an isomer other than that isolated in this work, *i.e.* *RSSS*, *RSSR* or *SSSS* (Scheme 1). We have recently isolated,[27] for the first time, a fourteen-membered tetraazamacrocyclic complex of Cu^{II} in the rare *RSSS* configuration of N-donors, but the electronic maximum of this complex (556 nm) is not consistent with that of the unidentified band (*ii*). This leaves the *SSSS* and *RSSR* isomers as being the remaining possibilities, but we have no further information which favours one isomer over the other.

Finally, we note that all of the complexes reported in this work were extremely resistant to acid-catalysed demetallation, and no change to their electronic spectra is observed in either neutral or acidic solution over periods of months. This behaviour is quite remarkable by comparison with that of the unsubstituted $[Cu(cyclam)]^{2+}$ complex[28] and its C-methylated analogues,[29] which dissociate over periods of only days under similar conditions. The presence of the pendant primary ammonium groups is clearly implicated in the stability of the copper(II) complexes in acidic solution. In similar systems it has been found that protonation of a single co-ordinated[30,31] or non-co-ordinated amine[32] renders the resulting complex more resistant to further protonation than is the precursor. Therefore, the presence of two sites of protonation in the complexes $[Cu(H_2L^1)]^{4+}$ and $[Cu(H_2L^2)]^{4+}$ is consistent with their resistance to acid-catalysed hydrolysis.

Conclusion

We have identified and separated a quite complex mixture of C- and N-based diastereomers of the copper(II) complexes of L^1 and L^2. Spectroscopic variations across the series reported in this work highlight a number of unusual features that are not readily explained by reference to changes in structure in the first co-ordination sphere. The non-co-ordinated pendant primary amines clearly play a number of important roles in the formation of inter- and intra-molecular hydrogen-bonds and also their presence serves to render their complexes resistant towards acid-catalysed dissociation.

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