N-Methylation of diamino-substituted macrocyclic complexes: intermolecular reactions

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Two N-based isomeric copper(II) complexes of the macrocycle *trans*-6,13-dimethyl-6,13-bis(dimethylamino)-1,4,8,11-tetraazacyclotetradecane (L^3) have been synthesized and characterised spectroscopically and structurally: α-[$CuL^3(OH_2)_2$]Cl_2, monoclinic, space group $C2/m$, $a = 12.908(4)$, $b = 12.433(2)$, $c = 7.330(2)$ Å, β = 105.87(2)°, $Z = 2$; β-[$CuL^3(OClO_3)_2$]·$2H_2O$, monoclinic, space group $P2_1/c$, $a = 9.708(3)$, $b = 9.686(3)$, $c = 14.202(4)$ Å, β = 106.17(1)°, $Z = 2$. The two isomers exhibit very similar co-ordination spheres but significantly different visible electronic maxima. This difference is attributed to an intramolecular N···H contact between the pendant dimethylamino group and an adjacent secondary amine H atom.

In previous investigations of the co-ordination chemistry of the potentially hexadentate macrocycle L^1 the conditions have been explored under which the pendant primary amines co-ordinate in addition to the macrocyclic secondary amines.[1,2] It has become clear that these pendant donor groups will generally co-ordinate in octahedral[3,4] metal complexes in sites above and below the macrocyclic plane, but remain unco-ordinated in complexes of metal ions preferring square-planar or tetragonally elongated geometries.[5] Recently, derivatives of this macrocycle have been developed by performing reactions on the pendant amines. For example, N-nitrosation of the copper(II) complex of L^1 results in either substitution of the primary amine with a hydroxyl group, or elimination leading to an alkene.[6] In this report, and the following paper, the reactions of [CuL^1]$^{2+}$ with formaldehyde are explored under conditions which lead to either N-methylated or methylene-bridged complexes, depending on whether inter- or intra-molecular condensation occurs. The present results illustrate an unexpected isomer-dependent structural organisation that is achieved through N-methylation reactions of these pendant amines. This also has consequences for the solution visible spectroscopy of these complexes.

Experimental

Syntheses

trans-6,13-Dimethyl-1,4,8,11-tetraazacyclotetradecane-6,13-diamine hexahydrochloride (L^1·6HCl) was prepared as previously described.[7]

A solution of $CuCl_2$·$2H_2O$ (2.4 g, 14 mmol), L^1·6HCl (6.0 g, 13 mmol) and KOH (4.4 g, 79 mmol) in methanol (100 cm^3) was stirred until all reagents had dissolved to afford a deep purple solution. This was evaporated to dryness then taken up in formic acid (100 cm^3) and aqueous formaldehyde (40 cm^3, 32%). The mixture was refluxed for 2 d then evaporated to dryness. The residue was dissolved in water (1 dm^3) then filtered to remove any paraformaldehyde or Cu(OH)$_2$ that had formed. The purple filtrate was charged onto a 10 × 3 cm column of Sephadex C-25 cation-exchange resin (Na$^+$ form). The eluent was 0.05 mol dm^{-3} trisodium citrate which resulted in a number of bands in the following order: 1, blue-green, Cu^{2+}(aq) which was discarded; 2, indigo, λ_{max} 561 nm, minor, discarded; 3, purple, λ_{max} 548 nm, minor, discarded; 4, indigo, λ_{max} 553 nm, minor, [CuL^2]$^{2+}$; a higher-yielding synthesis is given in the following paper; 5 and 6, see below.

Band 5. Maroon, λ_{max} 514 nm, α-[CuL^3]$^{2+}$. This solution was diluted ten-fold and charged on a Sephadex C-25 column

L^1 L^2

L^3
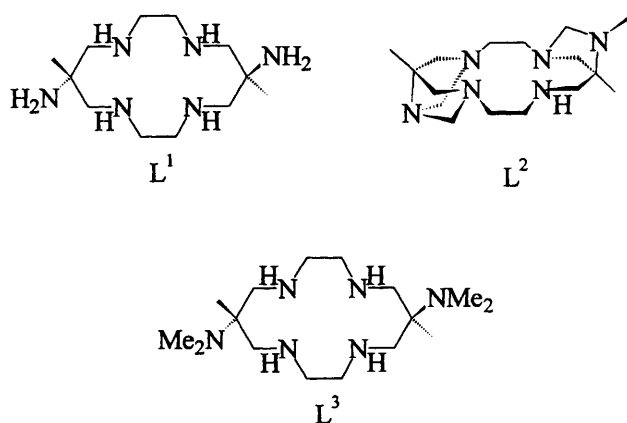
(10 × 2 cm). A single purple band was eluted with 0.5 mol dm^{-3} NaCl solution, which was concentrated to *ca.* 20 cm^3 to afford a purple precipitate on standing. This was filtered off, washed with EtOH and Et$_2$O and air dried (1.3 g). On standing, the filtrate afforded purple crystals suitable for X-ray analysis (Found: C, 38.2; H, 8.7; N, 16.7. Calc. for $C_{16}H_{38}Cl_2$-CuN_6·$3H_2O$: C, 38.2; H, 8.8; N, 16.7%). Electronic spectrum (water): λ_{max} 497 (ε 91.4) and 253 nm (4600 dm^3 mol^{-1} cm^{-1}). Note: the perchlorate salt of this compound is insoluble in water, so NaClO$_4$ solution cannot be used as an eluent.

Band 6. Purple, λ_{max} 522 nm, β-[CuL^3]$^{2+}$. This solution was diluted ten-fold and charged on a Sephadex C-25 column (10 × 2 cm). A single purple band was eluted with 0.5 mol dm^{-3} NaClO$_4$ solution and concentrated to *ca.* 20 cm^3 to afford a pink precipitate on standing. This was filtered off, washed with EtOH and Et$_2$O and air dried (0.25 g). The filtrate yielded purple crystals suitable for X-ray analysis (Found: C, 33.5; H, 6.9; N, 13.9. Calc. for $C_{16}H_{38}Cl_2N_6O_8$: C, 33.3; H, 6.6; N, 14.6%). Electronic spectrum (water): λ_{max} 508 (ε 77.8) and 253 nm (4220 dm^3 mol^{-1} cm^{-1}).

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, a E 505 dropping-mercury electrode, an Ag–AgCl reference electrode

and a platinum auxiliary electrode. All solutions for electro-chemistry 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. Infrared spectra of compounds dispersed as KBr discs were measured on a Perkin-Elmer 1600 FT instrument.

Molecular mechanics calculations

Trial structures were built with the program HYPERCHEM and minimised with MOMECPC[8] using a published force field.[9] Aqua ligands were modelled in all sites perpendicular to the CuN$_4$ plane so as to reproduce most accurately the solution structures of these species. Drawings of all strain-energy-minimised structures were produced with the program CHEMPLUS. The strain-minimised energies of each conformer are shown in Figs. 3 and 4.

Angular overlap model calculations

Calculations were performed on the two crystallographically determined geometries of α-[CuL^3(OH$_2$)$_2$]$^{2+}$ and β-[CuL^3-(OClO$_3$)$_2$] with the program CAMMAG.[10] The ligand-field parameters e_σ(Cu–N), e_σ(Cu–O), e_{d-s}(Cu–N) and e_{d-s}(Cu–O) were 6800, 100, 1700 and 25 cm^{-1} respectively, the spin–orbit coupling constant ζ was set to 800 cm^{-1} and no π-bonding parameters were employed.

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-θ scan mode. Data reduction was performed with the XTAL[11] package. Absorption corrections were applied with the program DIFABS.[12]

Structure solutions. Both structures were solved by heavy-atom methods with SHELXS 86[13] and refined by full-matrix least-squares analysis with SHELXL 93.[14] All non-H atoms were refined with anisotropic thermal parameters except minor contributors to perchlorate O-atom disorder in the structure of β-[CuL^3(OClO$_3$)$_2$]·2H$_2$O. All H atoms were included at estimated positions and their thermal parameters restrained to be 1.3 times that of their attached C, N or O atom, except water H atoms in the structure of β-[CuL^3(OClO$_3$)$_2$]·2H$_2$O, which were located and refined. The atomic nomenclature is defined in Figs. 1 and 2 drawn with PLATON.[15]

Crystal data. α-[CuL^3(OH$_2$)$_2$]Cl$_2$: C$_{16}$H$_{42}$Cl$_2$CuN$_6$O$_2$, $M = 485.0$, monoclinic, space group *C2/m*, $a = 12.908(4)$, $b = 12.443(2)$, $c = 7.330(2)$ Å, $\beta = 105.87(2)°$, $U = 1132.4(5)$ Å^3, $D_c(Z = 2) = 1.422$ g cm^{-3}, μ(Mo-Kα) = 12.24 cm^{-1}, $F(000) = 554$, $T = 293$ K. Specimen: purple prism $0.30 \times 0.20 \times 0.20$ mm, $A^*_{min,max}$ 0.87, 1.13; $N = 1052$, $N_o = 856$ [|F_o| > 2σ(|F_o|), 2 < θ < 25°], *hkl* −14 to 14, 0–14, 0–8. Final $R_1 = 0.053$, $wR_2 = 0.144$, $w^{-1} = \sigma(F_o)^2 + (0.1194P)^2 + 0.22P$ where $P = (F_o^2 + 2F_c^2)/3$, number of parameters = 60, goodness of fit = 1.055. Residual extrema +0.6, −0.9 e Å^{-3}.

β-[CuL^3(OClO$_3$)$_2$]·2H$_2$O. C$_{16}$H$_{42}$Cl$_2$CuN$_6$O$_{10}$, $M = 613.0$, monoclinic, space group *P2$_1$/c*, $a = 9.708(3)$, $b = 9.868(3)$, $c = 14.202(4)$ Å, $\beta = 106.17(1)°$, $U = 1306.7(7)$ Å^3, $D_c(Z = 2) = 1.558$ g cm^{-3}, μ(Mo-Kα) = 11.00 cm^{-1}, $F(000) = 646$, $T = 293$ K. Specimen: purple prism $0.30 \times 0.17 \times 0.17$ mm, $A^*_{min,max}$ 0.84, 1.16; $N = 2301$, $N_o = 1703$ [|F_o| > 2σ(|F_o|), 2 < θ < 25°], *hkl* −11 to 11, 0–11, 0–16. Final $R_1 = 0.050$, $wR_2 = 0.142$, $w^{-1} = \sigma(F_o)^2 + (0.1487P)^2$ where $P = (F_o^2 + 2F_c^2)/3$, number of parameters = 181, goodness of fit = 0.902. Residual extrema +0.5, −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 Instruction for Authors,
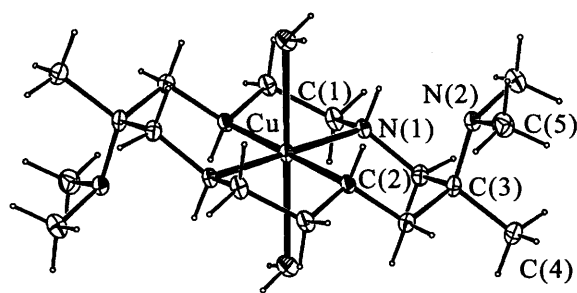

Fig. 1 View of the α-[CuL^3(OH$_2$)$_2$]$^{2+}$ ion showing 20% probability ellipsoids

J. Chem. Soc., Dalton Trans., 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 186/259.

Results

The standard Eschweiler–Clarke methylation procedure[16,17] (HCO$_2$H–CH$_2$O) applied to [CuL^1]$^{2+}$ afforded the isomeric bis(dimethylamino)-substituted analogues α- and β-[CuL^3]$^{2+}$ in good yield. The ratio of these two N-based isomers was dictated by that of the analogous α and β isomers† of the starting material [CuL^1]$^{2+}$, *i.e.* the kinetically determined ratio that is established upon mixing free L^1 with Cu^{2+}(aq). It has become apparent that the rate of N-based isomerisation between α- and β-[CuL^1]$^{2+}$ is negligible in neutral aqueous solution,[7] and that these isomers can be separated chromatographically and crystallised without re-equilibration. A similar inertness is observed in the N-methylated analogues α- and β-[CuL^3]$^{2+}$, with there being no noticeable isomerisation in solution over a period of several weeks. At present there is no experimental evidence to indicate which is the more stable isomer, but molecular mechanics calculations predict the α-isomer to be more stable (see below). One curious observation was that the perchlorate salt of α-[CuL^3]$^{2+}$ was totally insoluble in water, which necessitated isolation of the complex as its chloride salt. By contrast, β-[CuL^3(OClO$_3$)$_2$] was quite water soluble, even in the presence of an excess of perchlorate.

The infrared spectra of α-[CuL^3(OH$_2$)$_2$]Cl$_2$ and β-[CuL^3(OClO$_3$)$_2$]·2H$_2$O exhibited a number of peaks not seen in the spectra of their precursor complexes. Most notable was the appearance of prominent peaks at 2833 and 2788 cm^{-1} which may be assigned to C–H stretching vibrations of the N-methyl groups. Both isomers exhibit intense N–H vibrations at 3249 and 3247 cm^{-1} for the respective α and β isomers.

Crystal structural analyses of the complexes α-[CuL^3(OH$_2$)$_2$]Cl$_2$ and β-[CuL^3(OClO$_3$)$_2$]·2H$_2$O were performed. The α-[CuL^3(OH$_2$)$_2$]$^{2+}$ cation was found on a 2/m site (C_{2h} symmetry) and the unique chloride ion was located on a two-field axis. A view of the cation is shown in Fig. 1, where the coordination geometry is apparent. The four equivalent Cu–N bond lengths (Table 1) are significantly shorter than the unique axial Cu–O bond length, which is expected for pseudo-Jahn–Teller-distorted *trans*-CuN$_4$O$_2$ complexes,[18] but the Cu–N bond lengths are not unusual by comparison with other fourteen-membered tetraaza macrocyclic copper(II) complexes.[19,20] A notable feature of the structure is that the unique axial pendant dimethylamino group is disposed such that the amine lone pair is directed toward the adjacent secondary amine H atoms [N(2)···H(1N) 2.57 Å].

The crystal structure of β-[CuL^3(OClO$_3$)$_2$]·2H$_2$O revealed the complex on a centre of symmetry. In this case, the anions co-ordinate in axial sites relative to the macrocyclic plane (Fig. 2).

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† The α and β nomenclature refers to isomers where the pendant dimethylamino group is *cis* and *trans*, respectively, to the secondary amine H atoms which share the same six-membered chelate ring.

Table 1 Bond lengths (Å) and angles (°) for α-[CuL³(OH₂)₂]Cl₂

|			
Cu–N(1)	2.018(3)	N(2)–C(3)	1.476(8)
Cu–O(1)	2.451(4)	C(1)–C(1')	1.512(8)
N(1)–C(1)	1.476(5)	C(2)–C(3)	1.529(5)
N(1)–C(2)	1.480(5)	C(3)–C(2″)	1.529(5)
N(2)–C(5)	1.460(5)	C(3)–C(4)	1.546(8)
N(1)–Cu–N(1″)	93.2(2)	N(1)–C(1)–C(1″)	109.1(3)
N(1)–Cu–O(1)	89.7(1)	N(1)–C(2)–C(3)	114.2(3)
C(1)–N(1)–C(2)	111.4(3)	N(2)–C(3)–C(2)	109.8(3)
C(1)–N(1)–Cu	106.5(2)	C(2″)–C(3)–C(2)	110.7(4)
C(2)–N(1)–Cu	116.2(3)	N(2)–C(3)–C(4)	114.0(4)
C(5″)–N(2)–C(5)	107.9(5)	C(2)–C(3)–C(4)	106.2(3)
C(5)–N(2)–C(3)	114.7(3)		

Primes denote symmetry equivalents: '−x, y, −z and ″x, −y, z.

Table 2 Bond lengths (Å) and angles (°) for β-[CuL³(OClO₃)₂]·2H₂O

Cu–N(2)	2.012(3)	C(2)–C(3)	1.528(6)
Cu–N(1)	2.015(3)	C(3)–C(6)	1.536(5)
Cu–O(11)	2.506(3)	C(3)–C(4)	1.534(5)
N(1)–C(1)	1.473(5)	Cl(1)–O(14A)	1.25(3)
N(1)–C(2)	1.488(5)	Cl(1)–O(12A)	1.26(4)
N(2)–C(4)	1.479(4)	Cl(1)–O(13)	1.391(5)
N(2)–C(5)	1.485(5)	Cl(1)–O(11)	1.423(3)
N(3)–C(8)	1.447(6)	Cl(1)–O(12)	1.430(5)
N(3)–C(7)	1.475(6)	Cl(1)–O(14)	1.431(7)
N(3)–C(3)	1.501(5)	Cl(1)–O(13A)	1.54(4)
C(1)–C(5')	1.504(5)		
N(2)–Cu–N(1)	94.1(1)	N(3)–C(3)–C(6)	108.3(3)
N(2)–Cu–O(11)	91.9(1)	C(2)–C(3)–C(6)	109.2(3)
N(1)–Cu–O(11)	87.0(1)	N(3)–C(3)–C(4)	110.0(3)
C(1)–N(1)–C(2)	111.6(3)	C(2)–C(3)–C(4)	112.9(3)
C(1)–N(1)–Cu	106.8(2)	C(6)–C(3)–C(4)	110.7(3)
C(2)–N(1)–Cu	116.8(2)	N(2)–C(4)–C(3)	114.5(3)
C(4)–N(2)–C(5)	110.6(3)	N(2)–C(5)–C(1')	107.6(3)
C(4)–N(2)–Cu	117.0(2)	O(13)–Cl(1)–O(11)	111.6(3)
C(5)–N(2)–Cu	106.4(2)	O(13)–Cl(1)–O(12)	110.4(4)
C(8)–N(3)–C(7)	108.6(4)	O(11)–Cl(1)–O(12)	107.9(3)
C(8)–N(3)–C(3)	115.4(4)	O(13)–Cl(1)–O(14)	109.6(5)
C(7)–N(3)–C(3)	113.8(3)	O(11)–Cl(1)–O(14)	107.3(3)
N(1)–C(1)–C(5')	107.9(3)	O(12)–Cl(1)–O(14)	110.0(4)
N(1)–C(2)–C(3)	114.5(3)	Cl(1)–O(11)–Cu	139.7(2)
N(3)–C(3)–C(2)	105.5(3)		

Primes denote the symmetry equivalent −x, −y, −z.
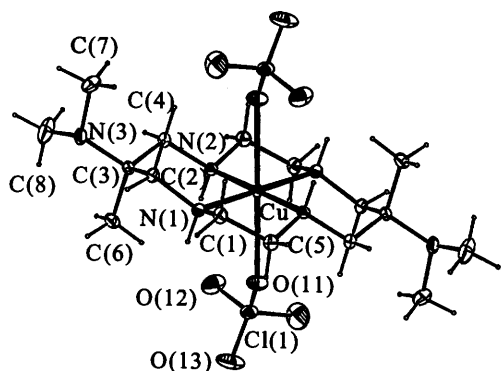
Fig. 2 View of the β-[CuL³(OClO₃)₂] molecule showing 20% probability ellipsoids

The Cu–N bond lengths (Table 2) are not significantly different from those found in the α isomer, and the axial Cu–O bonds to the perchlorate ligands are slightly longer than those to the aqua ligands in α-[CuL³(OH₂)₂]Cl₂, which may be attributable to steric repulsion with the somewhat more bulky perchlorate anion. The N–Cu–N bond angles within the six-membered chelate rings are slightly larger ($\approx 1°$) than those found in the α isomer, and, consequently, the corresponding bite angles
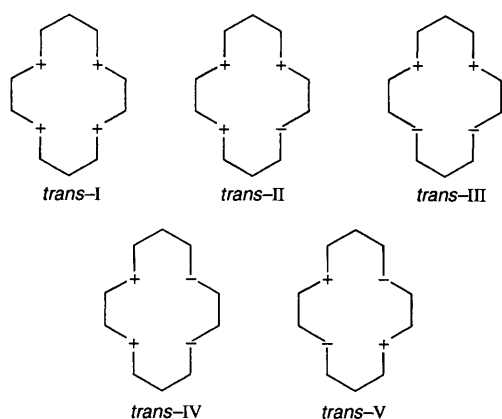

(a) 55.3 kJ mol⁻¹

(b) 102.3 kJ mol⁻¹

(c) 81.9 kJ mol⁻¹
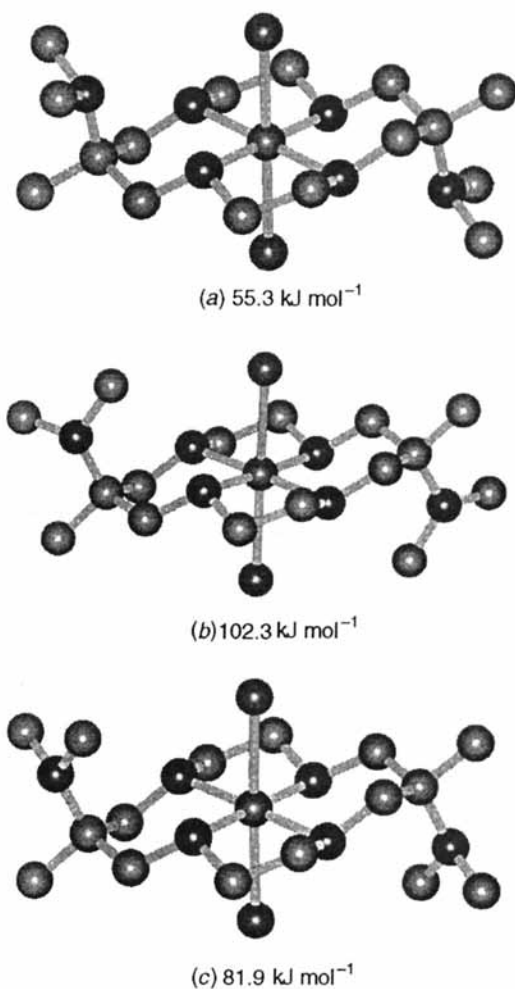
Fig. 3 Strain-minimised geometries and energies of α-[CuL³(OH₂)₂]²⁺ based on the orientation of the dimethylamino groups (H atoms omitted for clarity)

defined by the five-membered rings are contracted by the same amount. The remaining intraligand bond lengths and angles are virtually identical to those of the α isomer. One notable difference between the two structures is the 'twisted' disposition of the now equatorial dimethylamino group.

The various rotational isomers of α- and β-[CuL³(OH₂)₂]²⁺ based on the dispositions of the pendant dimethylamino groups were modelled with molecular mechanics and the results are summarised in Fig. 3. The crystallographically observed conformation of the fourteen-membered macrocyclic ring was maintained for the molecular mechanics analyses of both N-based isomers. All conformers exhibiting the eclipsed experimentally observed ring conformation are ≈ 5 kJ mol⁻¹ more stable than the corresponding staggered (C_2) conformations and ≈ 18 kJ mol⁻¹ more stable than the other eclipsed (C_{2h}) conformers, where one and both five-membered chelate rings have been inverted, respectively, relative to the macrocyclic ring conformations shown in Figs. 3 and 4. Indeed, the crystallographically observed ring conformation is invariably found in tetradentate co-ordinated fourteen-membered tetraaza macrocycles exhibiting the centrosymmetric $R(1)R(4)S(8)S(11)$ (trans-III) * configuration.

In both cases, the crystallographically observed rotational isomer possessed the lowest strain-minimised energy. The experimentally observed rotamer of α-[CuL³(OH₂)₂]²⁺ was at least 25 kJ mol⁻¹ more stable than any other rotamer. The

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* The five N-based isomers of co-ordinated fourteen-membered macrocycles. The + sign indicates that the attached H atom is above the macrocyclic plane, the − sign that the H atom is below the plane.

trans-I   trans-II   trans-III

trans-IV   trans-V

(a) 71.1 kJ mol⁻¹

(b) 66.4 kJ mol⁻¹

(c) 66.4 kJ mol⁻¹

(d) 68.5 kJ mol⁻¹

Fig. 4 Strain-mininised geometries and energies of β-[CuL^3(OH$_2$)$_2$]$^{2+}$ based on the orientation of the dimethylamino groups (H atoms omitted for clarity)

disposition of the pendant tertiary amines is such that the N-methyl groups both point away from the complex, and consequently the N lone pair is directed between the two adjacent secondary amine H atoms. Other rotamers result in considerable strain being imposed on the C–N–C and C–C–C(N) valence angles as a result of the methyl groups being brought into close proximity with the macrocycle and the axial aqua ligands. Therefore, it emerges that the crystallographically observed conformation will be rotationally locked by the orientation of the two dimethylamino groups. The conformational analysis of β-[CuL^3(OH$_2$)$_2$]$^{2+}$ revealed a somewhat more flexible molecule, with there being a range of only $\approx$5 kJ mol⁻¹ between the four non-degenerate rotamers (Fig. 4). In this respect the orientations of the dimethylamino groups would be expected to fluctuate between their rotational minima with relative freedom.

Cyclic voltammetry of the complexes α- and β-[CuL^3]$^{2+}$ revealed irreversible reduction waves around -1.1 and -0.9 V vs. Ag–AgCl respectively. No corresponding anodic waves were found on the reverse sweep. Direct current polarography identified broad, two-electron reduction processes for both complexes at $E_{\frac{1}{2}}$ -0.76 V vs. Ag–AgCl. This behaviour can be explained by an initial one-electron reduction of each complex followed by a rapid dissociation of the copper(I) complex, and ultimately a second one-electron reduction of the free Cu⁺(aq). This irreversible electrochemical behaviour is typical of secondary amine tetraazamacrocyclic complexes of Cu^{II} found in the trans-III configuration of N-donors. The relatively large Cu⁺ ion cannot be accommodated within the small cavity defined by the trans-III configuration and the complex dissociates rapidly. N-Methylated macrocyclic tertiary amine complexes of Cu^{II} exhibiting the trans-I form [21] and secondary amine complexes in the unusual trans-II configuration [22] do show reversible electrochemical behaviour, and this has been attributed to a greater degree of flexibility of these complexes where the metal does not sit in the centre of the macrocyclic ring, but is displaced out of the plane of the four N-donors. In these cases, changes in the Cu–N bond lengths and co-ordination geometry upon reduction are less inhibited by the macrocyclic configuration, and the copper(I) complexes survive long enough for anodic waves to be observed.

Discussion

By inspection of their respective crystal structures, the two isomers α-[CuL^3(OH$_2$)$_2$]$^{2+}$ and β-[Cu^3(OClO$_3$)$_2$] have the same Cu–N bond lengths and N–Cu–N angles within experimental error, yet their visible electronic maxima are significantly different. The differences in the spectra are not due to anion co-ordination, i.e. Cl⁻ for α-[CuL^3]$^{2+}$ and ClO$_4$⁻ for β-[CuL^3]$^{2+}$, as the addition of an excess of NaCl had no significant effect on either spectrum. The apparently stronger ligand field of the α isomer (in neutral solution) is mirrored by the solution spectra of the unmethylated isomers α- and β-[CuL^1]$^{2+}$ where the
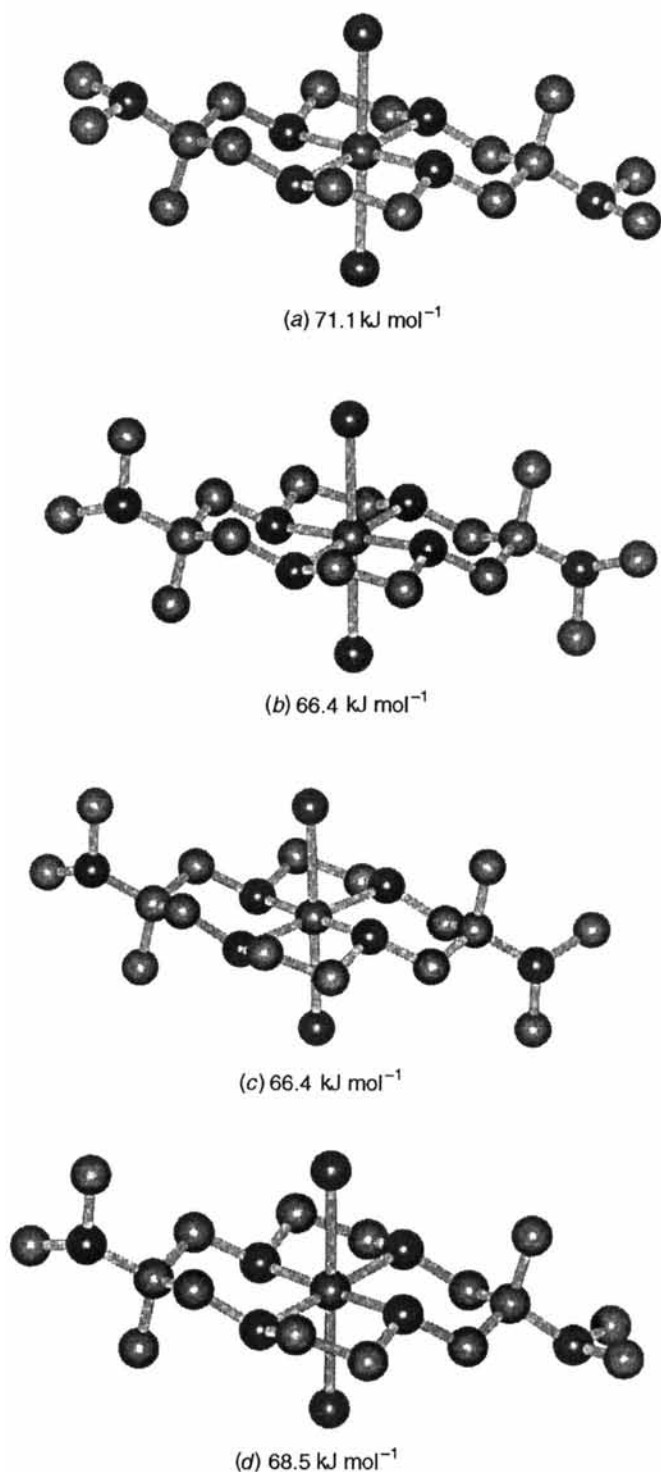
electronic maxima are 501 and 518 nm respectively. Similarly, the co-ordination geometries of α-[CuL^1(OH$_2$)$_2$]$^{2+}$ and β-[Cu(H$_2$L^1)(OClO$_3$)$_2$]$^{2+}$ exhibit the same Cu–N and Cu–O bond lengths within experimental error.[20,23,24]

However, a marked shift in the electronic maxima of the two isomers α- and β-[CuL^3]$^{2+}$ was found when their spectra were measured in 0.1 mol dm⁻³ HCl, where both pendant amines are protonated. In the case of α-[CuL^3]$^{2+}$ the maximum at 497 nm (0.1 mol dm⁻³ NaCl) shifts to 522 nm for α-[Cu(H$_2$L^3)]$^{4+}$ in 0.1 mol dm⁻³ HCl. A similar bathochromic shift from 508 (0.1 mol dm⁻³ NaCl) to 529 nm (0.1 mol dm⁻³ HCl) is observed for the spectrum of β-[CuL^3]$^{2+}$.

The effect of the crystallographically observed N–Cu–N bond-angle variation between the two isomers α- and β-[CuL³]²⁺ on the electronic transition energies was gauged with angular overlap model (AOM) calculations, by keeping all AOM parameters (e_σ, e_{d-s}, ζ) constant, and only changing the positional coordinates of the donor atoms. The calculations predict that there will be four closely spaced transitions from the $d_{x^2-y^2}$ ground state, with energies around 20 000 cm⁻¹. The centre of gravity of these four transition energies was taken to represent the observed electronic maximum. The assumption was made for the present analysis that variations in the relative intensities of the four components of this envelope of transitions would be common to both isomers, and would not result in specific differences between the two observed electronic maxima. The calculations predict that the *ca.* 1° difference in the N–Cu–N angles does not affect the centre of gravity of the four transition energies, and that the two complexes should exhibit identical visible spectra on this basis alone. In addition, varying the donor strength of the apically co-ordinated aqua ligands, $e_\sigma(OH_2)$, by a factor of two does not significantly affect the calculated electronic transition energies. It should be pointed out that a two-fold increase or decrease overestimates drastically the real change in e_σ upon varying the Cu–O bond length, r, by ≈2%. Generally, e_σ parameters have been found to vary as a function of r^{-n} ($n = 5$ or 6).[25,26] The weak bonding interactions made by the aqua ligands relative to the macrocyclic N-donors [$e_\sigma(OH_2):e_\sigma(NHR_2) \approx 1:70$], means that the spectrum will be effectively insensitive to minor variations in these parameters. That is, the differences in the crystallographically observed Cu–O bond lengths, which may not even be present in solution, are not responsible for the observed shift in electronic maximum. In summary, the experimentally observed 440 cm⁻¹ shift in the visible electronic maximum between the α and β isomers cannot be explained by the minor structural variations that were observed in the first co-ordination spheres of the two complexes.

Molecular mechanics calculations of the possible conformational isomers of α-[CuL³(OH₂)₂]²⁺ indicate that one conformer will be greatly preferred over the remaining possibilities. Therefore, it is fairly certain that the observed solid-state structure is retained in solution. As found in the crystal structure, the lone pair of the free tertiary amine is bifurcated by the pair of neighbouring *syn* secondary amine H atoms in the strain-energy-minimised structure (N···H 2.62 Å). Interestingly, the experimental structure is reproduced by the molecular mechanics calculation without the inclusion of hydrogen-bonding functions in the force field. Therefore, this N···H contact is not dependent on an attractive hydrogen-bonding interaction.

Instead, the preferred disposition of the pairs of *gem* N-methyl groups, so as to point away from the complex, orients the lone pair toward the secondary amine H atoms. The crystallographically observed N···H distance (2.57 Å) is close enough to be considered a hydrogen-bonding contact, but it emerges that the donor and acceptor are forced, albeit coincidentally, to be close enough for this bond to form. The N-based isomer β-[CuL³]²⁺ cannot achieve this same intramolecular hydrogen bond, since the pendant amine and the neighbouring pair of secondary amine H atoms, which are attached to the same six-membered chelate ring, are *trans* with respect to one another. In addition, the various rotamers based on the dispositions of the two dimethylamino groups in β-[CuL³]²⁺ possess similar minimised strain energies, so, unlike α-[CuL³]²⁺, there is no major preference for one rotamer over any other in this configuration.

In the absence of any significant structural differences between the two isomers, it seems that the intramolecular hydrogen bond found in the α isomer is responsible for the observed hypsochromic shift in the visible maximum on going from β- to α-[CuL³]²⁺. Qualitatively, it can be seen that a weakening of the N–H covalent bond through the formation of a Cu–N–H···N moiety (Scheme 1) will increase the donor strength of the ligating N atom, and hence shift the electronic maximum to higher energy. Recent reports have highlighted the importance of second-sphere co-ordination in complexes bearing ligands capable of undergoing hydrogen bonding.[27,28] The present results point to a similar second-sphere interaction occurring with α-[Cu³]²⁺ but not for β-[CuL³]²⁺ as a result of their differing stereochemistries. Specific solvation or anion co-ordination can result in significant differences between the electronic spectra of certain complexes. However, the same spectral differences found in water are also observed when the spectra are measured in Me₂SO and in aqueous 1 mol dm⁻³ NaCl solution which indicates that neither solvation nor anion co-ordination is responsible for the observed shift in maximum.

In acidic solution the *ca.* 800 cm⁻¹ bathochromic shift in the electronic maxima of both protonated isomers (relative to their spectra measured in neutral solution) is a separate issue. These shifts upon protonation are of comparable magnitude for both isomers, and point to a similar (non-specific) change in both complexes. It has been suggested that protonated (non-co-ordinated) amines within a macrocyclic ligand can function as sites for hydrogen bonding to axially bound anionic ligands such as Cl⁻ or HSO₄⁻.[29,30] This ditopic behaviour, where the anion is bound by both the metal and through a hydrogen-bonding interaction with the ligand, is a subject of considerable current interest.[31] In this case, chloride co-ordination

α isomer

β isomer
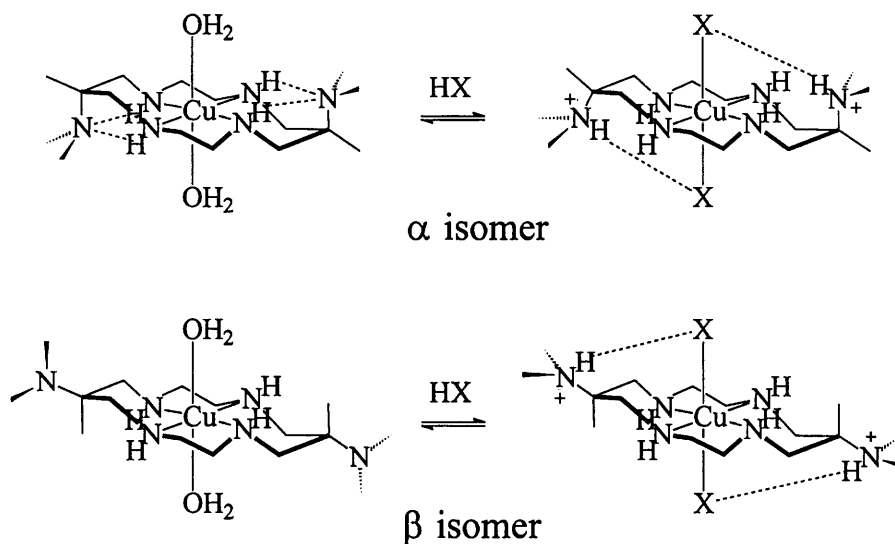
Scheme 1

appears to be the cause of the shift in the visible maximum of both α- and β-[CuL³]²⁺ in dilute HCl solution. However, axial co-ordination of Cl⁻ does not appear to occur to the dipositively charged complexes in neutral solution. This result implicates the positively charged ammonium substituents as playing an important role in stabilising the axially bound anionic ligand. A similar proposal has been put forward to explain the solution behaviour of a number of structurally similar nickel(II) complexes containing non-co-ordinated amines as part of the macrocyclic ring system.[29,30] As illustrated in Scheme 1, the differing stereochemistries do not prevent the protonated pendant amine of either isomer from interacting with an axially co-ordinated ligand, whereas the intramolecular hydrogen bond suggested in neutral solution can only occur in the α isomer.

The results presented herein indicate that some unusual structural and spectroscopic behaviour can result when functional groups attached to macrocyclic rings undergo subtle chemical transformations. In this case, an enhancement of the structural rigidity of the complex α-[CuL³]²⁺ was achieved as a result of locking the rotational disposition of the bulky dimethylamino substituents. This in turn effected an unusual hypsochromic shift in the visible electronic maximum of this isomer relative to that of the β isomer. The effect that N-methylation has on the ability of L³ to co-ordinate as a hexadentate ligand to metal ions preferring octahedral co-ordination, in a similar manner to that of the precursor L¹, is currently being explored.

Acknowledgements

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