

Transition Metal Complexes of Derivatized Chiral Dihydro-1,2,4-triazin-6-ones, Part IV [1]. Synthesis and Structural Characterization of a Copper(II) Complex of (*L*)-3-Acetyl-5-benzyl-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one Oxime

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Dihydro-1,2,4-triazin-6-one Oxime, Copper(II) Complex, Square Pyramidal Complex

Reaction of (*L*)-3-acetyl-5-benzyl-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one oxime (**1**) with copper acetate afforded the complex **5** in high yield. Single crystal X-ray structural analysis of **5** revealed a square-pyramidal geometry around the copper ion where the two oxime ligands are coordinated symmetrically to the Cu atom. The apex of the square-pyramid is occupied by a chloride ligand with the copper atom roofed above the center of the plane of the four coordinating nitrogens by about 0.22 Å. MS-FAB, magnetic and other analytical data are in accord with this solid-state structure.

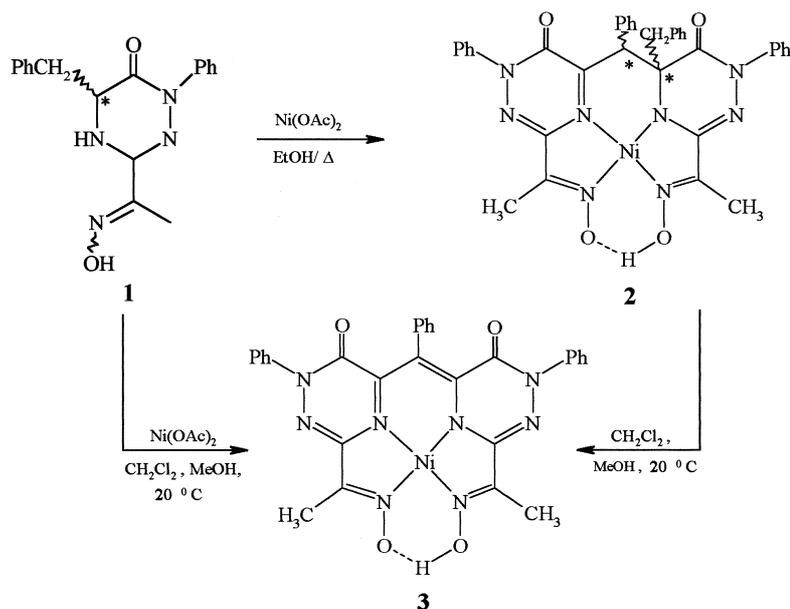
Introduction

We reported earlier on the reaction of oxime **1** with nickel(II) acetate in ethanol, whereby the square planar complex **2** was obtained in which the two oxime ligands coordinated in a symmetrical fashion (Scheme 1) [2]. An interesting structural feature of **2** is the formation of a carbon-carbon bond that links the benzylic carbon of one ligand to the stereocenter (C-5) of the other partner ligand as evidenced by an X-ray crystal structure analysis [2]. A similar reaction of oxime **1** with palladium acetate gave a square-planar complex in which the oxime ligands coordinated in an unsymmetrical manner and for which no carbon-carbon coupling was observed [3]. It was noticed that the brown-red colour of a solution of **2** in dichloromethane changed slowly to bright-red. The reaction of oxime **1** with nickel acetate in dichloromethane/methanol gave also the same bright-red coloured solution. The crude products obtained from both bright-red solutions were found to be mixtures and were purified on preparative silica gel tlc plates and the scarlet byproducts obtained

(10–15% yield) were found to be identical. The molecular ion (M^+) was found to be 604 which is consistent with the elimination of a toluene molecule from **2** to give **3** (Scheme 1). Similar behaviour was observed with the nickel(II) complex of the alanine analogue of oxime **1** and a structurally similar complex to **3** was obtained with M^+ 533 which is consistent with the elimination of methane [4].

These observations prompted us to investigate the reactions of oxime **1** with other transition metal ions such as copper(II) for which numerous examples of square-planar complexes of Cu(II) are known.

In this paper we report on the reaction of **1** with copper(II) acetate. We found that copper(II) behaves in a fashion analogous to nickel(II) with respect to the formation of the square-planar structural moiety ($M-4N$), present in **3**. In addition, a chlorine atom occupies a fifth coordination site giving rise to a square-pyramidal geometry around the copper(II) ion **5** (Scheme 2).



Scheme 1.

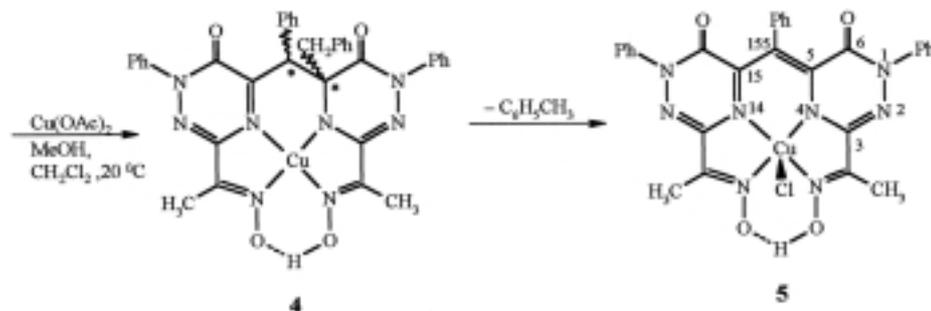
Results and Discussion

The reaction of oxime **1** with copper(II) acetate in dichloromethane gave a crude deep-red product which was identified as a mixture of complexes **4** and **5**, (**5** being obtained from **4** after the elimination of toluene, Scheme 2). Contrary to the nickel complex **2** which was obtained in large yields, the analogous complex of copper **4** was only accessible in minute quantities, *i.e.* as an impurity with **5**. It is also possible to obtain **5** by mixing the reactants in refluxing ethanol and as such both nickel and copper complexes behave similarly with regard to the loss of toluene.

Complex **5** has a molar conductance of $1.1\text{ s cm}^{-2}\text{ mol}^{-1}$ in dichloromethane which indicates a non-electrolyte nature of this complex [5]. The mag-

netic moment of **5** is 1.82 BM which is typical for Cu(II) (d^9 system). The molecular ion peak in the mass spectrum was found at $m/z = 646$, and this is consistent with the formula $\text{CuC}_{29}\text{H}_{22}\text{N}_8\text{O}_4$ (609) plus a chlorine atom.

An X-ray crystal structure analysis of **5** has been performed. The crystallographic data are summarized in Table 1. A molecular plot (Fig. 1) shows that the copper ion is coordinated to both ligands *via* the amidrazone ring nitrogen HN(4) and the oxime nitrogen. The bond lengths indicate π -bond formation between N14–C15, in addition to a π -bond linking the benzylic carbon C155 of one ligand to the ring carbon C5 of the other partner ligand as shown in structure **5** (Scheme 2 and Fig. 1). Comparison of the bond distances in the Ni-containing six-membered chelate ring in **2**



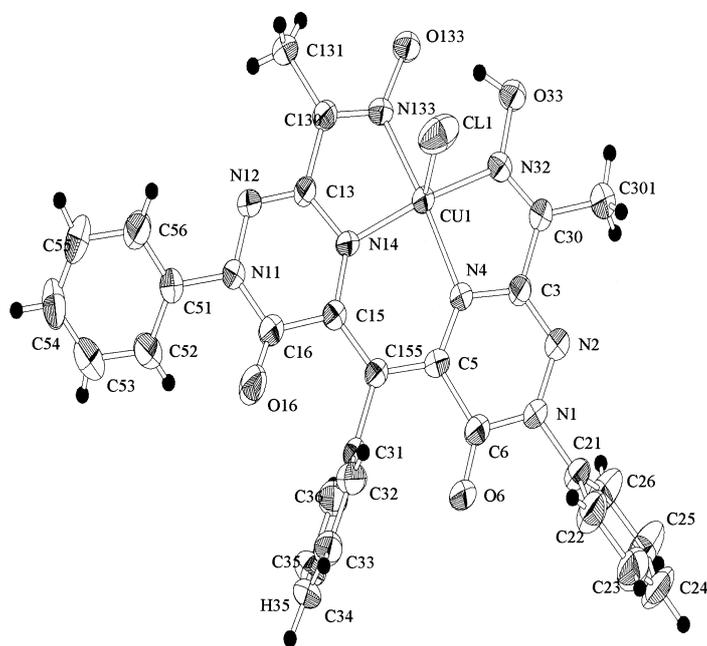
Scheme 2.

| | | | |
|--------------------|------------|---------------------|------------|
| Cu(1)–N(4) | 1.938(3) | N(4)–Cu(1)–N(14) | 92.63(12) |
| Cu(1)–N(14) | 1.920(3) | N(32)–Cu(1)–N(132) | 96.81(13) |
| Cu(1)–N(32) | 1.963(3) | N(4)–Cu(1)–N(132) | 166.91(12) |
| Cu(1)–N(132) | 1.946(3) | N(14)–Cu(1)–N(32) | 166.65(13) |
| Cu(1)–Cl(1) | 2.5938(11) | N(4)–Cu(1)–Cl(1) | 103.42(9) |
| N(4)–C(5) | 1.342(4) | N(14)–Cu(1)–Cl(1) | 101.95(9) |
| N(14)–C(15) | 1.351(4) | N(32)–Cu(1)–Cl(1) | 91.38(10) |
| N(4)–C(3) | 1.384(4) | N(132)–Cu(1)–Cl(1) | 89.66(9) |
| N(14)–C(13) | 1.377(4) | C(5)–N(4)–Cu(1) | 127.6(2) |
| N(32)–C(30) | 1.285(5) | C(15)–N(14)–Cu(1) | 127.5(2) |
| N(132)–C(130) | 1.295(5) | N(4)–C(5)–C(155) | 123.7(3) |
| N(32)–O(33) | 1.367(4) | N(14)–C(15)–C(155) | 123.8(3) |
| N(132)–O(133) | 1.337(4) | C(5)–C(155)–C(15) | 124.1(3) |
| C(5)–C(155) | 1.425(5) | C(5)–C(155)–C(31) | 118.7(3) |
| C(15)–C(155) | 1.421(5) | N(4)–C(5)–C(6) | 116.1(3) |
| C(3)–C(30) | 1.480(5) | N(14)–C(15)–C(16) | 115.5(3) |
| C(13)–C(130) | 1.477(5) | C(3)–N(4)–Cu(1) | 110.8(2) |
| C(5)–C(6) | 1.510(5) | C(13)–N(14)–Cu(1) | 111.0(2) |
| C(15)–C(16) | (5) | C(30)–N(32)–Cu(1) | 116.0(3) |
| N(4)–Cu(1)–N(32) | 83.4 (13) | C(130)–N(132)–Cu(1) | 114.8(2) |
| N(14)–Cu(1)–N(132) | 84.19(12) | O(33)–N(32)–Cu(1) | 124.5(2) |
| | | O(133)–N(132)–Cu(1) | 122.9(9) |

Table 1. Relevant bond lengths (Å) and angles (°).

(Scheme 1) [2] with those of the analogous Cu-containing ring in **5** (Scheme 2) indicates clearly that conjugation is only present in the ring of **5**. It seems that this conjugation, which is probably the driving force for the elimination of toluene from complex **4** to produce **5**, is the reason for the deep-red colour of complex **5**. This conjugation is evidenced from the bond lengths of C5–C155 and

C15–C155 which are about equal to 1.42 Å. This value is intermediate between single and double bonds. Likewise, the C5–N4 and C15–N14 bond lengths are about equal to 1.34 Å, which is also an intermediate value between C–N and C=N bond lengths. The data (Table 1) strongly support an almost complete delocalization of both C=C and C=N π -bonds and as such the chelate ring is por-

Fig. 1. ORTEP plot of the molecular structure of **5**.

phonic-type. Surprisingly, the molecular structure shows the presence of a chlorine atom bonded to the Cu center. The source of this Cl is not definitely known, but it could be from the chlorinated solvent used in the preparation and recrystallization processes [6]. The Cu–Cl bond distance is ~ 2.6 Å and it is slightly longer than a normal Cu–Cl bond length of ~ 2.3 Å. An interesting observation is the position of the Cu²⁺ ion being roofed above the center of the plane of the four coordinating nitrogens by about 0.221 Å. This phenomenon is known in the porphyrin complex of iron in heme proteins where iron is situated above the plane of the four coordinated N atoms of porphyrin by as much as 0.75 Å. This makes the overall geometry of complex **5** a slightly distorted square-pyramidal geometry. Finally, there is one solvent molecule each of CH₂Cl₂ and of C₆H₁₂ in the unit cell of **5** originating from the solvent-pair used in the recrystallization process. Their presence is probably due to the fact that the single crystal used in the X-ray work was taken straight from the solution and kept at 220 K during the process of data collection. These solvent molecules were not shown in the elemental analysis of a dry sample.

Trace element copper plays a vital role in living organisms where it serves as an essential metallo-enzyme active site “cofactor” [7]. Currently, copper complexes capable of cleaving or hydrolyzing nucleic acids, are receiving considerable interest [7]. Hence, the synthesis and bioassay of several type **3** copper(II) complexes, incorporating various masked α -amino acid residues such as tyrosine and histidine, are in progress.

Experimental Section

Melting points (uncorrected) were determined using a Gallenkamp melting point apparatus in one-end open glass capillaries. The magnetic moment was measured for a finely ground solid sample of **5** at ambient temperature using a Johnson Matthey Magnetic Susceptibility Balance. MS-FD spectra for M⁺ molecular ions were obtained using a Finnigan MAT TSQ-70 spectrometer at 70 eV; ion source temperature = 200 °C. MS-FAB spectra were obtained with a VG Analytical Ltd. ZAB HS mass spectrometer, equipped with xenon gun operating at 8 keV and 0.8 mA emission, using as the sample containing matrix CHCl₃, TG/G (thioglycerol/glycerol) or NBA (3-nitrobenzyl alcohol).

Molar conductivities (Λ_M) for the complexes were determined for 10⁻³ M solutions in dichloromethane using a JENWAY Conductivity Meter 4310. Elemental analyses were performed at the Laboratories of Quantitative Technologies Inc. (QTI), New Jersey, USA.

(*L*)-3-Acetyl-5-benzyl-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one oxime (**1**)

The preparation of this compound has been described previously [2].

Benzylidene-5,5'-[3-acetyloximato-6-oxo-1-phenyl-4,5-dihydro-1,2,4-triazine]chlorocopper(II) (**5**)

Copper(II) acetate monohydrate (1.0 g, 5 mmol) in methanol (60 ml) was added to a solution of the oxime (**1**) (3.22 g, 10 mmol) in dichloromethane–methanol solvent mixture (100 ml, 1:2 v/v). The resulting reaction mixture was stirred overnight at 20 °C. Evaporation of the organic solvents gave a deep-red solid which was purified by preparative TLC chromatography on precoated 0.5 mm silica gel glass plates (60 F₂₅₄, Merck), employing chloroform as the developing solvent. The fast moving scarlet coloured fraction ($R_f \sim 0.25$) was collected and recrystallized from dichloromethane/cyclohexane mixed solvent. Yield of pure product (1.7 g, 55%), m.p. = >300 °C; MS (pos. FAB in CH₂Cl₂, TG/G): $m/z = 646$ corresponding to [M+H]⁺, pos. FAB exact mass = 645.5447; these values are consistent with CuC₂₉H₂₂N₈O₄Cl (645.546). – CuC₂₉H₂₂N₈O₄Cl: calcd. C 53.96, H 3.44, N 17.36, Cl 5.49; found C 53.75, H 3.69, N 16.98, Cl 5.41.

Crystal structure determination of **5**

Deep-red needle-like crystals were grown by allowing a solution of **5** in dichloromethane/cyclohexane solvent pair (4:1 v/v) to stand at ambient temperature for 60 h (open flask); crystal dimensions: $0.2 \times 0.02 \times 0.03$ mm. Crystal data for C₂₉H₂₂N₈O₄CuCl, CH₂Cl₂, C₆H₁₂: FW = 814.62, monoclinic, space group $P2_1/n$, with $a = 11.1202$ (6), $b = 18.8120$ (12), $c = 17.6771$ (8) Å, $\alpha = 90^\circ$, $\beta = 92.711(6)^\circ$, $\gamma = 90^\circ$, $V = 3693.8$ (4) Å³, $Z = 4$, $d_{\text{calcd}} = 1.465$ g/cm³. Data collection was made at 220(2) K on a STOE IPDS diffractometer. $F(000) = 1680$, $\mu = 0.860$ mm⁻¹. 34495 independent reflections were collected within the scan range $\theta = 2.38$ – 25.89° using Mo- K_α radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods using the program SHELXS-86 [8]. All non-hydrogen atoms were refined anisotropically

by full-matrix least-squares procedure based on F^2 using all unique data with SHELXL-97 [9]. The hydrogen atoms were found in the difference Fourier maps and were refined isotropically. This resulted in R values $R_1 = 0.0896$, $wR_2 = 0.1315$ for all data and $0.0517(0.1181)$ for the 7030 observed reflections [$R_{\text{int}} = 0.1194$] and 560 variable parameters. GOF = 0.903, largest peak and hole in final Fourier difference map were 0.668 and $-0.394 \text{ e} \cdot \text{Å}^{-3}$, respectively.

Supplementary material

Further information on the X-ray crystal structure data of compound **5** can be ordered from the Cambridge Crystallographic Data Center (E-mail: deposit@ccdc.cam.ac.uk) under the depository number CCDC 180576.

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