

Preparations and structures of a series of novel, mono-substituted *cis,cis*-1,3,5-triaminocyclohexane-based complexes

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The complexation of triimine ligands based on *cis,cis*-1,3,5-triaminocyclohexane with copper salts caused a selective hydrolysis reaction producing new monoimine complexes, the single-crystal structures of which showed the ligand skeletons to be isostructural, with a well defined rigid superstructure adjacent to the metal centre.

Face capping N_3 ligands form the basis of many ligand systems, particularly in bioinorganic chemistry.¹ One such example is *cis,cis*-1,3,5-triaminocyclohexane (tach) which has been used recently in the modelling of metalloenzyme active sites,² and as a basis for an *in vivo* metal chelator.³ Our interest in tach lies in using it as a basis for preparing small molecule metalloenzyme models. One increasing challenge in modelling is the preparation of models which, in addition to the primary coordination sphere, begin to model the secondary co-ordination sphere of the metal centre.⁴ Herein, we report the synthesis and characterisation of a series of ligands based on tach, that work towards a methodology for producing such models.

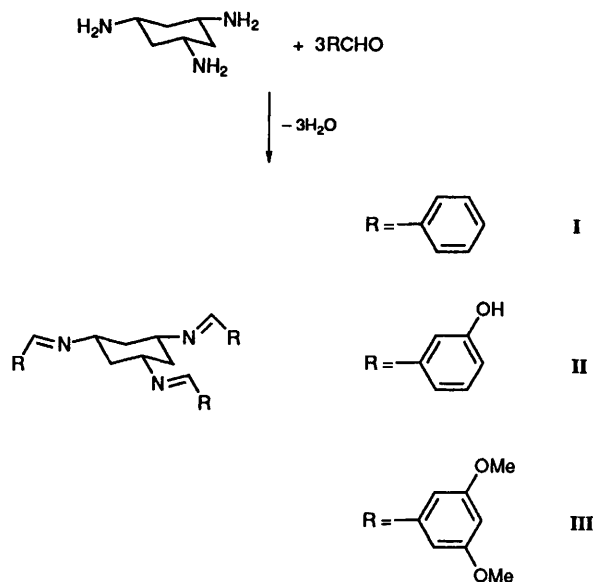
The ligand system is prepared by condensing tach⁵ with aldehydes to produce a series of triimine ligands, Scheme 1. As typical examples of this system, we present here the synthesis of *cis,cis*-1,3,5-tris[(*E*)-benzylideneamino]cyclohexane **I**,⁶ *cis,cis*-1,3,5-tris[(*E*)-3-hydroxybenzylideneamino]cyclohexane **II** and *cis,cis*-1,3,5-tris[(*E*)-3,5-dimethoxybenzylideneamino]cyclohexane **III**; these were prepared in yields of 60, 80 and 78% respectively.†

† Molecule **I** has been prepared before⁶ but **II** and **III** are new and were synthesised as follows. Compound **I** (0.50 g, 1.20 mmol, 60%), m.p. 80.0–80.5 °C (lit.,⁶ 87–89 °C).

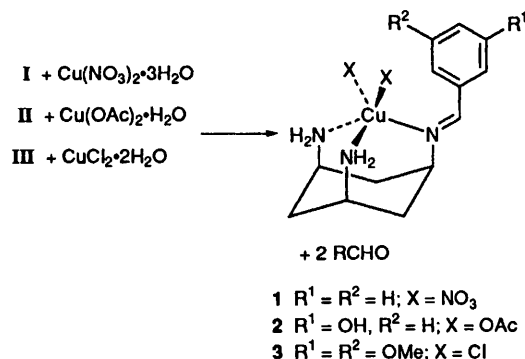
Compound **II** was obtained as a white powder by the reaction of *cis,cis*-1,3,5-triaminocyclohexane·3HCl (0.25 g, 1.05 mmol) in methanol (10 cm³) with an aqueous NaOH solution (2 cm³, 3.15 mmol) and a solution of 3-hydroxybenzaldehyde (0.385 g, 3.15 mmol) in methanol (50 cm³) for 1 h at reflux (0.37 g, 0.84 mmol, 80%), m.p. 161–162 °C (Found: C, 70.20; H, 6.50; N, 8.90. Calc. for C₂₇H₂₇N₃O₃·H₂O: C, 70.55; H, 6.35; N, 9.15%). ¹H NMR (CD₃OD, 270 MHz): δ 8.43 (s, 3 H, CH=N), 7.09 (m, 12 H, aromatic H), 4.95 (s, H₂O), 3.67 [tt, 3 H, ³J_{HH} = 12, ³J_{HH} = 4, CH(NH₂)], 2.04 [dt, 3 H, ²J_{HH} = 12, ³J_{HH} = 12, CH(H)], 1.90 [dt, 3 H, ²J_{HH} = 12, ³J_{HH} = 4 Hz, CH(H)]. IR (cm⁻¹, in KBr): 3500–3000s, 2940s, 2861s, 2734w, 2577w, 1644s, 1596s, 1453s, 1349m, 1291s, 1248s, 1174m, 1155m, 1025w, 998w, 864m, 783s, 685s. Positive ion mass spectrum (nitrobenzyl alcohol matrix): *m/z* = 442 (MH⁺).

Compound **III** was obtained as a white powder by the reaction of *cis,cis*-1,3,5-triaminocyclohexane·3HCl (1.00 g, 4.19 mmol) in methanol (25 cm³) with an aqueous solution of NaOH (2 cm³, 12.6 mmol) and a solution of 3,5-dimethoxybenzaldehyde (2.09 g, 12.60 mmol) in methanol (25 cm³) for 3.5 h at ambient temperature (1.86 g, 3.24 mmol, 78%), m.p. 150–150.5 °C (Found: C, 69.25; H, 6.50; N, 7.20. Calc. for C₃₃H₃₉O₆N₃: C, 69.10; H, 6.85; N, 7.35%). ¹H NMR (CD₃OD, 270 MHz): δ 8.43 (s, 3 H, CH=N), 7.00 (d, 6 H, ⁴J_{HH} = 2, aromatic H_a), 6.62 (t, 3 H, ⁴J_{HH} = 2, aromatic H_b), 3.85 (s, 18 H, OCH₃), 3.69 [tt, 3 H, ³J_{HH} = 12, ³J_{HH} = 4, CH(NH₂)], 2.05 (dt, 3 H, ²J_{HH} = 12, ³J_{HH} = 12 Hz, CH(H)], 1.91 [dt, 3 H, ²J_{HH} = 12 Hz, ³J_{HH} = 4 Hz, CH(H)]. IR (cm⁻¹, in KBr): 3625–3325w, 2936w, 2854w, 2839w, 1640m, 1593s, 1461s, 1428m, 1353m, 1317w, 1300m, 1206s, 1158s, 1065m, 840w, 680w. Positive ion mass spectrum (nitrobenzyl alcohol matrix): *m/z* = 574 (MH⁺).

Molecules **I**, **II** and **III** were complexed with copper(II) nitrate trihydrate, copper(II) acetate monohydrate and copper(II) chloride dihydrate respectively, in methanol at ambient temperature. The complexation step afforded three new complexes (Scheme 2), *r-c*-3,5-diamino-κ²*N,N'*-1-[(*Z*)-benzylideneamino-κ*N*]cyclohexanebis(nitrato-κ*O*)copper(II) (**1**; 85%), *r-c*-3,5-diamino-κ²*N,N'*-1-[(*Z*)-3-hydroxybenzylideneamino-κ*N*]cyclohexanebis(acetato-κ*O*)copper(II) (**2**; 60%) and *r-c*-3,5-diamino-κ²*N,N'*-1-[(*Z*)-3,5-dimethoxybenzylideneamino-κ*N*]cyclohexanedichlorocopper(II) (**3**;



Scheme 1 Reaction of tach with the aldehydes to give molecules **I**, **II** and **III**



Scheme 2 Complexation of molecules **I**, **II** and **III** to give complexes **1**, **2** and **3**

68%)* In all cases the complexation step caused the hydrolysis of two of the imine groups selectively producing an imine diamine complex. (Presumably hydrolysis relieves the strain in the intermediate copper complex formed with I, II or III.) Remarkably this reaction is quite general and can be accomplished with a variety of metal salts.† This simple reaction is notable inasmuch as the synthesis of similar face capping mono-substituted ligands, e.g. alcohol pendant cyclen (1,4,7,10-tetraazacyclododecane) ligands, is synthetically demanding requiring a multistep synthesis.⁷

Crystals of the complexes were grown by slow evaporation of methanolic solutions. The crystal structures‡ (Fig. 1) of

* Crystals of complex 1 were obtained by the reaction of copper nitrate trihydrate (0.25 g, 0.64 mmol) in methanol (*ca.* 8 cm³) with a solution of I (0.10 g, 0.25 mmol) in methanol (8 cm³). Blue crystals (0.22 g, 0.54 mmol, 85%), m.p. 214–215 °C (decomp.) (Found: C, 39.05; H, 4.45; N, 16.95. Calc. for C₁₃H₁₉CuN₅O₆: C, 38.55; H, 4.75; N, 17.30%). IR (cm⁻¹, in KBr): 3321s, 3269m, 3244m, 3203m, 3151m, 3129m, 2921s, 1634s, 1589m, 1580m, 1465s, 1454s, 1431s, 1384s, 1363s, 1341s, 1312s, 1282s, 1150s, 1107m, 1026m, 906m, 758s, 692s. Positive ion mass spectrum (nitrobenzyl alcohol matrix): *m/z* = 280 (peak from ⁶³Cu) (*M*⁺ – 2NO₃⁻). Measured density = 1.61(5) g cm⁻³.

Complex 2 was obtained as a deep blue powder by the reaction of copper acetate monohydrate (0.41 g, 2.00 mmol) in methanol (*ca.* 150 cm³) with a solution of II (0.9 g, 2 mmol) in methanol (50 cm³). Hexane (5 cm³) was added dropwise to precipitate a blue solid (0.50 g, 1.20 mmol, 60%), m.p. 202–204 °C (decomp.) (Found: C, 49.55; H, 5.95; N, 10.00. Calc. for C₁₇H₂₅CuN₃O₅: C, 49.20; H, 6.05; N, 10.15%). IR (cm⁻¹, in KBr): 3220s, 3136s, 2941w, 2921w, 2888w, 1689m, 1626m, 1612m, 1577s, 1426m, 1397s, 1381s, 1327m, 1301m, 1230w, 1176w, 923w, 857w, 796w, 693w, 665w. Positive ion mass spectrum (nitrobenzyl alcohol matrix): *m/z* = 296 (peak from ⁶³Cu) (*M*⁺ – 2CH₃CO₂⁻). Measured density = 1.51(5) g cm⁻³.

Complex 3 was obtained as a blue powder by the reaction of copper chloride dihydrate (0.44 g, 2.60 mmol) in methanol (*ca.* 150 cm³) with III (1.49 g, 6.00 mmol) for 0.5 h. Hexane (2 cm³) followed by methanol (1 cm³) was added to precipitate a blue solid (0.73 g, 1.77 mmol, 68%), m.p. 160–165 °C (decomp.) (Found: C, 42.75; H, 5.55; N, 9.80. Calc. for C₁₅H₂₃ClCuN₃O₂·0.5H₂O: C, 42.80; H, 5.50; N, 10.00%). IR (cm⁻¹, in KBr): 3422w (br), 3258m, 3215m, 3144m, 2924w, 2867w, 1629m, 1596s, 1468m, 1455m, 1418m, 1361w, 1338m, 1320w, 1305w, 1205m, 1159s, 1065s, 897w, 841m, 682w. Positive ion mass spectrum (nitrobenzyl alcohol matrix): *m/z* = 375 (peak from ⁶³Cu) (*M*⁺ – Cl), 340 (*M*⁺ – 2Cl). Measured density = 1.59(5) g cm⁻³.

† Other mono-substituted products using compound I have been prepared with ZnCl(BPh₄) (69%), Ni(NO₃)₂ (99%) and Cu(OAc)₂ (85%), all structures have been characterised by single-crystal X-ray diffraction.

‡ Crystal data: all data were collected on a Rigaku AFC6S diffractometer, 293(2) K, ω–2θ scan mode with graphite-monochromated Mo-Kα radiation. Unit cell indexed by least-squares refinement on diffractometer angles for 20 automatically centred reflections, λ = 0.710 69 Å. Solutions by Patterson methods with SAPI91 and expanded using Fourier techniques with DIRDIF. Full matrix least squares refinement on *F*² with SHELXL 93 with all non-hydrogen atoms anisotropic and hydrogens refined using a rigid model. Programs used are given in refs. 8 and 9. C₁₃H₁₉CuN₅O₆ 1, *M* = 404.87, triclinic, space group *P*1̄ (no. 2), *a* = 9.887(5), *b* = 10.444(4), *c* = 8.819(3) Å, α = 96.87(3), β = 93.67(4), γ = 66.43(3)°, *U* = 828.6(6) Å³, *Z* = 2, *D_m* = 1.61 g cm⁻³, *D_c* = 1.62 g cm⁻³, *F*(000) = 418. Blue block. Crystal dimensions 0.40 × 0.30 × 0.20 mm, μ(Mo-Kα) = 13.60 cm⁻¹, ω scan width = 1.21 + 0.30 tan θ, ω scan speed 1° min⁻¹; 3113 reflections measured (5.98 ≤ 2θ ≤ 50.00°), (*h*, *k*, +*l*), 2928 unique. The weighting scheme *w* = 1/[σ²(*F_o*²) + (0.0435*P*)² + 0.57*P*], *P* = [max(*I_o*, 0) + 2*F_c*²]/3 gave satisfactory agreement analysis. Final *R_F*, *wR₁* values on all data were 0.061, 0.096 and *R_F*, *wR₁* values on [*I_o* > 2σ(*I_o*)] data were 0.037, 0.085, goodness-of-fit on *F*² = 1.037. C₁₇H₂₅CuN₃O₅ 2, *M* = 414.95, orthorhombic, space group *Pnma* (no. 62), *a* = 20.183(11), *b* = 10.336(8), *c* = 8.737(3) Å, *U* = 1823(2) Å³, *Z* = 4, *D_m* = 1.50 g cm⁻³, *D_c* = 1.51 g cm⁻³, *F*(000) = 868. Blue block. Crystal dimensions 0.50 × 0.30 × 0.20 mm, μ(Mo-Kα) = 12.31 cm⁻¹, ω scan width = 1.16 + 0.30 tan θ, ω scan speed 1° min⁻¹; 1494 reflections measured (5.08 ≤ 2θ ≤ 50.00°), (+*h*, +*k*, +*l*), 1494 unique. The weighting scheme *w* = 1/[σ²(*F_o*²) + (0.0472*P*)² + 1.65*P*], *P* = [max(*I_o*, 0) + 2*F_c*²]/3 gave satisfactory agreement analysis. The thermal ellipsoid of O(4) is elongated along the axis perpendicular to the mirror plane. We have interpreted this as thermal motion/disorder in the crystal due to the hydrogen-bond contacts that can be made

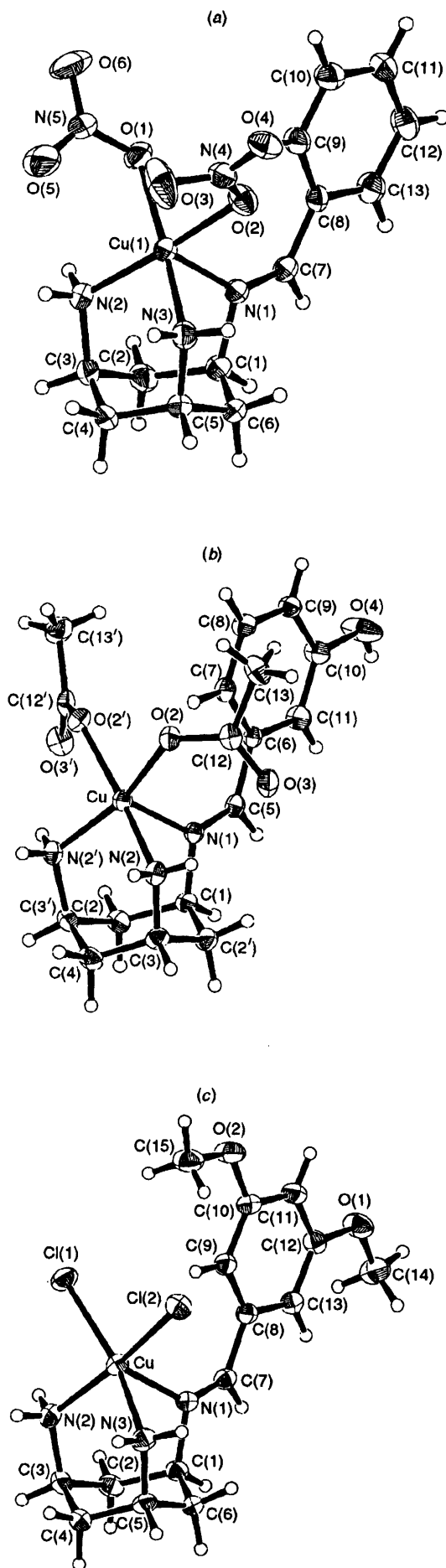


Fig. 1 ORTEP⁸ diagrams of complexes 1, 2 and 3 with 30% probability ellipsoids

complexes **1**, **2** and **3** all show a five-co-ordinate copper centre ligated to the three face capping nitrogens of the tach backbone. In each case the copper co-ordination geometry is square pyramidal distorted along the apical Cu(1)–N(1) bond with a distance of 2.318(3) in **1**, 2.395(4) in **2** and 2.446(3) Å in **3**. The other Cu–N distances, Cu(1)–N(2), Cu(1)–N(3) are 1.998(3) and 2.000(3) in **1**, 1.990(3) and 1.990(3) in **2** (2 lies on a crystallographic mirror plane) and 2.000(3) and 2.013(3) Å in **3**, respectively. In each structure the phenyl ring and the imine bond form a near planar unit with torsion angles of 179.1(4) [N(1)–C(7)–C(8)–C(13)] in **1**, 180 [N(1)–C(5)–C(6)–C(11)] in **2** and 177.1(3)° [N(1)–C(7)–C(8)–C(13)] in **3**. The N(1)–C(7)–C(8) angle is 129.1(3)° in **1**, the equivalent angle [N(1)–C(5)–C(6)] is 127.1(4)° in **2** and 128.4(3)° in **3** indicating some steric strain between the phenyl ring and the anions co-ordinated to the copper centre. In **3** the oxygen atom [O(2)] of the methoxy group is positioned 5.351(5) Å from the copper centre.

A comparison of the ligand skeleton of **1** with those of **2** and **3** shows them to be isostructural despite differing substitution, each demonstrating a rigid superstructure adjacent to the copper centre; this can be used as a platform to position groups in the secondary co-ordination sphere of the copper centre. It can be seen from the comparison of **2** with **3** that the use of a disubstituted phenyl derivative is required to ensure that a

between O(4) and both O(2), O(2') in an adjacent molecule. Final R_F , wR_1 values on all data were 0.059, 0.093 and R_F , wR_1 values on [$I_o > 2\sigma(I_o)$] data were 0.034, 0.081, goodness-of-fit on $F^2 = 1.008$. $C_{15}H_{23}Cl_2CuN_3O_2$ **3**, $M = 411.80$, triclinic, space group $P\bar{1}$ (no. 2), $a = 9.873(7)$, $b = 11.348(5)$, $c = 9.343(4)$ Å, $\alpha = 107.44(4)$, $\beta = 114.62(4)$, $\gamma = 73.35(4)^\circ$, $U = 891.9(9)$ Å³, $Z = 2$, $D_m = 1.59$ g cm⁻³, $D_c = 1.53$ g cm⁻³, $F(000) = 426$. Green block. Crystal dimensions 0.30 × 0.20 × 0.20 mm, $\mu(\text{Mo-K}\alpha) = 15.35$ cm⁻¹, ω scan width = 0.95 + 0.30 tan θ , ω scan speed 2° min⁻¹; 3338 reflections measured ($5.38 \leq 2\theta \leq 50.00^\circ$), ($h, k, +l$), 3141 unique [absorption correction (max., min. transmission factors = 1.00, 0.80)]. The weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.366P)^2 + 0.24P]$, $P = [\max(I_o, 0) + 2F_c^2]/3$ gave satisfactory agreement analysis. Final R_F , wR_1 values on all data were 0.057, 0.086 and R_F , wR_1 values on [$I_o > 2\sigma(I_o)$] data were 0.032, 0.073, goodness-of-fit on $F^2 = 1.047$. 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.

group is positioned above the metal centre. This type of ligand system allows the opportunity to exert control over exogenous ligands bound to the metal; this feature has been recognised as being important in the accurate modelling of metalloenzyme active sites.² In future studies we will prepare other derivatives of this ligand system with a view to modelling the secondary co-ordination sphere of metals in metalloproteins.

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