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Stereoselective assembly of a new pendant-arm macrocycle

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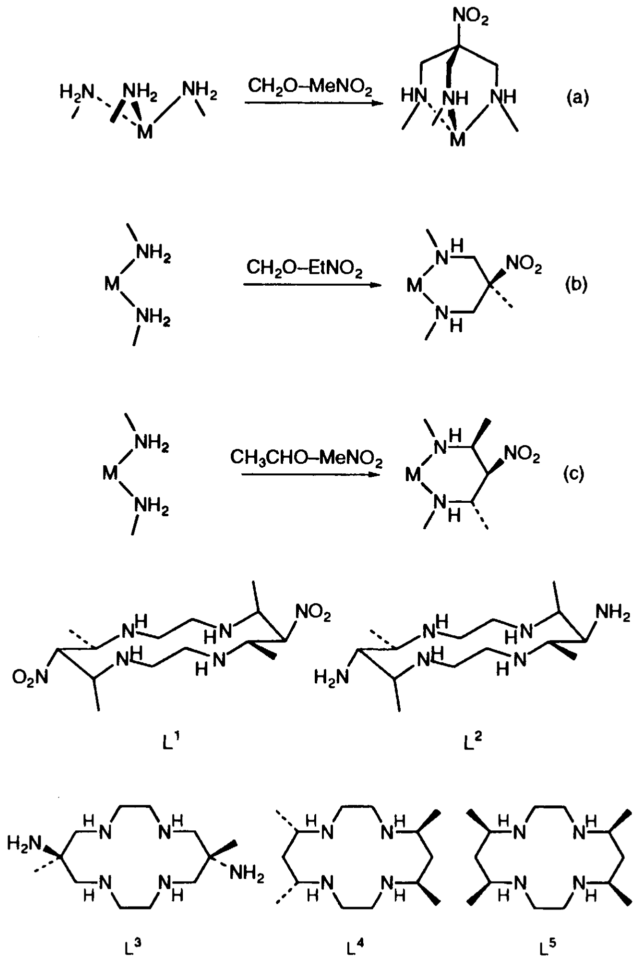
The new pendant-arm macrocycle (5*S*,7*S*,12*R*,14*R*)-tetramethyl-6,13-dinitro-1,4,8,11-tetraazacyclotetradecane (L^1) has been synthesised as its copper(II) complex and its crystal structure revealed a rare example of genuine square-planar co-ordination; reduction of $[CuL^1]^{2+}$ affords the metal-free diamino-substituted analogue.

Metal-directed condensations of co-ordinated primary amines with formaldehyde and nitroalkanes have become established as one of the most versatile and inexpensive routes toward C-functionalised macrocyclic amines.[1] The pendant amines which arise from reduction of the nitro-substituted analogues play an active role in the co-ordination chemistry of these ligands. In addition, the primary amine may be used as a reactive functional group at which further chemistry may be performed, without interfering with the co-ordinating ability of the macrocyclic N-donors.

In template reactions of types (a) and (b), the number of 'acidic' hydrogen atoms that may be substituted by the intermediate methylene imine residues is dictated by the degree of alkylation of the α-carbon atom, *i.e.* nitromethane (three) or nitroethane (two), leading to 'capped' or 'linked' nitro-substituted products, respectively. Linking only two co-ordinated imine residues with a tribasic acid, such as nitromethane [reaction (c)], offers the opportunity of a potentially nucleophilic centre attached to the macrocyclic ring at which further chemistry may be performed. However, reactions of formaldehyde and nitromethane with $[M(en)_2]^{2+}$ (M = Cu or Ni, en = ethane-1,2-diamine) have been unsuccessful, with side reactions leading to decomposition of the complex.

We report herein the synthesis of a new class of pendant-arm macrocycle, as its copper(II) complex $[CuL^1]^{2+}$, by the metal-directed condensation of $[Cu(en)_2]^{2+}$, nitromethane and acetaldehyde. To a methanolic solution of $[Cu(en)_2][NO_3]_2$ at 0 °C was added 4 equivalents of acetaldehyde. The reaction mixture was refluxed for 10 min then cooled again in an ice-bath. Two equivalents each of nitromethane and triethylamine were added, and the solution was stirred at 25 °C for 2 h to afford a purple precipitate of the macrocyclic product $[CuL^1][NO_3]_2$. Purification was achieved by cation-exchange column chromatography and the product was isolated as the perchlorate salt in 23% yield. Crystals suitable for X-ray diffraction analysis were grown by slow evaporation of a neutral aqueous sodium perchlorate solution of the complex.

The crystal structural analysis of $[CuL^1][ClO_4]_2$† found the cation at a centre of symmetry (Fig. 1). The copper atom lies in the plane of the four secondary amine nitrogen atoms and no contacts less than 2.75 Å are made between the anion oxygen atoms and the metal centre. Indeed, the anions are displaced laterally from the vacant co-ordination sites above and below the CuN_4 plane. Thus, the co-ordination geometry may be described as genuinely square plane with no significant differences between the two independent Cu–N bond lengths. The absolute configuration of the four methyl-substituted carbon atoms is *S*[C(3)]*S*[C(5)]*R*[C(3′)]*R*[C(5′)], which results in an alternating axial and equatorial disposition of the methyl groups relative to their respective six-membered chelate rings as one circles the macrocycle. The pendant *trans* nitro groups are *syn* to the adjacent secondary amine hydrogen atoms; a configuration that has been designated as α for structurally similar macrocyclic complexes.[4] Co-ordination by anions or water molecules in sites perpendicular to the CuN_4 plane is generally observed in complexes of this type; the more common geometries being tetragonally elongated octahedral



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† Crystal data. $C_{14}H_{30}Cl_2CuN_6O_{12}$, *M* 608.9, monoclinic, space group $P2_1/c$, $a = 9.270(4)$, $b = 10.342(2)$, $c = 12.845(5)$ Å, $\beta = 101.47(2)°$, $Z = 2$, $D_c = 1.676$ g cm^{-3}, μ(Mo-Kα) = 11.97 cm^{-1}, *F*(000) = 630, *T* = 296 K, final $R_1 = 0.0552$, $wR_2 = 0.1190$ for 1217 independent observed reflections [$|F_o| > 2\sigma(|F_o|)$, $2\theta < 50°$], $w^{-1} = \sigma(F_o)^2 + (0.0567P)^2 + 1.0323P$ where $P = (F_o^2 + 2F_c^2)/3$. Data were collected on an Enraf-Nonius CAD4 diffractometer using graphite-monochromated Mo-Kα radiation and employing the ω–2θ scan mode. The structure was solved by direct methods with SHELXS 86[2] and refined by full-matrix least squares with SHELXL 93.[3] All non-hydrogen atoms were refined with anisotropic thermal parameters, whereas the hydrogen atoms were constrained at estimated positions. Complete 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.*, 1996, Issue 1.

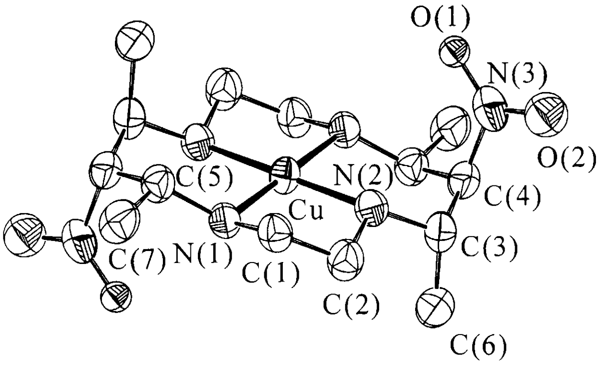

Fig. 1 View of the [CuL^1]$^{2+}$ cation (hydrogen atoms omitted for clarity). Selected bond lengths (Å): Cu–N(1) 2.014(5), Cu–N(2) 2.004(5), C–C 1.51–1.54 and C–N 1.48–1.49

[4 + 2] or square pyramidal [4 + 1]. However, in the present case, the axially oriented methyl groups [C(6) and C(6′)] block access by the perchlorate anions to these sites to provide a rare example of square-planar co-ordination in a tetraazamacrocyclic copper(II) complex.

The aqueous-solution visible spectrum of [CuL^1][ClO$_4$]$_2$ (λ_{max} 519 nm, ε 59.6 dm^3 mol^{-1} cm^{-1}) is similar to that measured in the poorly co-ordinating solvent nitromethane (λ_{max} 513 nm, ε 156 dm^3 mol^{-1} cm^{-1}). The geometry of the closely related six-co-ordinate complex α-[CuL^3(OH$_2$)$_2$][ClO$_4$]$_2$ has been identified by a crystal-structure analysis,[5] and there is no reason to suspect that its co-ordination number changes upon dissolution in water. However, the visible spectrum of the α-[CuL^3(OH$_2$)$_2$]$^{2+}$ cation in water (λ_{max} 500 nm, ε 82.9 dm^3 mol^{-1} cm^{-1}) is significantly different from that measured in nitromethane (λ_{max} 478 nm, ε 106 dm^3 mol^{-1} cm^{-1}). The marked blue shift in the visible maximum upon dissociation of α-[CuL^3(OH$_2$)$_2$][ClO$_4$]$_2$ in nitromethane suggests that the two aqua ligands dissociate and that a square-planar geometry of α-[CuL^3]$^{2+}$ is favoured in non-co-ordinating solvents. The insensitivity of the visible maximum of [CuL^1]$^{2+}$ to the co-ordinating ability of the solvent is supportive of there being no change in co-ordination number of the cation going from the solid state to aqueous solution to non-aqueous solution.

Reduction of [CuL^1]$^{2+}$ with zinc and HCl afforded the hexaamine L^2, which has been isolated as its hexahydrochloride salt. The proton-decoupled distortionless enhancements by polarisation transfer (DEPT) ^{13}C NMR spectrum of the ligand (Fig. 2) reveals the expected seven resonances for the C_i symmetric ligand, with the most prominent feature being the two chemically distinct methyl groups (axial and equatorial) at high field. Significantly, it appears that the original template synthesis is highly stereoselective. A number of possibilities could have arisen from this reaction, when the various combinations of chirotopic (*R* or *S*), methyl-substituted carbon atoms are considered. Indeed, other combinations have been identified crystallographically in structurally similar macrocycles, namely the *SRRS* and *SRSR* isomers, L^4 and L^5.[6,7] However, the present structure appears to be unique for macrocycles of this type in that the *SSRR* isomer has been formed exclusively.

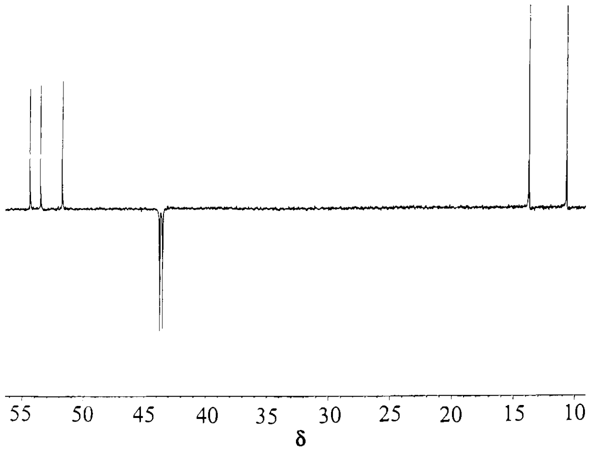

Fig. 2 DEPT ^{13}C NMR spectrum of L^2 in D$_2$O (pD ≈ 2)

An additional feature of the synthesis of [CuL^1]$^{2+}$ is that the hydrogen atom *gem* to the nitro group remains, and further chemistry at the potentially nucleophilic carbon atom may be envisioned. Reaction with formaldehyde, to form a hydroxymethyl group *gem* to the nitro group, is a particularly desirable goal. Conversion of the pendant nitro group to a ketone (Nef reaction) is also now possible. Similarly, the hexaamine L^2 offers a number of new possibilities for the elaboration of its inherently more reactive primary amines (attached to secondary carbon atoms) relative to L^3, and further investigations with this ligand system are currently underway.

Acknowledgements

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