Chiral heterocyclic ligands. XII. Metal complexes of a pyrazine ligand derived from camphor.

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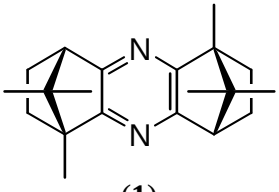
Dedicated to Jim Coxon with fond memories of our earlier 'positively charged' involvement with camphor.

Abstract
The synthesis and X-ray crystal structures of copper(II) nitrate, copper(I) iodide and zinc(II) bromide complexes of the chiral ligand **2** are described.

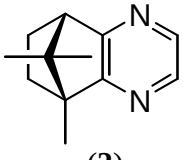
Keywords: chirality, pyrazine, bornane, N-ligand, crystal structure.

Introduction

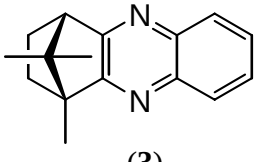
Chiral heterocyclic ligands have found many applications in chemistry, most notably in the area of asymmetric catalysis.[1] Such compounds are usually synthesised from readily available, naturally occurring compounds from the chiral pool.[2] Monoterpenes serve as a useful source of inexpensive synthons for such studies.[3] For example, von Zelewsky and co-workers have prepared a vast library of chelating and bridging heterocyclic ligands which contain a fused pinane subunit within their structures.[4] Similarly, we have synthesised many chiral ligands, using camphor as a source of the chirality.[5] Accordingly, by fusing a pyrazole ring to the bornane skeleton we have prepared many bidentate and tridentate chelating ligands, as well as a number of bridging ligands containing this subunit.[6]



(**1**)



(**2**)



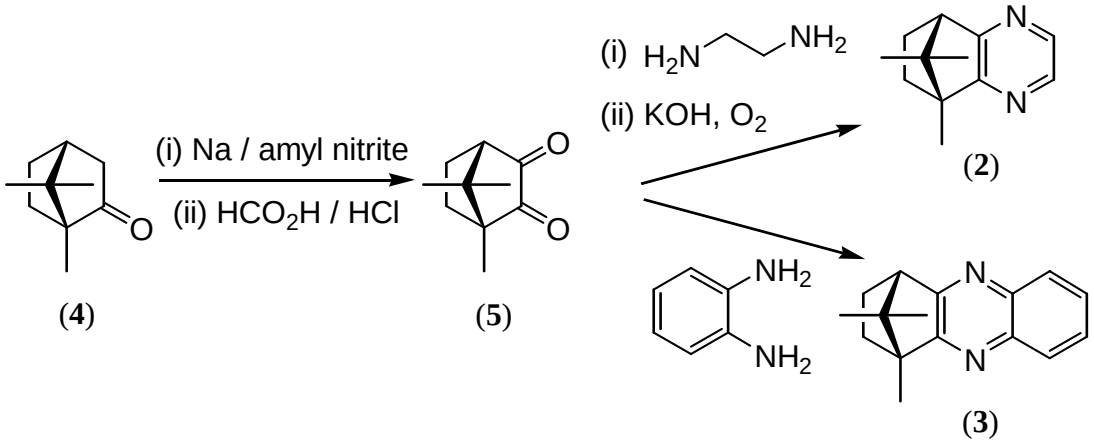
(**3**)

More recently, we have turned our attention to fusing the bornane skeleton to azine rings and have reported the synthesis of the first chiral 2,2'-bipyrimidine.[7] We have also

fused bornane units to a pyrazine ring and have described the preparation of some chiral coordination polymers, using the C_2-symmetric ligand **1** as a bridging ligand.[8] In contrast, the C_1-symmetric ligand **2** proved less useful for the construction of chiral coordination polymers,[8] because of the difficulty for this ligand to faithfully assemble in a single orientation, due to the similar, but subtly different, nature of the two nitrogen donors. However, this ligand can successfully be used as a monodentate ligand for the construction of discrete, rather than polymeric, coordination compounds. In this context, we have studied the coordination chemistry of **2** and the related quinoxaline **3** with various transition metals and now report the synthesis and X-ray crystal structures of copper and zinc mononuclear complexes and a tetranuclear copper complex in which ligand **2** acts as a monodentate donor.

Results and Discussion

Ligands **2** and **3** were prepared from (1R)-(+)-camphor (**4**), as shown in Scheme 1, *via* camphorquinone (**5**). Although **4** can be oxidised directly to **5** using selenium dioxide,[9] we chose to carry out this conversion in two steps involving nitrosation to an intermediate quinone-monoxime,[10] followed by hydrolysis.[11] The quinone was then condensed with ethylenediamine to give a dihydropyrazine[12] followed by oxidation to **2**, in 69% overall yield.[13] Condensation of **5** with *o*-phenylenediamine furnished **3** directly in 54% yield.[13]



Scheme 1. Syntheses of ligands **2** and **3**.

The coordination chemistry of **2** and **3** was explored with various transition metal reagents. No complexes of **3** were able to be isolated, possibly due to the highly hindered nature of both nitrogen donors. However, three crystalline products were isolated in good yields from reactions of **2**. Reaction with a methanolic copper(II) nitrate solution produced very thin blue plates of complex **6**. Reaction with copper(I) iodide in acetonitrile gave yellow crystals of complex **7**. The ^{1}H NMR spectrum of **7** showed only one set of signals for the organic ligand, whereas electrospray mass spectrometry

indicated the presence of a range of species involving various combinations of copper, ligand **2** and acetonitrile. A colourless complex **8** was obtained by reaction with a methanol solution of zinc(II) bromide. The structures of these complexes were determined by X-ray crystallography.

The light-blue crystals of the copper(II) nitrate complex, **6**, were very thin and diffracted only weakly. Nevertheless, the structure of **6** was unambiguously established as that shown in Figure 1. The complex crystallizes in the orthorhombic space group $C222_1$, with the asymmetric unit containing half a copper atom, one molecule of **2**, a coordinated monodentate nitrate and a coordinated water molecule, which is disordered over two sites. The copper atom lies on a two-fold rotation axis that generates the other half of the complex.

The copper atom is octahedral with a N2O4 coordinating environment. The chiral ligand molecules coordinate through the less hindered nitrogen atom, with a Cu-N bond length of 2.06(1) Å, while the remaining nitrogen atom of the ligand is non-coordinating. The bulky chiral ligands adopt a *trans* realtionship about the copper atom, with a N-Cu-N angle that is almost linear [173.5(9)°]. The coordinated oxygen atoms are in a plane, with the nitrate anions being *cis* and having a Cu-O distance of 2.13(1) Å and an O-Cu-O angle of 89.6(6)°. The coordinated water molecules are disordered over two sites, with the major contributing water molecule occupied 60% of the time. The major contributing water molecule has a Cu-O bond length of 1.96(6) Å. The minor contributing water molecule is further away from the copper atom, with a Cu-O distance of 2.48(8) Å.

The copper(I) iodide complex, **7**, crystallizes in the monoclinic space group C2, with four molecules of **2** and four copper iodides in the asymmetric unit. The complex consists of Cu_4I_4 clusters with each of the copper atoms coordinated by one molecule of

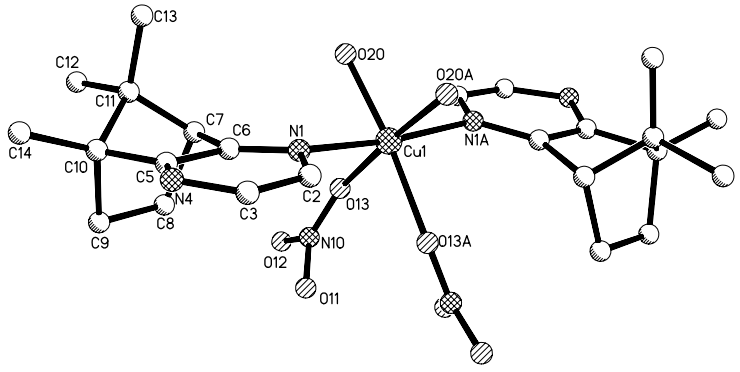


Figure 1. Perspective view of the mononuclear complex **6**, showing the major component of the disordered water molecules. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and bond angles (°): Cu1-N1 2.06(1), Cu1-O13 2.13(1), Cu1-O20 1.94(6), N1A-Cu1-N1 173.1(10), O20-Cu1-N1 96.7(8), O20-Cu1-O13 85.9(6), N1-Cu1-O13 93.9(5), O20-Cu1-O20A 99.3(10), O13-Cu1-O13A 89.9(7).

2. The asymmetric unit contains two independent half $Cu_4L_4I_4$ clusters, one of which is shown in Figure 2.

The four copper and four iodine atoms of each cluster form a distorted cube-like structure with the copper atoms forming a tetrahedron. The two independent clusters each sit astride a two-fold axis and have similar geometries, with Cu···Cu distances in the range 2.670(3) – 2.738(3) Å for one cluster, and 2.648(3) – 2.776(3) Å for the other. The copper atoms all have tetrahedral coordination geometry, and are each coordinated by three iodine atoms, with Cu-I bond lengths in the range 2.655(2) – 2.769(2) Å. The remaining site of the tetrahedral copper is occupied by the less hindered nitrogen atom of **2**, with Cu-N distances between 2.030(9)Å and 2.043(9) Å.

The distorted cube-like cluster is the most common structure found for tetranuclear copper(I) halide complexes, and is more common for iodide complexes than for those of other halides.[14] The cube-like Cu_4I_4 cluster has potential S_4 point symmetry, and the formation of the clusters occupying crystallographic S_4 sites has been observed for a number of complexes utilising nitrogen-donor ligands.[15] However, the coordination to the copper atoms of the chiral ligand, **2**, precludes any possible S_4 symmetry. The two

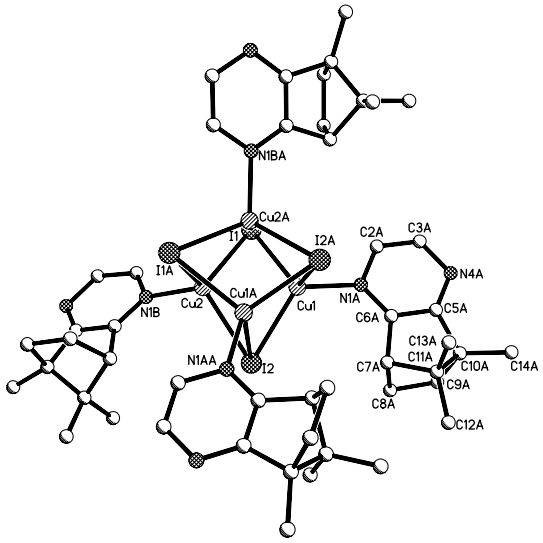


Figure 2. Perspective view of the structure of one of the two independent $Cu_4L_4I_4$ units of **7**. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and bond angles (º): Cu1-N1A 2.053(8), Cu2-N1B 2.034(8), Cu1-I1 2.706(2), Cu1-I2 2.655(2), Cu1A-I2 2.750(2), Cu2-I1 2.673(2), Cu2A-I1 2.716(2), Cu2-I2 2.684(2), N1A-Cu1-I2 120.0(2), N1A-Cu1-I1 105.8(2), I2-Cu1-I1 105.44(5), N1A-Cu1-I2A 95.6(2), I2-Cu1-I2A 113.45(5), I1-Cu1-I2A 116.75(5), N1B-Cu2-I1 108.6(2), N1B-Cu2-I2 110.0(2), I1-Cu2-I2 105.54(5), N1B-Cu2-I1A 101.0(2), I1-Cu2-I1A 112.71(5), I2-Cu2-I1A 118.70(5).

independent copper clusters, which are not related by symmetry, differ principally in the relative orientation of the molecules of **2** that are coordinated to the copper atoms. Similar differences have been observed in the copper(I) iodide complex of pyridine, which crystallizes in the orthorhombic space group $P2_12_12_1$ with one cluster in the asymmetric unit.[16]

The zinc dibromide complex, **8**, crystallizes in the chiral monoclinic space group $P2_1$, with four molecules of **2** and two zinc dibromide moieties in the asymmetric unit. The complex consists of two independent zinc atoms, each coordinated by two chiral ligand molecules and two bromine atoms, one unit of which is shown in Figure 3. The zinc atoms are coordinated by two molecules of **2**, through the least hindered nitrogen atoms, with Zn-N bond lengths of 2.080(6) and 2.086(7) Å for one Zn atom, and 2.089(7) and 2.105(6) Å for the other. The zinc atoms are also coordinated by two bromine atoms, with Zn-Br bond lengths in the range 2.3439(2) – 2.3585(2) Å. The zinc atoms have slightly distorted tetrahedral coordination environments, with the largest distortion being the angles between the bromine atoms, which are 119.54(6)º and 118.20(6)º for Zn1 and Zn2, respectively. The bond lengths and bond angles of this complex are similar to those found in the tetrahedral zinc dibromide complex of the less sterically hindered molecule pyrazine.[17] However, this complex is a one-dimensional polymer, which in the present case is not formed, presumably due to the more sterically hindered coordination environment of the non-coordinating nitrogen atom.

In conclusion, we have shown that the chiral ligand **2** can bind to transition metals to form discrete complexes in which **2** acts as a monodentate ligand, with coordination through the less hindered of the two nitrogen atoms.

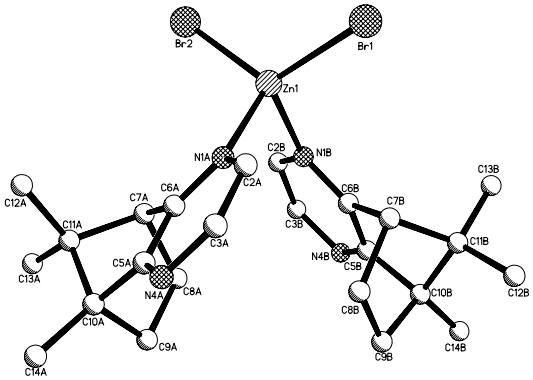
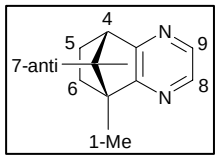


Figure 3. Perspective view of one of the independent zinc complexes **8**, with atomic numbering shown. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and bond angles (º): Zn1-N1B 2.081(6), Zn1-N1A 2.089(7), Zn1-Br2 2.3435(13), Zn1-Br1 2.3583(14), N1B-Zn1-N1A 94.4(3), N1B-Zn1-Br2 108.4(2), N1A-Zn1-Br2 110.8(2), N1B-Zn1-Br1 111.3(2), N1A-Zn1-Br1 109.5(2), Br2-Zn1-Br1 119.56(6).

Experimental Section

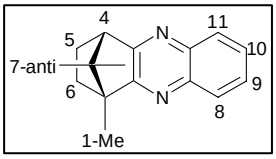
General Procedures. NMR spectra were recorded with a Varian 300 MHz NMR spectrometer. Melting points were performed on an Electrothermal melting point apparatus and are uncorrected. Elemental analyses were performed by the Campbell microanalytical laboratory at the University of Otago.

Preparation of 2:



The intermediate dihydropyrazine[12] (4.35g, 22.8mmol) and potassium hydroxide (3.21g, 57.2mmol) were stirred in dry ethanol (50mL) at 50°C as oxygen was bubbled through the solution for 24hrs. The solvent was removed *in vacuo* and the residue extracted with CH_2Cl_2 (2x50mL). The organic phase was washed with water (25mL), dried (Na_2SO_4) and the solvent removed *in vavuo* to give a colourless crystalline solid. This was recrystallized from 1:1 pet ether/EtOAc to give **2** as colourless crystals. Yield 3.21g (75%). M.p. 59°C (lit.[18] 52-55°C). ^{1}H NMR (300MHz, $CDCl_3$): δ 8.12 (2H, m, H8,H9), 2.94 (1H, d, H4), 2.21 (1H, m, $H6_{exo}$), 1.96 (1H, m, $H5_{exo}$), 1.32 (3H, s, H1-Me), 1.27 (2H, dd, $H5_{endo}$, $H6_{endo}$), 1.03 (3H, s, H7-*anti*), 0.57 (3H, s, H7-*syn*). ^{1}H NMR (300MHz, CD_3CN): δ 8.16 (2H, m, H8,H9), 2.94 (1H, d, H4), 2.21 (1H, m, $H6_{exo}$), 2.04 (1H, m, $H5_{exo}$), 1.34 (3H, s, H1-Me), 1.24 (2H, dd, $H5_{endo}$, $H6_{endo}$), 1.09 (3H, s, H7-*anti*), 0.59 (3H, s, H7-*syn*).

Preparation of 3:



Camphorquinone (1.66g, 10.0mmol) and freshly sublimed *o*-phenylenediamine (1.09g, 10.1mmol) were refluxed in acetic acid (20mL) for 4 hours. The reaction mixture was neutralised with NaOH and extracted with ether (2x50mL). The organic phase was dried to give a yellow oil, which solidified on standing. This was purified by column chromatography (20g silica, 1:3 pet ether/EtOAc) to give **3** as a colourless crystalline solid. Yield 1.41g (59%). M.p. 76°C (lit.[13] 78°C). ^{1}H NMR (300MHz, $CDCl_3$): δ 8.05 (2H, m, H8,H11), 7.61 (2H, m, H9,H10), 3.05 (1H, d, H4), 2.30 (1H, m, $H6_{exo}$), 2.06 (1H, m, $H5_{exo}$), 1.44 (3H, s, H1-Me), 1.43 (2H, dd, $H5_{endo}$, $H6_{endo}$), 1.12 (3H, s, H7-*anti*), 0.63 (3H, s, H7-*syn*).

Preparation of 6:

Reaction of **2** (9.6mg, 0.051mmol) dissolved in hot methanol with copper(II) nitrate (24.8mg, 0.10mmol) dissolved in hot methanol gave a blue solution. A crystalline product suitable for X-ray crystal structure analysis appeared on evaporation of the reaction mixture. Yield 12.2mg (80%). M.p. >200°C (dec.). Anal. Found: C, 31.24; H, 4.28; N, 13.26. Calc. for $C_{36}H_{48}N_{14}O_{24}Cu_4.4H_2O.2MeOH$: C, 31.45; H, 4.45; N, 13.51.

Preparation of 7:
Reaction of **2** (18.7mg, 0.1mmol) dissolved in acetonitrile with copper(I) iodide (19.3mg, 0.10mmol) dissolved in hot acetonitrile gave a yellow solution. Crystals suitable for X-ray diffraction were obtained by slow evaporation of the reaction mixture. Yield 21.6mg (73%). M.p. 208-209°C. Anal. Found: C, 38.09; H, 4.29; N, 7.39. Calc. for $C_{12}H_{16}N_2CuI$: C, 38.06; H, 4.26; N, 7.40. ^{1}H NMR (300MHz, CD_3CN): δ 8.35 (2H, m, H8,H9), 3.36 (1H, d, H4), 2.28 (1H, m, $H6_{exo}$), 2.05 (1H, m, $H5_{exo}$), 1.36 (3H, s, H1-Me), 1.27 (2H, dd, $H5_{endo}$, $H6_{endo}$), 1.11 (3H, s, H7-*anti*), 0.60 (3H, s, H7-*syn*).

Preparation of 8:
Reaction of **2** (9.3mg, 0.05mmol) dissolved in methanol with zinc bromide (23.4mg, 0.10mmol) dissolved in hot methanol gave a colourless solution. Crystals suitable for X-ray diffraction were obtained by slow evaporation of the reaction mixture. Yield 15.6mg (64%). M.p. 223-224°C. Anal. Found: C, 46.68; H, 5.38 N, 9.05. Calc. for $C_{24}H_{36}N_2ZnBr_2.H_2O$: C, 46.59; H, 5.21; N, 9.07.

X-Ray Crystallography. Data were collected with a Siemens SMART CCD area detector, using graphite monochromatized MoKα radiation (λ = 0.71073 Å). The intensities were corrected for Lorentz and polarization effects and for absorption.[19] The structure was solved by direct methods using SHELXS[20] and refined on F^2, using all data, by full-matrix least-squares procedures using SHELXTL.[21] All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in calculated positions, with isotropic displacement parameters 1.2 times the isotropic equivalent of their carrier carbons. Complete crystallographic data, as a CIF file, have been deposited with the Cambridge Crystallographic Data Centre (CCDC Nos 278409 - 278411). Copies can be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (e-mail: deposit@ccdc.cam.ac.uk).

Crystal data for 6: $C_{24}H_{32}CuN_6O_8$, MW 596.10, orthorhombic, $C222_1$, thin blue plate, 0.45 x 0.14 x 0.01 mm, *a* = 7.494(6), *b* = 30.58(3), *c* = 12.065(11) Å, V = 2765(4) Å ^{3}, Z = 8, T = -105°C, F(000) = 1244, μ (MoKα) = 0.847 mm^{-1}, D_{calcd} = 1.432 g.cm^{-3}, $2\theta_{max}$ 48° (CCD area detector, 99.9% completeness), wR(F^2) = 0.299 (all 2176 data), R = 0.124 (1447 data with I > 2σI).

Crystal data for 7: $C_{48}H_{64}Cu_4I_4N_8$, MW 1514.83, monoclinic, C2, yellow plate, 0.58 x 0.46 x 0.04 mm, *a* = 27.931(8), *b* = 12.439(4), *c* = 15.743(5) Å, β = 100.842(4) °, V = 5372(3) Å ^{3}, Z = 4, T = -105°C, F(000) = 2944, μ (MoKα) = 3.901 mm^{-1}, D_{calcd} = 1.873 g.cm^{-3}, $2\theta_{max}$ 50.5° (CCD area detector, 99.8 % completeness), wR(F^2) = 0.096 (all 8954 data), R = 0.040 (8046 data with I > 2σI).

Crystal data for 8: $C_{24}H_{32}Br_2N_4Zn$, MW 601.73, monoclinic, $P2_1$, colourless block, 0.51 x 0.36 x 0.11 mm, *a* = 10.559(4), *b* = 19.801(8), *c* = 12.833(5) Å, β = 103.811(5) °, V = 2605.5(17) Å ^{3}, Z = 4, T = -105°C, F(000) = 1216, μ (MoKα) = 4.027

mm^{-1}, D_{calcd} = 1.534 $g.cm^{-3}$, $2\theta_{max}$ 50° (CCD area detector, 99.7% completeness), $wR(F^2)$ = 0.225 (all 9148 data), R = 0.091 (8394 data with $I > 2\sigma I$).

Acknowledgement

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Graphical Abstract

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