

Rigidity extremes in coordination chemistry: a fine energetic balance in the isolation of a trapped ligand inversion intermediate[†]

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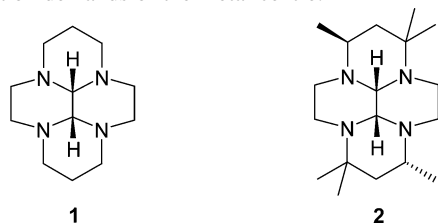
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An unusual copper(II) complex of a highly rigid and bulky ligand (a macrocycle–glyoxal condensate) has been synthesized and investigated via DFT calculations and structural characterisation.

Rigid ligand systems impose geometric constraints on metal ion coordination.¹ At extremes of ligand rigidity the degree of distortion from the 'preferred' metal ion geometry may be influenced by the stability of ligand conformation.

Rigid bidentate amine ligands have been exploited in the modelling of copper enzyme active sites.² They have been used, along with the more prevalent tridentate ligands of Kitajima³ and Tolman,⁴ to produce copper μ -hydroxo, μ -oxo, or μ -peroxo bridged dimers or even trimers that mimic active site geometries or reactivities. In an effort to produce novel restricted geometry copper complexes, tetracyclic ligands formed by the condensation of glyoxal with tetraazamacrocycles have been prepared.⁵ Such ligands *e.g.* **1**, formed from unsubstituted macrocycles (cyclam, cyclen), act as bidentate ligands to copper(II) with two chlorides completing the square planar coordination geometry. As part of an investigation of the potential for distortion from planarity, we report similar complexations using highly substituted macrocycle–glyoxal condensates in order to modify the cavity in which the copper(II) binds. One of these complexes is reported and shows a conformational departure from the free ligand structure that was not predicted. We propose that the structurally characterized product is a trapped intermediate in the known inversion equilibrium of ligands of this type, Fig. 1. We also report a consideration of the energetic implications of the ligand conformation relative to the coordination demands of the metal centre.



Copper and palladium complexes with the *cis*-glyoxal condensate of 1,4,8,11-tetraazacyclotetradecane (cyclam) have previously been synthesized and characterized as the first complexes

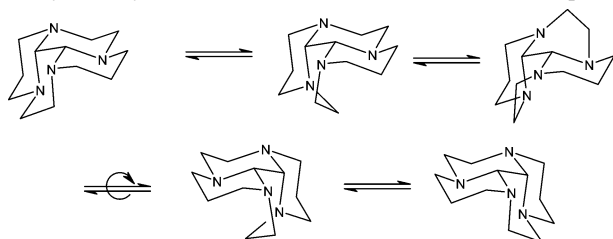


Fig. 1 The proposed inversion sequence for a tetraazamacrocycle–glyoxal condensate.⁷

[†] Electronic supplementary information (ESI) available: Experimental, crystallographic and computational details. See <http://www.rsc.org/supp-data/cc/b4/b405358c/>

with ligands of this type.⁵ Typically, the ligands act as bidentate donors with the metal ion residing in the cleft of the ligand. The tetracyclic nature of these ligands makes them highly rigid. The lowest energy folded structure orients two nonadjacent nitrogens into the concave cleft while the other nonadjacent pair direct their lone pairs from the convex face.⁶ This conformation, retained upon complexation, has all four six-membered rings in chair conformations and is observed in the solid state structure of the free ligand.⁷

The glyoxal condensate (1,1,3,6,6,8-hexamethyldecahydro-3a,5a,8a,10a-tetra-azapyrene) of the tetA (*cis*-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane) macrocycle **2** contains an additional six methyl groups around the 14-membered macrocyclic ring compared to the cyclam analogue. Semi-empirical calculations and analogous studies have suggested that the additional steric hindrance caused by the six methyl groups may either preclude complexation with a metal ion or provide a highly distorted geometry.^{5,8} Complexation of copper(II) with unsubstituted glyoxal–macrocycle condensates occurs at room temperature in methanol.^{5a} Anticipating difficulty in complexation with **2**, the methanol reaction mixture was held at reflux overnight resulting in a yellow–green crystalline product of X-ray quality upon cooling. ‡ We initially expected complexation to non-adjacent nitrogen positions with distorted square planar coordination geometry around the copper but instead discovered coordination of adjacent nitrogens and a distinct conformational change in the ligand upon binding.

An X-ray structural determination of the crystalline solid, shown in Fig. 2(h), revealed the copper bound by two short bonds to adjacent nitrogens with a longer bond to a third and two of the four six-membered rings exhibiting the higher energy twist-boat conformation. This conformation is proposed to occur in an intermediate structure during inversion of the ligand from one enantiomer to the other. However, in the known crystal structures the rings are always observed in the chair conformation.^{7,10} It should be noted that a related conformational change to the two chair and two boat conformation can be forced upon a closely related highly substituted ligand (the *cis*-tetB–glyoxal condensate) by stepwise methylation of nonadjacent nitrogens.⁸ To further explore the finely balanced energetics of these compounds, DFT calculations were carried out on the copper complexes for each of the two possible conformations of **1** and **2**.

Calculations of the relative stabilities of the two cyclam glyoxal condensate (**1**) copper complexes, Fig. 2(c) and (g), show that the all chair conformation is 51 kJ mol⁻¹ (42 kJ mol⁻¹) more stable than the boat/chair complex at the UBP86/TZP (UB3LYP/LanL2DZ) level. This was very much as expected. However, calculations on the tetA–glyoxal condensate (**2**) copper complexes show that the all chair conformation is only 21 kJ mol⁻¹ (11 kJ mol⁻¹) more stable than the boat/chair complex at the UBP86/TZP (UB3LYP/LanL2DZ) level – a considerably smaller energy difference than for the cyclam–glyoxal condensate (**1**) complexes. For the all chair conformation (top row, Fig. 2), there are varying degrees of distortion from planarity in the copper coordination geometry. The calculated structure for CuICl₂ shows less distortion than the solid state structure suggesting that distortion requires only small energy changes.

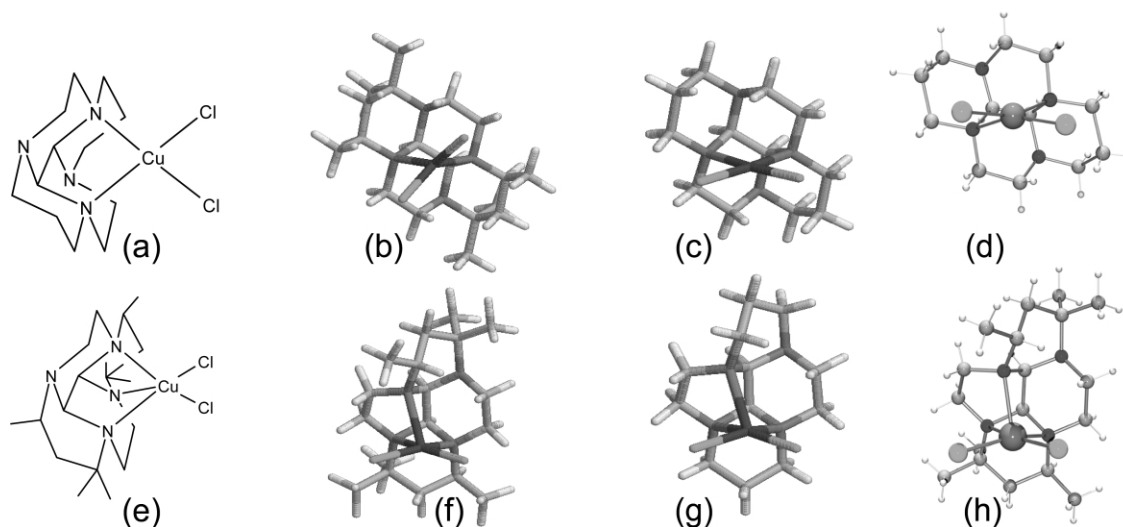


Fig. 2 (a) Schematic of isolated compound Cu1Cl_2 (all chair); (b) calculated structure of Cu2Cl_2 (all chair); (c) calculated structure of Cu1Cl_2 (all chair); (d) X-ray structure of Cu1Cl_2 (all chair);^{5a} (e) schematic of isolated compound Cu2Cl_2 (two twist boat); (f) calculated structure of Cu2Cl_2 (two twist boat); (g) calculated structure of Cu1Cl_2 (two twist boat); (h) X-ray structure of Cu2Cl_2 (two twist boat). Selected bond lengths (Å) and angles (°) for X-ray structure of Cu2Cl_2 : Cl(1)–Cu(1) 2.2506(4), Cl(2)–Cu(1) 2.2374(5), N(1)–Cu(1) 2.1833(12), N(2)–Cu(1) 2.3170(12), N(4)–Cu(1) 2.0831(13), N(4)–Cu(1)–N(1) 65.15(4), N(1)–Cu(1)–Cl(2) 97.40(3), N(4)–Cu(1)–Cl(1) 97.88(3), Cl(2)–Cu(1)–Cl(1) 99.067(17).

A bond energy analysis[†] for complex formation with CuCl_2 shows a higher binding energy of **2** (boat/chair) vs. **2** (all chair), with the latter having the least favourable binding energy of all four molecules studied. This is due to a significantly smaller electrostatic and orbital interaction than in the other systems. In the absence of copper, the chair conformation of **1** is 63 kJ mol⁻¹ more stable than the free boat/chair conformation with the more compact nature of the chair shape giving rise to stronger bonding. The energy difference between the free conformations in **2** is almost exactly the same. The experimentally isolated complex is probably determined by the kinetics.

Tetracyclic tetraamines produced from the condensation of glyoxal with various tetraazamacrocycles have been studied for more than two decades.⁹ An interesting aspect of these *cis*-fused tetracyclic structures is their inversion from one enantiomeric form to the other. The unsubstituted cyclam–glyoxal condensate has C_2 symmetry (axis perpendicular to the ethylene bridge bond) and is therefore chiral. Weisman *et al.* used this characteristic to explain the temperature dependent NMR spectra of the molecule and to assign its configuration as *cis*-fused since the *trans*-fused isomer cannot undergo inversion without bond-breakage.^{6b} Riddell *et al.* explored the energetics of this inversion and its probable stepwise path.⁷ A likely path for the inversion was proposed, Fig. 1. Overall, all four nitrogens and both piperazine rings become inverted, and both hexahydropyrimidine rings retain their initial geometric states.⁷

Several other unsubstituted tetracycles of differing ring sizes undergo related inversion processes with similar energies of activation.^{10a} Yet, no such dynamic process has been reported for systems in which alkyl substituents are appended to the ring carbons. The isolation of the observed conformation shows a ring inversion intermediate conformation trapped by complex formation and suggests the inversion process described for the unsubstituted tetracycles also occurs for the substituted systems.

Further investigations of distorted copper complexes are underway with particular interest in the degree of alkylation required to isolate distorted square planar complexes and the resultant effects on the formation of bridged dimers.

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Notes and references

[†] Satisfactory elemental analyses were obtained for all compounds. *Crystal data*: $\text{Cu2Cl}_2 \cdot \text{C}_{18}\text{H}_{34}\text{Cl}_2\text{CuN}_4$, 150(2) K, monoclinic, $P2_1/n$, $a = 8.5250(8)$, $b = 18.9082(17)$, $c = 12.7881(13)$, $\beta = 97.997(8)^\circ$, $V = 2041.3(3) \text{ \AA}^3$, $Z = 4$, $F(000) = 932$, 45368 reflections measured of which 8731 were independent on F^2 , final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0354$, $wR_2 = 0.0792$, R indices (all data): $R_1 = 0.0640$, $wR_2 = 0.0856$. The structure was solved by direct methods (SHELXS) and refined against F^2 (SHELXL97) using WinGX.¹¹ CCDC 238909. See <http://www.rsc.org/suppdata/cc/b4/b405358c/> for crystallographic data in .cif or other electronic format.

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