

Available online at www.sciencedirect.com



INORGANIC CHEMISTRY COMMUNICATIONS

Inorganic Chemistry Communications 9 (2006) 1173-1177

www.elsevier.com/locate/inoche

# Synthesis, structure and magnetic properties of the first copper(II) complex with an (E)-4-aryl-4-oxo-2-butenoato ligand

Zoran M. Miodragović<sup>a,\*</sup>, Goran A. Bogdanović<sup>b</sup>, Bojana B. Krajčinović<sup>c</sup> Branko J. Drakulić<sup>c</sup>, Vladan B. Kusigerski<sup>b</sup>, Djenana U. Miodragović<sup>a</sup> Vojislav V. Spasojević<sup>b</sup>, Ismet M. Hodžić<sup>a</sup>, Ivan O. Juranić<sup>a</sup>

<sup>a</sup> Faculty of Chemistry, University of Belgrade, P.O. Box 158, 11001 Belgrade, Serbia and Montenegro <sup>b</sup> VINČA Institute of Nuclear Sciences, Laboratory of Theoretical Physics and Condensed Matter Physics, P.O. Box 522, 11001 Belgrade, Serbia and Montenegro

<sup>c</sup> Department of Chemistry, Institute of Chemistry, Technology and Metallurgy, University of Belgrade, Njegoševa 12, 11000 Belgrade, Serbia and Montenegro

Received 9 June 2006; accepted 22 July 2006

# Abstract

A new binuclear Cu(II) complex with an (*E*)-4-(2,4-diisopropylphenyl)-4-oxo-2-butenoato ligand (L) was successfully synthesized and characterized by elemental analysis and IR-spectroscopy. The structures of (*E*)-4-(2,4-diisopropylphenyl)-4-oxo-2-butenoic acid (HL), and the corresponding (*tetrakis*)- $\mu$ -[(*E*)-4-(2,4-diisopropylphenyl)-4-oxo-2-butenoato]-bis(ethanol)-copper(II) complex, [Cu<sub>2</sub>L<sub>4</sub>(-C<sub>2</sub>H<sub>5</sub>OH)<sub>2</sub>], were determined by single crystal X-ray analyses and are preliminarily discussed. This is the first complex of a transition metal with ligand L, as well as the first determined crystal structure of a metal complex with this type of ligand. Analysis of the magnetic susceptibility measurements of the isolated [Cu<sub>2</sub>L<sub>4</sub>(C<sub>2</sub>H<sub>5</sub>OH)<sub>2</sub>] · H<sub>2</sub>O complex shows the existence of a strong anti-ferromagnetic intradimer coupling, with an exchange integral value 2*J* of  $-260 \text{ cm}^{-1}$ .

© 2006 Elsevier B.V. All rights reserved.

Keywords: (E)-4-(2,4-diisopropylphenyl)-4-oxo-2-butenoato ligand; Cu(II) complexes; X-ray analysis; Magnetic properties

The interest in copper(II) polynuclear complexes containing carboxylato bridging ligands was triggered by the intriguing magnetic and catalytic properties of these compounds [1]. 4-Aryl-4-oxo-2-butenoic acids (aroylacrylic acids) exert antibacterial [2] and antineoplastic activity [3]. The mode of action is ascribed to the Michael-type addition of free sulfahydrile groups (–SH) to the  $\beta$ -position of the ketovinyl moiety (–C(O)–CH=CH–) of the molecules [4,5]. In a previous paper, *in vitro* antiproliferative activity of 19 (*E*)-4-aryl-4-oxo-2-butenoic acids toward human cervix carcinoma HeLa cells was reported [3]. The compounds influenced the proliferation of the target cells in the concentration range  $4.5-40 \,\mu$ M/L (IC<sub>50</sub> values). The QSAR (Quantitative Structure Activity Relationships) results show linear dependences between the antiproliferative activity of the compounds and their lipophilicity (using estimated log *P* values). As an extension of these investigations, a series of new congeners were synthesized and used as precursors for the syntheses of more active compounds [6]. In this communication, the structure of one of these precursors, resolved by the single crystal X-ray diffraction method, is reported.

Within the framework of studies aimed at gaining a deeper insight into the previously reported [3,6] bioactive scaffolds behavior within biological systems, the interactions of the molecules with metal ions, as integral components of cells, were investigated. Thus, a number of Cu(II) and Zn(II) complexes with phenyl-substituted (E)-4-phenyl-4-

<sup>\*</sup> Corresponding author. Tel.: +381 11 3336 782; fax: +381 11 184 330. *E-mail address:* zoranmio@chem.bg.ac.yu (Z.M. Miodragović).

<sup>1387-7003/\$ -</sup> see front matter  $\odot$  2006 Elsevier B.V. All rights reserved. doi:10.1016/j.inoche.2006.07.029

oxo-2-butenoato ligands were recently synthesized (manuscript in preparation). In this communication, the synthesis and preliminary characterization of the Cu(II) complex with (*E*)-4-(2,4-diisopropylphenyl)-4-oxo-2-butenoato ligand (L) is presented. 4-Aryl-4-oxo-2-butenoic acids have been known for a long time. The first synthesis of the basic compound, 4-phenyl-4-oxo-2-butenoic acid was reported in 1882 [7]. Nevertheless, to the best of our knowledge, there has, hitherto, only been one report of metal complexes with these compounds as ligands [8]. In the present paper, for the first time, the crystal structure of one metal complex with the mentioned type of ligand, as well as its variable temperature magnetic behavior is described.

The complex was synthesized by instilling an aqueous solution containing 42.6 mg (0.25 mmol) of  $CuCl_2 \cdot 2H_2O$ into a solution of NaL prepared by dropping an aqueous solution containing 20.0 mg (0.5 mmol) of NaOH into a water suspension of 130.2 mg (0.5 mmol) of HL [3] under continuous stirring at room temperature, whereby a pH of 6-7 was obtained. After continuous stirring at room temperature for 1 h, the crude pale greenish-blue microcrystalline product was separated by suction and purified by rinsing first with ethanol and finally with water, giving a complex with the formula  $[Cu_2L_4(C_2H_5OH)_2] \cdot H_2O$ . Yield: 53.0 mg (33.7%) calculated with respect to HL. A rather poor yield is the consequence of relative good solubility of the complex in ethanol. Green single crystals of the  $[Cu_2L_4(C_2H_5OH)_2]$  complex were obtained by slightly changing the composition of  $[Cu_2L_4(C_2H_5OH)_2] \cdot H_2O$ microcrystals during recrystallization from ethanol. Yield: 25.0 mg (15.9%) calculated with respect to the starting amount of HL.

The characteristic bands of the asymmetric ( $\bar{v}_{a}(COO)$ ) and symmetric ( $\bar{v}_{s}(COO)$ ) skeletal vibration of the carboxvlate group in the IR spectra (KBr discs, Perkin-Elmer FT-IR 1726x spectrometer) of the title complex were found at  $1606 \text{ cm}^{-1}$  and  $1408 \text{ cm}^{-1}$  and of the corresponding potassium salt KL at  $1582 \text{ cm}^{-1}$  and  $1384 \text{ cm}^{-1}$ . The identical values of  $\Delta \bar{v} (\Delta \bar{v} = \bar{v}_a(\text{COO}) - \bar{v}_s(\text{COO}))$  of 198 cm<sup>-1</sup> for the free and coordinated carboxylato group indicate that the coordination mode of the carboxylato group of the ligand L is bridging bidentate [9]. This is unlike the tris- $(\beta$ -benzoylacrylato)-europium(III) complex in which, on the basis of IR-data, the carboxylato groups were coordinated in a chelate bidentate manner [8]. However, in the case of binuclear copper(II) complexes, the bridging bidentate mode of coordination of four carboxylato groups forming a cage structured coordination sphere is well known [1a,1b,10].

The single crystal X-ray data were collected on an Enraf-Nonius CAD-4 diffractometer [11] using Mo K $\alpha$  radiation ( $\lambda = 0.71073$  Å) and  $\omega/2\theta$  scans in the 1.42–25.01°  $\theta$  range for compound HL and the 1.41–25.97°  $\theta$  range for the [Cu<sub>2</sub>L<sub>4</sub>(C<sub>2</sub>H<sub>5</sub>OH)<sub>2</sub>] complex. The cell constants and the orientation matrix for the data collection, obtained from 23 centered reflections in the  $\theta$  range of 10.45–16.83° for HL and 12.37–16.84° for complex, corre-

spond to orthorhombic and monoclinic cells, respectively. The unit cell dimensions and other crystallographic data for both compounds are given in Table 1. The data were corrected for Lorentz and polarization effects [12].

The crystal structures were solved by direct methods [13a] and by difference Fourier methods and refined on  $F^2$  by the full-matrix least-square method [13b]. In HL, all H atoms were easily determined from the  $\Delta F$  maps but in the final stage of refinement, they were placed at calculated positions (in order to decrease the number of refined parameters) using a riding model. The H atom belonging to COOH was refined isotropically without any constraint. In the crystal structure of the [Cu<sub>2</sub>L<sub>4</sub>-(C<sub>2</sub>H<sub>5</sub>OH)<sub>2</sub>] complex, all H atoms were included in the refinement at their geometrically calculated positions but the H atom from the OH group (in the ethanol ligand) was taken from the  $\Delta F$  map and refined isotropically with the O-H distance fixed at 0.85 Å. The methyl groups in both structures were treated with the HFIX 137 instruction. All non-hydrogen atoms in both crystal structures were refined with anisotropic thermal parameters. A Gaussian-type absorption correction [14,15] based on the crystal morphology was applied to the X-ray data of the

Table 1

Crystallographic data for compounds HL and [Cu<sub>2</sub>L<sub>4</sub>(C<sub>2</sub>H<sub>5</sub>OH)<sub>2</sub>]

	Ligand (HL)	Complex
		$[Cu_2L_4(C_2H_5OH)_2]$
Empirical formula	C <sub>16</sub> H <sub>20</sub> O <sub>3</sub>	C68H88 Cu2O14
Formula weight	260.32	1256.46
Crystal size (mm <sup>3</sup> )	$0.16 \times 0.30 \times 0.30$	0.10  imes 0.32  imes 0.54
Temperature (K)	293 (2)	293 (2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Orthorhombic	Monoclinic
Space group	Pbca	$P2_1/n$
Unit cell dimensions		
a (Å)	9.263 (2)	16.060 (4)
b (Å)	11.222 (3)	11.794 (5)
<i>c</i> (Å)	28.712 (6)	19.279 (3)
α (°)	90	90
β (°)	90	112.23 (2)
γ (°)	90	90
$V(Å^3)$	2985 (1)	3380.2 (17)
Ζ	8	2
$D_{\rm calc} ({\rm Mg}{\rm m}^{-3})$	1.159	1.234
Absorption coefficient (mm <sup>-1</sup> )	0.079	0.689
Theta range for	1.42-25.01	1.41-25.97
data collection (°)		
Index ranges	$0 \leftarrow h \leftarrow 11$ ,	$0 \leftarrow h \leftarrow 19$ ,
	$0 \leftarrow k \leftarrow 13$ ,	$0 \leftarrow k \leftarrow 14$ ,
	$-4 \leftarrow l \leftarrow 34$	$-23 \leftarrow l \leftarrow 21$
Reflections collected	3071	6858
Independent reflections	2612 ( $R_{int} = 0.0374$ )	6615 ( $R_{int} = 0.0448$ )
Data/parameters	2612/188	6615/389
Goodness-of-fit on $F^2$	0.961	0.918
Final <i>R</i> indices $[I > 2\sigma(I)]$	$R_1 = 0.0501,$	$R_1 = 0.0558$
	$wR_2 = 0.1241,$	$wR_2 = 0.1279$
Largest difference peak and hole (e $Å^{-3}$ )	0.212 and -0.181	0.376 and -0.292

 $[Cu_2L_4(C_2H_5OH)_2]$  complex ( $T_{min} = 0.8027$ ,  $T_{max} = 0.9313$ ). The software packages used for the preparation of the crystallographic material for publication were: PLA-TON [14], WinGX [15], PARST [16] and ORTEPIII [17].

As shown in Fig. 1, the molecules of the uncoordinated ligand HL form dimers, with two strong  $O-H\cdots O$  intermolecular hydrogen bonds. The crystal structure of the  $[Cu_2L_4(C_2H_5OH)_2]$  complex indicates that this is a binuclear Cu(II) complex with two centrosymmetrically related halves (Fig. 2), with a rather short Cu $\cdots$ Cu distance of 2.6350(12) Å. Each Cu(II) has a square-pyramidal coordination geometry consisting of one C<sub>2</sub>H<sub>5</sub>OH in the apical position and four oxygen atoms from the bridging carboxylato groups. The details of a comparative analysis of the geometrical parameters and hydrogen bonds for both

crystal structures will be discussed in a forthcoming full paper concerning Cu(II) and Zn(II) complexes with a series of differently substituted (E)-4-aryl-4-oxo-2-butenoato ligands.

Biologically active small and relatively rigid molecules of low polarity have a similar conformation within their site of action (cocrystallized with the receptors) and when the same molecules are crystallized without the receptor. Such similarity is described in the literature [18]. The environment of the active site forces the bioactive conformation. Consequently, when discussing a bioactive ligand and a corresponding complex having a carboxylate group (treated as the part of the molecule (L) which interacts with the cation moiety within the active site) complexed with the metal ion (treated as the cationic moiety within the active



Fig. 1. The molecular geometry of the HL ligand and an illustration of the dimer formed by two  $O-H \cdots O$  intermolecular hydrogen bonds. Displacement ellipsoids are drawn at the 40% probability level for non-H atoms. C and H atoms are not labeled for clarity.



Fig. 2. The molecular geometry of the  $[Cu_2L_4(C_2H_5OH)_2]$  complex (Symmetry code for centrosymmetric half of complex molecule: -x + 1, -y - 1, -z). Displacement ellipsoids are drawn at the 40% probability level for non-H atoms. For clarity, C and H atoms are not labeled.

site), it can be considered useful to compare the conformations of the free ligand and the complexed one. Quantitative similarity analysis assessed by the superimposition of all non-H atoms of the free HL and of the corresponding complexed ligand, using crystal structure data, was performed employing the similarity search facility implemented in the Vega ZZ 2.0.6 program [19]. The RMS (root mean square) distance between the related atom pairs (free ligand vs. complexed one) was 0.322. This difference is the consequence of the different orientation of the 4-*i*-Prgroup and of the different orientation of the aryl ring towards the aroyl keto group ( $\theta = 42.82^{\circ}$  complexed ligand;  $\theta = 31.35^{\circ}$  free ligand), as can be seen in Fig. 3 [20].

Magnetic measurements of the isolated [Cu<sub>2</sub>L<sub>4</sub>(- $C_2H_5OH_2$  complex were performed using a SQUID-based Quantum Design magnetometer MPMS XL-5 with an applied field of 1000 Öe in the temperature range 5-350 K. The experimental data were corrected for the underlving diamagnetic contribution using Pascal's constants [21], and the so-obtained values are shown in Fig. 4 as  $\chi_{mol}T$ . The magnetic data were analyzed on the basis of the Bleaney-Bowers equation, which describes the magnetic susceptibility of the exchange coupled pair of Cu(II) ions starting from the isotropic Heisenberg Hamiltonian  $\mathbf{H} = -2J\mathbf{S}_1 \cdot \mathbf{S}_2$ , and assuming a spin value S = 1/2 [21]. A modified form of this equation which includes a term for the fraction  $\rho$  of monomeric Cu(II) impurities, as well as a contribution from the temperature independent paramagnetism  $\chi_{\text{TIP}}$  of copper(II) ions [22] is

$$\chi_{\rm mol}T = 2Cg^2[3 + e^x]^{-1}(1 - \rho) + Cg^2\rho/2 + \chi_{\rm TIP}T,$$
(1)

where  $C = N_A \beta^2 / k_B$  and  $x = -2 J / k_B T$  were employed. The experimental data were successfully fitted to Eq. (1) and the least-squares best-fit curve is shown in Fig. 4. The obtained



Fig. 4. Experimental (dots) and fitted (solid line) temperature dependence of  $\chi_{mol}T$ .

values of the fitting parameters are  $\rho = 0.032$ ,  $\chi_{\text{TIP}} = 1.1 \times 10^{-3}$  emu/mol Oe, g = 2, and 2J = -260cm<sup>-1</sup>. The 2J value indicates the existence of a strong antiferromagnetic intradimer interaction, which is somewhat stronger than that of the corresponding [*tetrakis* (µ-1-phenylcyclopropane-1-carboxylato-O, O')bis(ethanol-O) dicopper(II)] complex ( $2J = -242 \text{ cm}^{-1}$ ), having the same coordination sphere, but with a shorter Cu···Cu distance (2.6009(4) Å) [1a]. In the related binuclear compound [*tetrakis*-(1-phenyl-1-carboxylato- $\mu$ -O, O'-cyclopentane)-bis-(ethanol-O) dicopper(II)bis(ethanol) having a Cu···Cu distance of 2.6203(5) Å, a 2J value of  $-284 \text{ cm}^{-1}$  was found [1b].



Fig. 3. Superimposed free ligand HL (black, stick presentation) over one of the complexed ligands within the complex (gray, stick presentation), using the X-ray structure data. Rendering by Vega ZZ 2.0.6 [19].

## Supplementary data

Crystallographic data for the structural analysis are deposited at the Cambridge Crystallographic Data Centre, CCDC Nos. 606031 and 606030 for compounds HL and  $[Cu_2L_4(C_2H_5OH)_2]$ , respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

#### Acknowledgement

This work is supported by the Ministry of Science, Technology and Environmental Protection of the Republic of Serbia (Grants: 142010, 142028, and 141027).

### References

 (a) F.P.W. Agterberg, H.A.J. Provo Kluit, W.L. Driessen, H. Oevering, W. Buijs, M.T. Lakin, A.L. Spek, J. Reedijk, Inorg. Chem. 36 (1997) 4321;

(b) F.P.W. Agterberg, H.A.J. Provo Kluit, W.L. Driessen, J. Reedijk, H. Oevering, W. Buijs, N. Veldman, M.T. Lakin, A.L. Spek, Inorg. Chim. Acta 267 (1998) 183;

(c) I.A. Koval, P. Gamez, O. Roubeau, W.L. Driessen, M. Lutz, A.L. Spek, J. Reedijk, Inorg. Chem. 42 (2003) 868;

(d) S. Reinoso, P. Vitoria, J.M. Gutiérrez-Zorrilla, L. Lezama, L. San Felices, J.I. Beitia, Inorg. Chem. 44 (2005) 9731;

(e) S. Youngme, C. Chailuecha, G.A. van Albada, C. Pakawatachai, N. Chaichit, J. Reedijk, Inorg. Chim. Acta 358 (2005) 1068;

- (f) B. Li, X. Wang, Y. Zhang, S. Gao, Y. Zhang, Inorg. Chim. Acta 358 (2005) 3519.
- [2] (a) H. Rinderknecht, J.L. Ward, F. Bergel, A.L. Morrison, Biochem. J. 41 (1947) 462;
  - (b) F.K. Kirchner, J.H. Bailey, C.J. Cavallito, J. Amer. Chem. Soc. 71 (1949) 1210;
  - (c) K. Bowden, M.P. Henry, ACS Adv. Chem. 114 (1972) 130;
  - (d) A. Dal Pozzo, M. Acquasaliante, G. Donezzeli, P. De Maria, C. Nicoli, J. Med. Chem. 30 (1978) 1674;

(e) K. Bowden, M.S. Dixon, J.R. Runson, J. Chem. Res. (1979) (S) 8, (M) 169;

(f) K. Bowden, A. DelPozzo, C.K. Duah, J. Chem. Res. (1990) (S) 377, (M) 2801.

- [3] Z. Juranić, Lj. Stevović, B. Drakulić, T. Stanojković, S. Radulović, I. Juranić, J. Serb. Chem. Soc. 64 (1999) 505.
- [4] I.L. Pinto, R.L. Jarvest, B. Clarke, C.E. Dabrowski, A. Fenwick, M.M. Gorzyca, J.L. Jennings, P. Lavery, E.J. Sternberg, D.G. Tew, A. West, Bioor. Med. Chem. Lett. 9 (1999) 449.
- [5] (a) B.M. Anderson, M.L. Tanhcoo, A. DelPozzo, Biochem. Biophys. Acta 703 (1982) 204;
  (b) B.M. Anderson, C.D. Anderson, G. Donzzeli, A. DelPozzo,

Biochem. Biophys. Acta 787 (1984) 215.

- [6] B.J. Drakulić, Z.D. Juranić, T.P. Stanojković, I.O. Juranić, J. Med. Chem. 48 (2005) 5600.
- [7] H. von Peschman, Berichte der Deutschen Chemischen Gesellschaft 15 (1882) 881.
- [8] X. Zhi, L. Wen-Xian, L. Ying-Ping, Neimenggu Daxue Kexuebao, Ziran Kexueban 34 (2) (2003) 152.
- [9] G.B. Deacon, R.J. Philips, Coord. Chem. Rev. 33 (1980) 227.
- [10] (a) G. Morgant, N.-H. Dung, J.-C. Daran, B. Viossat, X. Labouze, M. Roch-Arveiller, F.T. Greenaway, W. Cordes, J.R.J. Sorenson, J. Inorg. Biochem. 81 (2000) 11;
  (b) O. Kristiansson, L.-E. Tergenius, J. Chem. Soc., Dalton Trans.
- (2001) 1415.[11] Enraf-Nonius CAD4 Software, Version 5.0, Enraf-Nonius, Delft, The Netherlands, 1989.
- [12] CAD-4 Express Software, Enraf-Nonius, Delft, The Netherlands, 1994.
- [13] (a) G.M. Sheldrick, SHELXS97. Program for the Solution of Crystal Structures, University of Göttingen, Germany, 1997;
  (b) G.M. Sheldrick, SHELXL97. Program for the Refinement of Crystal Structures, University of Göttingen, Germany, 1997.
- [14] (a) A.L. Spek, Acta Cryst. A 46 (1990) C34;
  (b) A.L. Spek, PLATON, A. Multipurpose: Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, 1998.
- [15] L.J. Farrugia, J. Appl. Cryst. 32 (1999) 837.
- [16] M. Nardelli, PARST, J. Appl. Cryst. 28 (1995) 659.
- [17] L.J. Farrugia, ORTEPIII for Windows, J. Appl. Cryst. 30 (1997) 565.
- [18] (a) J. Wouters, F. Ooms, Cur. Pharm. Des. 7 (2001) 529;
  (b) G. Klebe, in: H.-B. Bürgi, J.D. Dunitz (Eds.), Structure Correlation, vol. 2, VCH, New York, 1994, p. 543.
- [19] A. Pedretti, L. Villa, G. Vistoli, J. Comp. Aid. Mol. Des. 18 (3) (2004) 167, VegaZZ available from: <a href="http://www.ddl.unimi.it">http://www.ddl.unimi.it</a>>.
- [20] The above-described comparison is not strict enough, because other factors influence the differences between the conformation of the free and complexed ligands; a more detailed analysis of this type will be presented in a full paper.
- [21] O. Kahn, Molecular Magnetism, VCH, New York, 1993.
- [22] M. Barquín, M.J. González Garmendia, S. Pacheco, E. Pinilla, S. Quintela, J.M. Seco, M.R. Torres, Inorg. Chim. Acta 357 (11) (2004) 3230.