Monatshefte für Chemie 129, 843–853 (1998)

Monatshefte für Chemie
Chemical Monthly

Printed in Austria

Crystal Structures of Copper(II) Complexes of Some 2-Methyl-8-quinolinols and Implications for their Antifungal Activity

Massud Shoja[1,*], **Herman Gershon**[1,2], **Diana Bray**[1], and **Donald D. Clarke**[1]

[1] Department of Chemistry, Fordham University, Bronx, NY 10458, USA
[2] New York Botanical Garden, Bronx, NY 10458, USA

Summary. A hypothesis that the geometry of a potential fungicide must be consistent with that of the pores of the fungal spore wall in order to penetrate it and be toxic has been developed. Certain *bis*(8-quinolinolato)copper(II) complexes seemed to contradict this. To resolve this issue, structures of *bis*(7-fluoro-8-quinolinolato)copper(II) (**1**), *bis*(2-methyl-8-quinolinolato)copper(II) (**2**), and *bis*(2-methyl-7-nitro-8-quinolinolato)copper(II) (**3**) were solved. The ligands of **1** are square planar with copper at the center of symmetry. In **2** and **3** the methyl group at C2 interacts with the other 8-quinolinol ligand, producing a significant distortion of the square planar geometry which causes a rotation about the N-Cu-N axis and allows the molecules to be polar, more compact, and manifest their toxicity. Bis(7-Nitro-8-quinolinolato)copper(II) is square planar and nontoxic.

Keywords. Crystal structures; Bis(8-quinolinolato)copper(II) complexes; Bis(7-fluoro-8-quinolinolato)copper(II); Bis(2-methyl-7-nitro-8-quinolinolato)copper(II); Bis(2-methyl-8-quinolinolato)copper(II).

Kristallstrukturen der Kupfer(II)-Komplexe einiger 2-Methyl-8-chinolinole und ihre Bedeutung für deren fungizide Eigenschaften

Zusammenfassung. Einer Hypothese zufolge muß die Geometrie eines potentiellen Fungizids mit jener der Poren in der Sporenwand der Pilze übereinstimen, um sie durchdringen und seine fungizide Wirkung entfalten zu können. Die Eigenschaften gewisser *Bis*(8-chinolinolato)kupfer(II)-Komplexe schienen dem zu widersprechen. Zur Auflösung dieser Diskrepanz wurden die Kristallstrukturen von *Bis*(7-fluoro-8-chinolinolato)kupfer(II) (**1**), *Bis*(2-methyl-8-chinolinolato)kupfer(II) (**2**) und *Bis*(2-methyl-7-nitro-8-chinolinolato)kupfer(II) (**3**) bestimmt. Die Liganden von **1** sind quadratisch-planar mit Kupfer im Symmetriezentrum. In **2** und **3** tritt eine sterische Wechselwirkung der Methylgruppe an C2 mit dem jeweils anderen 8-Chinolinol-Liganden auf, die zu einer deutlichen Verzerrung der quadratisch-planaren Struktur führt. Die dadurch auftretende Rotation um die N-Cu-N-Achse macht das Molekül polarer, kompakter und toxisch. *Bis*(7-nitro-8-chinolinolato)kupfer(II) ist quadratisch-planar und ungiftig.

* Corresponding author

Introduction

It has been hypothesized that the fungal spore wall is a barrier to certain potential antifungal agents, including 8-quinolinolato complexes of copper(II) [1]. These complexes are known generally to be square planar and be equally charged at opposite ends of the long axis [2]. It was suggested that the spore wall has pores with zero net charge composed of alternate positive and negative charges around the peripheries of the pores. The complexes, when placed in a growth medium along with fungal spores, are brought parallel to the pores by electrostatic attraction. When the axes of the complex are smaller than the pore diameters, the complex can penetrate the spore; otherwise, the complex is excluded. Dipolar complexes can penetrate the spore at an angle dependent on the net charge at one end of the compound. Thus, polar molecules having longer axes would be able to penetrate the spore wall, whereas nonpolar molecules with shorter axes cannot. If a potentially toxic compound is excluded from the cell is cannot be toxic. That the pores are not circular has been reported in subsequent studies [3–5].

To gain further insight, the copper(II) complexes of 2-methyl-8-quinolinols with fluoro, chloro, bromo, iodo, and nitro substituents in positions 5 and 7 have been prepared and characterized [6]. Antifungal evaluation of these compounds (unpublished data) yielded results demonstrating significant fungitoxicity which could not be explained by the spore wall hypothesis. This was based on dimensions calculated for *bis*(8-quinolinolato)copper(II) complexes of 5- and 7-nitro-8-quinolinols which were considered to be square planar and found not to be fungitoxic [1, 7]. Hence, the copper(II) complexes of 2-methyl-5- and 7-nitro-8-quinolinols were not expected to be fungitoxic, assuming that they were square planar and even larger than compounds with an H atom at C2. It was important to determine whether or not copper(II) complexes of 2-methyl-8-quinolinols were square planar. Therefore X-ray crystal structures of *bis*(7-fluoro-8-quinolinolato)-copper(II) (**1**), *bis*(2-methyl-8-quinolinolato)copper(II) (**2**), and *bis*(2-methyl-7-nitro-8-quinolinolato)copper(II) (**3**) were determined. The fluoro compound was included to confirm that the nonmethylated *bis*-complexes are square planar.

Results and Discussion

The ligands in **1** (Fig. 1) are arranged similarly to those in zinc 8-quinolinolate dihydrate [9] which also has the metal ion located at the center of symmetry, giving $Z = 2$. Copper 8-quinolinolate is reported to show a twist along the N-Cu-N axis [10], but other results indicate a square planar arrangement of the ligands [2]. Compounds **2** and **3** (Figs. 2 and 3) exhibit a twist around the O-Cu-O axis, resulting in a significant distortion of the planar arrangement. **1**, **2** and **3** form monoclinic crystals (space group: $P2_1/c$; lattice constants: $a = 10.409(1)$ Å, $b = 5.420(1)$ Å, $c = 16.161(1)$ Å, $\beta = 127.48(1)^\circ$, $Z = 2$ for **1**; $a = 7.551(7)$ Å, $b = 24.761(3)$ Å, $c = 11.800(2)$ Å, $\beta = 129.36(6)^\circ$, $Z = 4$ for **2**; $a = 20.178(2)$ Å, $b = 10.796(2)$ Å, $c = 13.497(2)$ Å, $\beta = 129.79(2)^\circ$, $Z = 4$ for **3**.

On comparing the three structures, the most striking feature is the effect of the substituent at C2. In **1**, fluorine causes no distortion of the coordination sphere. The ligands are square planar with copper located at the center of symmetry. In **2** and **3**

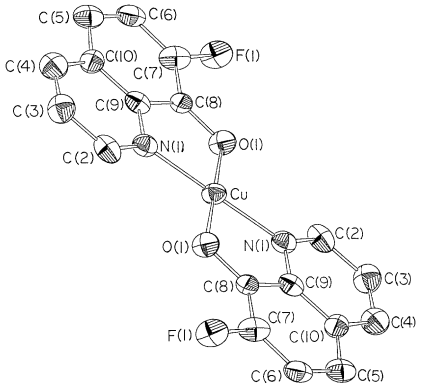

Fig. 1. ORTEP view of $Cu(C_{18}H_{10}O_2N_2F_2)$ (**1**)

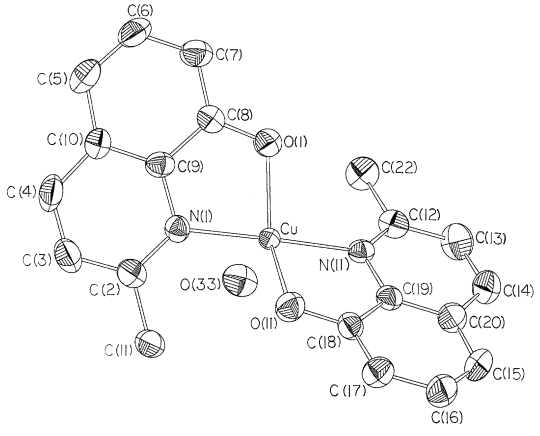

Fig. 2. ORTEP view of $Cu(C_{20}H_{16}O_2N_2) \cdot H_2O$ (**2**)

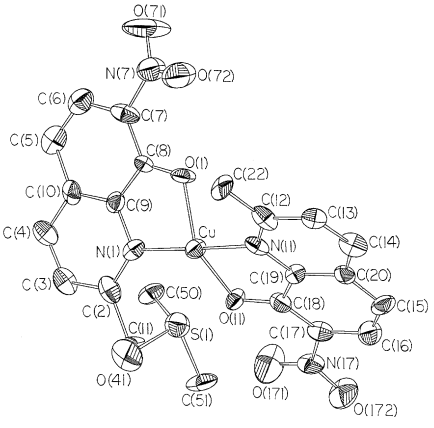

Fig. 3. ORTEP view of $Cu(C_{20}H_{14}O_6N_4) \cdot C_2H_6OS$ (**3**)

Table 1. Minimal antifungal activity (mmol/l (μg/ml)) of copper(II) complexes of 2-methyl-8-quinolinols and 2-unsubstituted 8-quinolinols is *Saboraud* dextrose broth at 28°C in shake cultures after six days[a]

Copper(II) *bis*-complexes	*A. niger*	*A. oryzae*	*M. verrucaria*	*T. viride*	*M. cirinelloides*	*T. mentagrophytes*
8-Quinolinol	0.034 (5)	0.034 (5)	0.028 (4)	0.041 (6)	>0.69 (>10^2)	0.021 (3)
7-Fluoro-8-quinolinol	>0.61 (>10^2)	>0.61 (>10^2)	<0.0061 (<1)	>0.61 (>10^2)	>0.61 (>10^2)	<0.0061 (<1)
5-Nitro-8-quinolinol	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)
7-Nitro-8-quinolinol	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)	>0.50 (>10^2)
2-Methyl-8-quinolinol	0.19 (30)	0.19 (30)	0.19 (30)	0.31 (50)	0.38 (60)	0.13 (20)
2-Methyl-5-nitro-8-quinolinol	>0.46 (>10^2)	<0.0046 (<1)	<0.0046 (<1)	0.014 (3)	>0.46 (>10^2)	<0.0046 (<1)
2-Methyl-7-nitro-8-quinolinol	>0.46 (>10^2)	>0.46 (>10^2)	<0.0046 (<1)	>0.46 (>10^2)	>0.46 (>10^2)	<0.0046 (<1)

[a] Test levels: 10 and 10^2 μg/ml; levels from 10–10^2 μg/ml were carried out in increments of 10 and from 1–10 in increments of 1 μg/ml

the methyl group at C2 interacts with the other substituted 8-quinolinol ligand, producing a significant distortion of the square planar arrangement. This distortion takes the form of a rotation about the N1-Cu-N11 axis (178°). The two ligand oxygens are bent out of the plane with O1-Cu-O11 by 135.5(7)° and 138.9(8)° for **2** and **3**, respectively. The dihedral angle between the planes formed by Cu-O1-C8-C9-N1 and Cu-O11-C18-C19-N11 is 45.6(4)° for **2** and 41.4(5)° for **3**. Whereas other substituted *bis*(8-quinolinolato)copper(II) complexes have been suggested to be nonplanar based on their stability constants [11], these are the first nonplanar structures for this type of complex which have been established rigorously.

Table 1 contains the antifungal properties of the *bis*-complexes of copper(II) with seven ligands (8-quinolinol and its 7-fluoro, 5- and 7-nitro analogues as well as 2-methyl-8-quinolinol and its 5- and 7-nitro analogues) against six fungi: *Aspergillus niger*, *A. oryzae*, *Myrothecium verrucaria*, *Trichoderma viride*, *Mucor cirinelloides*, and *Trichophyton mentagrophytes*. It should be noted that square planar *bis*(8-quinolinolato)copper(II) and its 7-fluoro analogue did not inhibit *M. cirinelloides* at over 10^2 μg/ml, whereas *bis*(2-methyl-8-quinolinolato)copper(II) which is not square planar did so at 60 μg/ml. This is consistent with previous results that non-polar *bis*(8-quinolinolato)copper(II) is not toxic to *M. cirinelloides*, and the mixed ligand complexes (8-quinolinolato)(salicylato)copper(II), (8-quinolinolato)(3-hydroxy-2-naphthoato)copper(II), (8-quinolinolato)(4-bromo-3-hydroxy-2-naphthoato)copper(II), and (8-quinolinolato)(3,5-diiodosalicylato)copper(II) which are polar are toxic to *M. cirinelloides* [12]. The copper(II) complexes of 5- and 7-nitro-8-quinolinols did not inhibit the six fungi at over 10^2 μg/ml. *Bis*(2-methyl-7-nitro-8-quinolinolato)copper(II) completely inhibited *M. verrucaria* and *T. mentagrophytes* at concentrations below 1 μg/ml and none of the rest above 10^2 μg/mL. *Bis*(2-methyl-5-nitro-8-quinolinolato) copper(II) inhibited *A. oryzae*, *M. verrucaria*, and *T. mentagrophytes* below 1 μg/ml and *T. viride* at 3 μg/ml. *A. niger* and *M. cirinelloides* were not inhibited above 10^2 μg/ml. It is thus evident that the geometry and polarity of a potential toxicant plays a significant role in its ability to penetrate the spore walls of fungi and thus to express its toxicity.

Surface layers (S-layers) have been found in bacterial cell envelopes and in cell walls and spore coats of algae. Due to the crystalline nature of the S-layers, they possess uniform pore morphologies and can behave as protective coats to the organism with sharp exclusion limits [13, 14]. These cells can thus be protected against biocides the shapes of which are incompatible with the geometries of the pores. S-layers have not yet been reported in the filamentous fungi including those employed here.

Experimental

X-Ray structure determinations

Crystals suitable for X-ray analysis were obtained by crystallization from dimethyl formamide (**1**) and dimethyl sulfoxide (**2** and **3**). Intensities were collected on an Enraf-Nonius CAD4 diffractometer using the $\omega-2\theta$ mode. A summary of crystal and intensity collection data is given in Table 2.

Table 2. Crystallographic data

	1	**2**	**3**
Formula	$CuC_{18}H_{10}O_2N_2F_2$	$CuC_{20}H_{16}O_2N_2\ H_2O$	$CuC_{20}H_{14}O_6N_4 \cdot C_2H_6OS$
Molecular weight	387.83	397.92	548.03
Crystal dimensions (mm)	$0.2 \times 0.2 \times 0.1$	$0.4 \times 0.4 \times 0.2$	$0.2 \times 0.2 \times 0.05$
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$
a (Å)	10.409 (1)	7.551 (7)	20.178(2)
b (Å)	5.420(1)	24.761(3)	10.796(2)
c (Å)	16.161(1)	11.800(2)	13.497(2)
β (°)	127.48(1)	129.36(6)	129.79(2)
V (Å^3)	723.5(2)	1706.0(2)	2259.5(6)
Z	2	4	4
D_c (g.cm^{-3})	1.788	1.549	1.611
λ (Å)	0.71073	0.71073	0.71073
Temperature (°C)	20	20	20
$(\sin\theta)/\lambda$	1.08	1.08	0.90
Total reflections collected	1493	3376	2406
Unique reflections collected	1268	2987	2097
Observed reflections ($I > 3\sigma$)	1001	1535	1131
Final R	0.029	0.035	0.041
Final R_w	0.033	0.039	0.046
S	0.818	1.76	2.71

Structures were solved by direct methods using the XTAL 3.4 system of programs [15] which showed all non-hydrogen atoms, including a water molecule in **2** and a molecule of dimethyl sulfoxide in **3**. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares methods. The hydrogen atoms were located on a difference electron density map. In the last cycle of refinement, H atoms were fixed at idealized positions (0.95 Å) except for hydrogens associated with the water molecule in **2** which resulted in the highest peaks in the difference map (0.9 Å^{-3} after the last cycle of least squares). These peaks were near the oxygen of the water molecule, but could not be resolved into discrete hydrogen positions, and any inclusion of these peaks with partial occupancy didn't improve agreement between the model and the data. The quantity minimized in the least squares calculations for all three compounds was $\Sigma w(|F_o|-|F_c|)^2$. All calculations were performed on a Dell OptiPlex GXpro. The final fractional atomic coordinates for non-hydrogen atoms are given in Table 3. Selected bond distances and bond angles for the three compounds are given in Table 4.

Antifungal testing

Methods previously employed [3,5] were used to establish the activity of copper(II) complexes against six fungi, *Aspergillus niger* (ATCC 1004), *A. oryzae* (ATCC 1101), *Myrothecium verrucaria* (ATCC 9095), *Trichoderma viride* (ATCC 8678), *Mucor cirinelloides* (ATCC 7941), and *Trichophyton mentagrophytes* (ATCC 9129).

Table 3. Fractional coordinates

Compound **1**

Atom	*x*	*y*	*z*	*U*
Cu	0.50000	1.00000	0.50000	0.0317(3)
F	0.7488(3)	0.4026(4)	0.7680(2)	0.051(1)
O(1)	0.5930(3)	0.7811(5)	0.6183(2)	0.038(1)
N(1)	0.6172(3)	0.7933(6)	0.4648(2)	0.033(1)
C(2)	0.6230(5)	0.8046(8)	0.3853(3)	0.042(2)
C(3)	0.7111(5)	0.6354(9)	0.3729(3)	0.047(2)
C(4)	0.7957(5)	0.4536(8)	0.4445(3)	0.045(2)
C(5)	0.8747(5)	0.2481(8)	0.6091(3)	0.041(2)
C(6)	0.8553(5)	0.2444(8)	0.6855(3)	0.043(2)
C(7)	0.7628(4)	0.4216(7)	0.6894(3)	0.038(2)
C(8)	0.6826(4)	0.6116(7)	0.6180(3)	0.033(2)
C(9)	0.7011(4)	0.6103(7)	0.5375(3)	0.032(2)
C(10)	0.7946(4)	0.4341(7)	0.5312(3)	0.036(2)

Compound **2**

Atom	*x*	*y*	*z*	*U*
Cu	0.8042(1)	0.7480(1)	0.3043(8)	0.0227(9)
N(1)	0.7123(9)	0.8261(4)	0.2985(6)	0.031(4)
N(11)	0.8830(9)	0.6731(4)	0.2970(6)	0.029(4)
C(3)	0.4769(15)	0.9028(4)	0.2450(10)	0.048(4)
O(1)	1.1040(8)	0.7841(3)	0.3872(5)	0.041(3)
O(11)	0.6707(8)	0.7163(3)	0.3878(5)	0.041(3)
C(17)	0.6278(13)	0.6296(3)	0.4583(8)	0.042(4)
C(7)	1.2883(14)	0.8708(4)	0.4579(9)	0.045(4)
C(2)	0.5080(13)	0.8467(3)	0.2455(8)	0.038(4)
C(6)	1.2705(15)	0.9266(4)	0.4651(10)	0.051(4)
C(22)	1.0614(17)	0.6914(4)	0.1870(11)	0.045(4)
C(4)	0.6525(15)	0.9374(4)	0.2980(10)	0.051(5)
C(5)	1.0671(15)	0.9505(4)	0.4134(9)	0.049(5)
C(8)	1.1023(11)	0.8369(3)	0.4004(7)	0.033(4)
C(12)	0.9813(12)	0.6533(3)	0.2442(8)	0.037(4)
C(10)	0.8723(13)	0.9178(3)	0.3553(9)	0.037(4)
C(11)	0.3119(15)	0.8085(4)	0.1858(10)	0.041(4)
C(20)	0.8349(14)	0.5824(4)	0.3534(9)	0.042(4)
C(18)	0.6985(11)	0.6632(3)	0.3998(7)	0.033(3)
C(9)	0.8902(12)	0.8615(3)	0.3490(8)	0.034(4)
C(19)	0.8084(12)	0.6386(3)	0.3499(8)	0.031(4)
C(15)	0.7604(14)	0.5496(4)	0.4145(9)	0.049(4)
C(14)	0.9436(14)	0.5619(4)	0.2983(9)	0.049(5)
C(13)	1.0131(17)	0.5970(4)	0.2446(11)	0.054(5)
C(16)	0.6599(15)	0.5736(4)	0.4650(9)	0.049(5)
O(33)	0.5538(7)	0.7505(4)	0.0545(4)	0.048(3)

Table 3. (*continued*)

Compound **3**

Atom	*x*	*y*	*z*	*U*
Cu	0.2443(1)	0.5989(2)	0.3235(2)	0.031(1)
C(9)	0.4012(8)	0.6187(13)	0.3716(12)	0.031(8)
N(1)	0.3579(7)	0.6817(11)	0.4022(10)	0.032(6)
O(1)	0.2811(6)	0.4868(8)	0.2545(8)	0.041(5)
C(22)	0.1842(13)	0.3019(18)	0.2970(16)	0.052(11)
C(2)	0.3946(9)	0.7780(15)	0.4796(13)	0.040(9)
C(5)	0.5245(9)	0.5767(16)	0.3834(14)	0.040(9)
C(8)	0.3550(8)	0.5108(12)	0.2925(11)	0.028(7)
C(11)	0.3473(13)	0.8458(19)	0.5160(17)	0.051(10)
N(11)	0.1314(7)	0.5179(11)	0.2402(10)	0.031(6)
C(7)	0.3979(10)	0.4458(12)	0.2585(13)	0.037(8)
C(6)	0.4809(11)	0.4774(16)	0.3044(15)	0.049(10)
C(4)	0.5221(12)	0.7534(17)	0.5001(16)	0.044(9)
C(3)	0.4780(11)	0.8151(17)	0.5282(16)	0.045(10)
O(11)	0.1751(5)	0.7494(8)	0.2724(8)	0.031(5)
O(41)	0.2939(5)	0.5577(8)	0.5245(8)	0.039(5)
S(1)	0.2343(2)	0.5333(4)	0.5514(4)	0.044(2)
C(51)	0.1893(12)	0.6805(16)	0.5451(18)	0.049(10)
C(50)	0.3013(19)	0.509(3)	0.7201(18)	0.083(16)
C(13)	0.0263(10)	0.3571(17)	0.1573(15)	0.034(10)
O(171)	0.1203(8)	0.9819(10)	0.2161(13)	0.096(8)
C(15)	−0.0849(10)	0.6623(17)	0.0448(15)	0.038(9)
C(18)	0.0939(9)	0.7298(13)	0.2008(12)	0.034(9)
C(16)	−0.0596(11)	0.7825(18)	0.0631(15)	0.046(10)
N(17)	0.0462(10)	0.9482(11)	0.1545(12)	0.044(7)
C(17)	0.0284(9)	0.8154(14)	0.1396(13)	0.034(9)
C(20)	−0.0217(8)	0.5681(13)	0.1032(12)	0.031(8)
N(7)	0.3608(9)	0.3421(13)	0.1725(13)	0.055(8)
O(172)	−0.0116(7)	1.0233(11)	0.1114(11)	0.069(7)
C(12)	0.1136(8)	0.3951(14)	0.2307(11)	0.034(8)
C(10)	0.4841(9)	0.6510(15)	0.4188(12)	0.036(9)
C(14)	−0.0379(10)	0.4410(15)	0.0945(14)	0.035(10)
O(71)	0.3817(10)	0.3167(13)	0.1087(15)	0.098(10)
C(19)	0.0661(8)	0.6027(13)	0.1795(11)	0.023(7)
O(72)	0.3045(7)	0.2851(11)	0.1597(11)	0.073(7)

Table 4. Bond distances (Å) and angles (°)

Compound **1**			
Cu–O(1)	1.936(3)	C(4)–C(10)	1.412(8)
Cu–N(1)	1.977(4)	C(10)–C(5)	1.421(5)
F(1)–C(7)	1.369(6)	C(5)–C(6)	1.367(8)
O(1)–C(8)	1.311(5)	C(6)–C(7)	1.388(7)
N(1)–C(2)	1.325(7)	C(7)–C(8)	1.384(5)
N(1)–C(9)	1.370(4)	C(8)–C(9)	1.426(7)
C(2)–C(3)	1.394(8)	C(9)–C(10)	1.411(6)
C(3)–C(4)	1.358(6)		
N(1)–Cu–O(1)	84.9(1)	F(1)–C(7)–C(8)	118.6(4)
Cu–O(1)–C(8)	110.8(3)	C(6)–C(7)–C(8)	124.1(5)
Cu–N(1)–C(2)	130.8(3)	O(1)–C(8)–C(7)	126.1(5)
Cu–N(1)–C(9)	110.3(3)	O(1)–C(8)–C(9)	119.8(3)
C(2)–N(1)–C(9)	118.9(4)	C(7)–C(8)–C(9)	114.1(4)
N(1)–C(2)–C(3)	122.1(4)	N(1)–C(9)–C(8)	114.2(4)
C(2)–C(3)–C(4)	119.8(5)	N(1)–C(9)–C(10)	122.4(4)
C(3)–C(4)–C(10)	120.5(5)	C(8)–C(9)–C(10)	123.5(3)
C(6)–C(5)–C(10)	118.8(4)	C(4)–C(10)–C(5)	125.3(4)
C(5)–C(6)–C(7)	121.2(4)	C(4)–C(10)–C(9)	116.3(3)
F(1)–C(7)–C(6)	117.3(3)	C(5)–C(10)–C(9)	118.3(5)
Compound **2**			
Cu–O(1)	1.997(6)	C(7)–C(8)	1.39(1)
Cu–O(11)	1.985(8)	C(8)–C(9)	1.44(1)
Cu–N(1)	1.99(1)	C(9)–C(10)	1.41(1)
Cu–N(11)	2.01(1)	N(11)–C(12)	1.33(1)
O(1)–C(8)	1.32(1)	N(11)–C(19)	1.37(1)
O(11)–C(18)	1.32(1)	C(12)–C(13)	1.41(1)
N(1)–C(2)	1.34(1)	C(12)–C(22)	1.49(2)
N(1)–C(9)	1.38(1)	C(13)–C(14)	1.36(2)
C(2)–C(3)	1.41(1)	C(14)–C(20)	1.43(2)
C(2)–C(11)	1.50(1)	C(20)–C(15)	1.42(2)
C(3)–C(4)	1.35(1)	C(15)–C(16)	1.36(2)
C(4)–C(10)	1.42(1)	C(16)–C(17)	1.40(1)
C(10)–C(5)	1.42(1)	C(17)–C(18)	1.39(1)
C(5)–C(6)	1.38(1)	C(18)–C(19)	1.42(1)
C(6)–C(7)	1.40(1)	C(19)–C(20)	1.40(1)
N(1)–Cu–O(1)	83.1(3)	N(11)–C(12)–C(22)	119.0(9)
O(1)–Cu–N(11)	98.4(3)	O(1)–C(8)–C(9)	117.5(7)
O(11)–Cu–N1	97.9(3)	C(7)–C(8)–C(9)	117.4(7)
N(11)–Cu–O(11)	83.2(3)	N(11)–C(12)–C(22)	119.0(9)
O(1)–Cu–O(11)	135.2(2)	N(11)- C(12)–C(13)	120.0(9)
N(1)–Cu–N(11)	176.6(2)	C(22)–C(12)–C(13)	121.0(9)
Cu–N(1)–C(2)	130.3(6)	C(4)–C(10)–C(5)	124.0(8)
Cu–N(1)–C(9)	111.2(6)	C(4)–C(10)–C(9)	115.8(8)
C(2)–N(1)–C(9)	118.3(9)	C(5)–C(10)–C(9)	119.1(8)
Cu–N(11)–C(12)	129.6(7)	C(19)–C(20)–C(15)	119.1(9)
Cu–N(11)–C(19)	110.6(6)	C(19)–C(20)–C(14)	117.0(9)

Table 4. (*continued*)

C(12)–N(11)–C(19)	119.7(9)	C(15)–C(20)–C(14)	123.7(9)
C(2)–C(3)–C(4)	120.7(9)	O(11)–C(18)–C(17)	124.4(9)
Cu–O(1)–C(8)	112.6(5)	O(11)–C(18)–C(19)	118.4(8)
Cu–O(11)–C(18)	111.9(6)	C(17)–C(18)–C(19)	117.2(7)
C(18)–C(17)–C(16)	121.1(9)	N(1)–C(9)–C(8)	115.5(7)
C(6)–C(7)–C(8)	121.5(9)	N(1)–C(9)–C(10)	123.4(8)
N(1)–C(2)–C(3)	121.1(8)	C(8)–C(9)–C(10)	121.0(7)
N(1)–C(2)–C(11)	118.5(8)	N(11)–C(19)–C(20)	123.1(9)
C(3)–C(2)–C(11)	120.4(8)	N(11)–C(19)–C(18)	115.9(7)
C(7)–C(6)–C(5)	121.6(9)	C(20)–C(19)–C(18)	122.0(9)
C(3)–C(4)–C(10)	120.6(8)	C(20)–C(15)–C(16)	118.9(9)
C(6)–C(5)–C(10)	119.4(8)	C(20)–C(14)–C(13)	119.0(9)
O(1)–C(8)–C(7)	125.1(8)	C(12)–C(13)–C(14)	121.1(9)
O(1)–C(8)–C(9)	117.5(7)	C(17)–C(16)–C(15)	122.0(9)
C(7)–C(8)–C(9)	117.4(7)		

Compound **3**

Cu–N(1)	2.02(1)	C(4)–C(10)	1.39(2)
Cu–O(1)	1.94(1)	O(11)–C(18)	1.28(2)
Cu–N(11)	1.98(1)	C(13)–C(12)	1.42(2)
Cu–O(11)	1.957(9)	C(13)–C(14)	1.35(2)
C(9)–N(1)	1.36(3)	O(171)–N(17)	1.21(2)
C(9)–C(8)	1.45(2)	C(15)–C(16)	1.36(3)
C(9)–C(10)	1.40(2)	C(15)–C(20)	1.41(2)
N(1)–C(2)	1.32(2)	C(18)–C(17)	1.37(2)
O(1)–C(8)	1.25(2)	C(18)–C(19)	1.44(2)
C(22)–C(12)	1.49(2)	C(16)–C(17)	1.41(2)
C(2)–C(11)	1.51(4)	N(17)–C(17)	1.46(2)
C(2)–C(3)	1.42(3)	N(17)–O(172)	1.22(2)
C(5)–C(6)	1.36(2)	C(20)–C(14)	1.40(2)
C(5)–C(10)	1.43(3)	C(20)–C(19)	1.41(2)
C(8)–C(7)	1.40(3)	N(7)–O(71)	1.21(3)
N(11)–C(12)	1.36(2)	N(7)–O(72)	1.20(2)
N(11)–C(19)	1.37(2)	O(41)–S(1)	1.49(1)
C(7)–C(6)	1.41(3)	S(1)–C(51)	1.80(2)
C(7)–N(7)	1.43(2)	S(1)–C(50)	1.77(2)
C(4)–C(3)	1.35(4)		
N(1)–Cu–O(1)	82.7(5)	C(16)–C(15)–C(20)	119.0(15)
N(1)–Cu–N(11)	178.0(6)	O(11)–C(18)–C(19)	128.1(9)
N(1)–Cu–O(11)	97.6(4)	O(11)–C(18)–C(19)	117.2(9)
O(1)–Cu -N(11)	96.1(5)	C(17)–C(18)–C(19)	115.0(9)
O(1)–Cu- O(11)	138.9(5)	C(15)–C(16)–C(17)	122.2(16)
N(11)–Cu–O(11)	82.3(4)	O(171)–N(17)–C(17)	118.0(8)
N(1)–C(9)–C(8)	113.0(9)	O(171)–N(17)–O(172)	121.1(8)
N(1)–C(9)–C(10)	123.9(9)	C(17)–N(17)–O(172)	121.3(15)
C(8)–C(9)–C(10)	124.1(12)	C(18)–C(17)–C(16)	123.1(9)
Cu–N(1)–C(9)	1120.7(8)	C(18)–C(17)–N(17)	122.2(9)
Cu–N(1)–C(2)	130.1(9)	C(16)–C(17)–N(17)	115.1(8)

Table 4. (*continued*)

C(9)–N(1)–C(2)	119.0(10)	C(15)–C(20)–C(14)	125.0(9)
Cu–O(1)–C(8)	113.2(9)	C(15)–C(20)–C(19)	119.1(10)
N(1)–C(2)–C(11)	119.1(12)	C(14)–C(20)–C(19)	116.0(10)
N(1)–C(2)–C(3)	119.1(14)	C(7)–N(7)–O(71)	121.2(15)
C(11)–C(2)–C(3)	12.0(13)	C(7)–N(7)–O(72)	118.0(16)
C(6)–C(5)–C(10)	119.2(15)	O(71)–N(7)–O(72)	121.1(16)
C(9)–C(8)–O(1)	120.0(14)	C(22)–C(12)–N(11)	121.0(9)
C(9)–C(8)–C(7)	114.9(9)	C(22)–C(12)–C(13)	120.2(17)
O(1)–C(8)–C(7)	126.2(9)	N(11)–C(12)–C(13)	119.0(9)
Cu–N(11)–C(12)	128.0(10)	C(9)–C(10)–C(5)	119.0(8)
Cu–N(11)–C(19)	111.2(9)	C(9)–C(10)–C(4)	117.2(15)
C(12)–N(11)–C(19)	120.1(10)	C(5)–C(10) -C(4)	124.1(16)
C(8)–C(7)–C(6)	123.0(9)	C(13)–C(14)–C(20)	122.0(15)
C(8)–C(7)–N(7)	123.1(15)	N(11)–C(19)–C(18)	115.1(9)
C(6)–C(7)–N(7)	114.0(16)	N(11)–C(19)–C(20)	123.1(9)
C(5)–C(6)–C(7)	122.2(16)	C(18)–C(19)–C(20)	123.2(9)
C(3)–C(4)–C(10)	119.0(15)	O(41)–S(1)–C(51)	107. 0(9)
C(2)–C(3)–C(4)	122.1(14)	O(41)–S(1)–C(50)	105.1(10)
Cu–O(11)–C(18)	114.1(8)	C(51)–S(1)–C(50)	98.0(10)
C(12)–C(13)–C(14)	121.3(16)		

Acknowledgments

Partial support for this work came from NSF, DUE#9650684.

References

[1] Gershon H, Parmegiani R, Weiner A, D'Ascoli RD (1966) Contrib Boyce Thompson Inst **23**: 219
[2] Kanamaru F, Ogawa K, Nitta I (1963) Bull Chem Soc Japan **36**: 422
[3] Gershon H, McNeil MW, Hinds Y (1969) J Med Chem **12**: 1115
[4] Gershon H (1972) Pestic Chem. Proc Int Congr Pestic Chem, 2nd edn, p 363
[5] Gershon H (1974) J Med Chem **17**: 824
[6] Gershon H, McNeil MW (1972) J Heterocycl Chem **9**: 659
[7] Bis(7-nitro-8-quinolinolato)copper(II) was prepared from the ligand [8] by standard methods and an X-ray crystal structure determination showed it to be square planar. Because that work was done after the present manuscript was completed it will be reported later.
[8] Gershon H, McNeil MW (1971) J Heterocycl Chem **8**: 129
[9] Palenik GJ (1964) Acta Cryst **17**: 696
[10] Palenik GJ (1964) Acta Cryst **17**: 687
[11] Gershon H, McNeil MW, Schulman SG, Parkes JW (1972) Anal Chim Acta **62**: 43
[12] Gershon H, Clarke DD, Gershon M (1989) J Pharm Sci **78**: 975
[13] Sleytr VB, Messner P (1988) J Bact **170**: 2891
[14] Küpcü S, Mader C, Sára M (1995) Biotechnol Appl Biochem **21**: 275
[15] Hall SR, King GSD, Stewart JM Editors (1995) Xtal 3.4 User's Manual University of Western Australia, Lamb, Perth

Received January 20, 1998. Accepted (revised) April 29, 1998