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Inorganica Chimica Acta 272 (1998) 24–32

Inorganica Chimica Acta

Cu^{II}–herbicide complexes: structure and bioactivity

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Received 16 October 1996; revised 3 February 1997; accepted 17 March 1997

Abstract

Copper complexes with the commercial auxin herbicides 2,4-dichlorophenoxy-acetic acid (2,4-D), 3,4-dichlorophenoxy-acetic acid (3,4-D), 2,4,5-trichlorophenoxy-acetic acid (2,4,5-T), 2-methyl-4-chloro-phenoxy-acetic acid (MCPA), 2,3-dichlorophenoxy-acetic acid (2,3-D) and 2-(2,4-dichlorophenoxy)-propanoic acid (2,4-DP) in the presence or not of 2,2′-bipyridine (bipy), an antimicrobial agent, were prepared and characterized. The available evidence supports a dimeric structure for the 2,3-D complex, while the presence of bipy leads to monomeric forms. The solution behaviour of dinuclear complexes in dimethylformamide (DMF) has shown that the complexes are converted to monomeric compounds by the addition of more than 1:2 of bipy. The cyclic voltammograms of dimers in DMF suggest that the complexes retain the dimeric structure in solution. The electron spin resonance spectra of the compound (aqua)(2,2′-bipyridine)bis(2-methyl-4-chlorophenoxyacetato)copper(II) (1) show features characteristic of the presence of an $S=1$ triplet state. The crystal structure of 1 was determined and refined by least-squares methods using three-dimensional Mo Kα data. 1 crystallizes in the space group $C2/c$, in a cell of dimensions $a=40.49(1)$, $b=7.286(3)$, $c=19.617(6)$ Å, $\beta=103.23(1)°$, $V=5634(3)$ Å^3, $Z=8$. Study of the antimicrobial activity showed that the presence of bipy increases the efficiency 4–8 times.

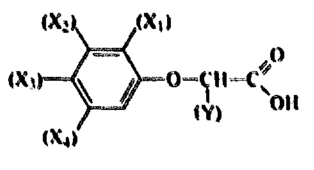
Keywords: Copper complexes; Herbicide complexes; Crystal structures; Bioactivity

1. Introduction

Many dinuclear Cu(II) carboxylate compounds have been isolated and their magnetostructural correlation studied [1–3]. In most cases the formula of the complexes is $Cu_2(OOCR)_4L_2$ ($L=H_2O$, dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and pyridine (Py)). The isolation of mononuclear carboxylato-compounds has also confirmed the existence of unidentate and bidentate coordination modes of the ligands [4–7]. The electrochemical behaviour of dinuclear complexes as one means of determining differences in reactivity between dinuclear and mononuclear complexes has also attracted great interest [8–20]. Phenoxyalkanoic acids interact with Cu(II) ions to form complexes which have been shown to have diverse stereochemistries [21–31].

We have initiated studies on drug–metal interaction in an attempt to examine their mode of binding and possible synergetic effects [32–37].

In this paper we report the solid and solution behaviour of mononuclear Cu(II) complexes with the commercial auxin herbicides 2,4-dichlorophenoxy-acetic acid (2,4-D), 3,4-dichlorophenoxy-acetic acid (3,4-D), 2,4,5-trichlorophenoxy-acetic acid (2,4,5-T), 2-methyl-4-chloro-phenoxy-acetic acid (MCPA), 2,3-dichlorophenoxy-acetic acid (2,3-D) and 2-(2,4-dichlorophenoxy)-propanoic acid (2,4-DP)



2,4-DP: $X_1=Cl$, $X_2=H$, $X_3=Cl$, $X_4=H$, $Y=CH_3$
2,3-D: $X_1=Cl$, $X_2=Cl$, $X_3=H$, $X_4=H$, $Y=H$
2,4-D: $X_1=Cl$, $X_2=H$, $X_3=Cl$, $X_4=H$, $Y=H$
3,4-D: $X_1=H$, $X_2=Cl$, $X_3=Cl$, $X_4=H$, $Y=H$
2,4,5-T: $X_1=Cl$, $X_2=H$, $X_3=Cl$, $X_4=Cl$, $Y=H$
MCPA: $X_1=CH_3$, $X_2=H$, $X_3=Cl$, $X_4=H$, $Y=H$

Scheme 1.

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PII S0020-1693(97)05847-7

in the presence of 2,2′-bipyridine (bipy) as ligands, the antimicrobial behaviour and possible structural relations (Scheme 1).

We also report the molecular and crystal structure of (aqua)(2,2′-bipyridine)bis(2-methyl-4-chloro-phenoxyacetato)copper(II) **1** compound.

2. Experimental

2.1. *Materials*

The chemicals for the synthesis of the compounds were used as purchased. Acetonitrile (CH_3CN) was distilled from calcium hydride (CaH_2) and CH_3OH from magnesium (Mg) and was stored over 3 Å molecular sieves. Diethyl ether, anhydrous grade and absolute ethanol were used without any further purification. 2,4-D, 3,4-D, 2,4,5-T, MCPA, 2,3-D, 2,4-DP, bipy, and $CuCl_2 \cdot 2H_2O$ were purchased from Aldrich Co. All chemicals and solvents were reagent grade.

2.2. *Physical measurements*

IR spectra (200–4000 cm^{-1}) were recorded on a Perkin-Elmer FT-IR 1650 spectrometer with samples prepared as KBr pellets. UV–Vis spectra were recorded on a Shimadzu-160A dual beam spectrophotometer. Electron spin resonance (ESR) spectra were recorded on a Bruker ESR 300 spectrometer equipped with a Varian variable temperature controller. Diphenylpicrylhydrazyl was used as an external standard. Room temperature magnetic measurements were carried out using Faraday's method with mercury tetrathiocyanatocobaltate(II) as calibrant. C, H and N elemental analysis was performed on a Perkin-Elmer 240B elemental analyser; Cu was determined by atomic absorption spectroscopy on a Perkin-Elmer 1100B spectrophotometer. Electric conductance measurements were carried out with a WTW model LF 530 conductivity outfit and a type C cell, which had a cell constant of 0.996. This represents a mean value calibrated at 25°C with potassium chloride. All temperatures were controlled with an accuracy of ±0.1°C using a Haake thermoelectric circulating system. Cyclic voltammetry studies were completed on an Eco chemie Autolab Electrochemical analyser. Cyclic voltammetric experiments were carried out in a three-electrode cell. The working electrode was platinum, and a platinum wire was used as the counter electrode. In all cases, an Ag/AgCl electrode saturated with KCl was used as the reference. The supporting electrolyte, tetraethylammonium perchlorate (teap) was purchased from Carlo Erba. Prior to its use, it was recrystallized twice from ethanol and dried under vacuum. Oxygen was removed by purging the solutions with pure nitrogen which had been previously saturated with solvent vapour. All electrochemical measurements were performed at 25.0±0.2°C. The temperature was controlled by a thermostatically controlled water bath.

The antimicrobial efficiency of the complexes was tested by their ability to inhibit the growth of microorganisms in the cultivation medium Mueller–Hinton broth (Imuna). The tests were performed according to the minimum inhibitory concentrations in μg ml^{-1} with four bacteria species: *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Proteus bulgaris*.

The concentration of microorganisms in the cultivation medium was 10^5–10^6 cfu ml^{-1}. Concentrations of 1600, 800, 400, 200, 100 and 50 μg ml^{-1} of the complexes in propyleneglycol were tested and the minimum inhibitory concentrations (MIC) were determined. Propyleneglycol showed no antimicrobial action at concentrations up to 1600 μg ml^{-1}.

2.3. *Preparation of the ligands*

The sodium salts of the ligands were prepared by the reaction of the protonated ligand with NaOH or $NaOCH_3$ in methanol. The white solids were recrystallized from methanol and dried in air.

2.4. *Synthesis of the (aqua)(2,2′-bipyridine)bis[(2-methyl-4-chlorophenoxy)acetato] copper(II) (1)*

MCPA (2.00 g, 10 mmol) was dissolved in CH_3OH (50 cm^3) and CH_3ONa (0.54 g, 10 mmol) was added. After 30 min stirring $CuCl_2 \cdot 2H_2O$ (0.85 g, 5 mmol) in CH_3OH (25 cm^3) was added dropwise. The reaction mixture was stirred for 1 h and reduced in volume under vacuum. Microcrystalline product of $Cu[C_6H_3(CH_3)Cl\text{-}OCH_2COO]_2(H_2O)_2$ was deposited and collected by filtration. $Cu[C_6H_3(CH_3)Cl\text{-}OCH_2COO]_2(H_2O)_2$ (3 mmol) in CH_3CN (50 cm^3) was dissolved and bipy (0.47 g, 3 mmol) in CH_3CN (25 cm^3) was added and the mixture was stirred for 1 h and left for slow evaporation. Crystals of $Cu[C_6H_3(CH_3)Cl\text{-}OCH_2COO]_2(NH_4C_5\text{-}C_5H_4N)(H_2O)$ (**1**) suitable for X-ray structure determination were deposited in a week. Yield 60%. Formula weight: 636.95. Calc. for $C_{28}H_{26}Cl_2N_2O_7Cu$: C, 52.80; H, 4.10; N, 4.40; Cu, 10.00. Found: C, 52.45; H, 3.80; N, 4.35; Cu, 9.60%. IR: ν_{max} (cm^{-1}) $\nu_{as}(CO_2)$: 1635 (vs); $\nu(C{=}N)$: 1490 (vs), 1450 (vs); $\nu_{sym}(CO_2)$: 1400 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 15.15(55); 33.10(2475).

The class of complexes was prepared in a similar way.

$Cu(2,3\text{-}D)_2(bipy)(H_2O)$ (**2**). Yield 55%. Formula weight: 677.82. Calc. for $C_{26}H_{20}Cl_4N_2O_7Cu$: C, 46.05; H, 2.95; N, 4.15; Cu, 9.40. Found: C, 46.10; H, 2.90; N, 4.25; Cu, 9.10%. ν_{max} (cm^{-1}) $\nu_{as}(CO_2)$: 1630 (vs); $\nu(C{=}N)$: 1475 (vs), 1455 (vs); $\nu_{sym}(CO_2)$: 1385 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}). DMF solution: 15.15(50); 33.10(2455).

$Cu(2,4\text{-}DP)_2(bipy)(H_2O)$ (**3**). Yield 60%. Formula weight: 705.83. Calc. for $C_{28}H_{24}Cl_4N_2O_7Cu$: C, 47.60; H, 3.40; N, 4.00; Cu, 9.00. Found: C, 47.90; H, 3.60; N, 4.25; Cu, 9.60%. ν_{max} (cm^{-1}) $\nu_{as}(CO_2)$: 1638 (vs); $\nu(C{=}N)$: 1477 (vs), 1446 (vs); $\nu_{sym}(CO_2)$: 1388 (vs) (KBr pellet).

UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 15.10(80); 33.10(2500).

Cu(2,4,5-T)$_2$(bipy)(H$_2$O) (**4**). Yield 60%. Formula weight: 746.75. Calc. for $C_{26}H_{18}Cl_6N_2O_7Cu$: C, 41.80; H, 2.45; N, 3.75; Cu, 8.50. Found: C, 41.90; H, 2.25; N, 3.70; Cu, 8.10%. ν_{max} (cm^{-1}) ν_{as}(CO$_2$): 1645 (vs); ν(C=N): 1475 (vs), 1445 (vs); ν_{sym}(CO$_2$): 1385 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 14.75(65); 33.10(2485).

Cu(2,4-D)$_2$(bipy)(H$_2$O) (**5**). Yield 60%. Formula weight: 677.82. Calc. for $C_{26}H_{20}Cl_4N_2O_7Cu$: C, 46.05; H, 2.95; N, 4.15; Cu, 9.40. Found: C, 46.40; H, 2.70; N, 3.95; Cu, 8.70%. ν_{max} (cm^{-1}) ν_{as}(CO$_2$): 1635 (vs); ν(C=N): 1475 (vs), 1445 (vs); ν_{sym}(CO$_2$): 1405 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 15.10(50); 33.10(2455).

2.5. *Synthesis of bis(2,2′-bipyridine)[(2-methyl-4-chlorophenoxy)acetato] copper(II) chloride (6)*

MCPA (2.00 g, 10 mmol) was dissolved in CH$_3$OH (50 cm^3) and CH$_3$ONa (0.54 g, 10 mmol) was added. After 30 min stirring CuCl$_2$·2H$_2$O (0.85 g, 5 mmol) and bipy (1.56 g, 10 mmol) in CH$_3$OH (25 cm^3) were added dropwise. The reaction mixture was refluxed for 1 h. The blue solution was reduced in volume and left for slow evaporation. Yield 60%. Formula weight: 611.0. Calc. for $C_{29}H_{24}Cl_2N_4O_3Cu$: C, 57.00; H, 3.95; N, 9.15; Cu, 10.40. Found: C, 57.10; H, 4.05; N, 9.25; Cu, 10.00%. ν_{max} (cm^{-1}) ν_{as}(CO$_2$): 1600 (vs); ν(C=N): 1475 (vs), 1445 (vs); ν_{sym}(CO$_2$): 1400 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 10.85(20); 14.30(65); 31.25(2030).

[Cu(2,4,5-T)(bipy)$_2$]Cl (**7**). Formula weight: 665.9. Calc. for $C_{28}H_{20}Cl_4N_4O_3Cu$: C, 50.50; H, 3.05; N, 8.40; Cu, 9.50. Found: C, 50.20; H, 3.10; N, 8.10; Cu, 9.10%. ν_{max} (cm^{-1}) ν_{as}(CO$_2$): 1615 (vs); ν(C=N): 1480 (vs), 1460 (vs); ν_{sym}(CO$_2$): 1395 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 10.85(15); 14.70(55); 31.35(2025).

[Cu(2,4-DP)(bipy)$_2$]Cl·3H$_2$O·2CH$_3$OH (**8**). Formula weight: 763.54. Calc. for $C_{31}H_{37}Cl_3N_4O_8Cu$: C, 48.70; H, 4.85; N, 7.35; Cu, 8.30. Found: C, 48.50; H, 5.20; N, 7.65; Cu, 8.00%. ν_{max} (cm^{-1}) ν_{as}(CO$_2$): 1590 (vs); ν(C=N): 1477 (vs), 1444 (vs); ν_{sym}(CO$_2$): 1404 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 10.95(35); 14.20(80); 31.25(2040).

[Cu(2,4-D)(bipy)$_2$]Cl (**9**). Formula weight: 631.4. Calc. for $C_{28}H_{21}Cl_3N_4O_3Cu$: C, 53.25; H, 3.35; N, 8.90; Cu, 10.05. Found: C, 52.90; H, 3.40; N, 8.65; Cu, 9.80%. ν_{max} (cm^{-1}) ν_{as}(CO$_2$): 1620 (vs); ν(C=N): 1480 (vs), 1440 (vs); ν_{sym}(CO$_2$): 1390 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 10.65(25); 14.10(50); 31.45(2020).

[Cu(2,3-D)(bipy)$_2$]Cl (**10**). Formula weight: 631.4. Calc. for $C_{28}H_{21}Cl_3N_4O_3Cu$: C, 53.25; H, 3.35; N, 8.90; Cu, 10.05. Found: C, 52.85; H, 3.60; N, 8.75; Cu, 9.80%. ν_{max} (cm^{-1}) ν_{as}(CO$_2$): 1615 (vs); ν(C=N): 1495 (vs), 1460 (vs); ν_{sym}(CO$_2$): 1410 (vs) (KBr pellet). UV–Vis: λ (cm^{-1}) (ε, dm^3 mol^{-1} cm^{-1}), DMF solution: 10.80(15); 14.20(30); 31.00(2000).

2.6. *X-ray crystal structure determination*

A dark blue prismatic crystal of Cu[C$_6$H$_3$(CH$_3$)Cl-OCH$_2$COO]$_2$(NH$_4$C$_5$-C$_5$H$_4$N)(H$_2$O) (**1**) with approximate dimensions 0.20×0.30×0.40 mm was mounted in air. Diffraction measurements were taken with a Crystal Logic dual goniometer diffractometer using graphite monochromated Mo radiation. Crystal data and parameters for data collection are reported in Table 1. Unit cell dimensions were determined and refined using the angular settings of 25 automatically centred reflections in the range 11° < 2θ < 23°. Intensity data were recorded using θ–2θ scanning to 2θ(max.) = 50° with a scan speed of 3.3° min^{-1} and a scan range of 2.5 plus $\alpha_1\alpha_2$ separation. Three standard reflections monitored every 97 reflections showed less than 3.0% intensity fluctuation and no decay. Lorentz and polarization correction were applied using Crystal Logic software.

Symmetry equivalent data were averaged with R_{int} = 0.0150 to give 4963 independent reflections from a total of 5128 collected. The structure was solved by direct methods using the program SHELXS86 [38] and refined by full-matrix least-squares techniques on F^2 with SHELXL-93 [39] using 4962 reflections and refining 466 parameters. All hydrogen atoms were located by difference maps and their positions were refined isotropically. All non-hydrogen atoms were refined anisotropically. The final values for R, R_w and GOF, for all data, are 0.0430, 0.1011 and 1.079, respectively. The maximum and minimum residual peaks in the final dif-

Table 1
Crystallographic data for **1**

	1
Formula	$C_{28}H_{26}Cl_2N_2O_7Cu$
a (Å)	40.494(14)
b (Å)	7.286(3)
c (Å)	19.617(6)
α (°)	
β (°)	103.23(1)
γ (°)	
V (Å^3)	5634(3)
T (K)	298
Space group	$C2/c$
Z	8
Formula weight	636.95
λ	0.71073
ρ_{obs} (g cm^{-3})	1.49
ρ_{calc} (g cm^{-3})	1.502
μ (cm^{-1})	10.14
R [a] indices (4232 reflections $I > 2\sigma(I)$)	R_1 = 0.0344, wR_2 = 0.0935

[a] $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ and $P = (\max(F_o^2, 0) + 2F_c^2)/3$, a = 0.04444, b = 4.972. $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

Table 2
Positional parameters ($\times 10^4$) and equivalent thermal parameters ($Å^2 \times 10^3$) of the non-H atoms of **1**

Atom	x	y	z	U_{eq}
Cu	4097(1)	1167(1)	9234(1)	42(1)
N(1)	4452(1)	1290(2)	10138(1)	40(1)
N(2)	3830(1)	151(3)	9884(1)	44(1)
O(1)	4412(1)	2231(3)	8734(1)	52(1)
O(4)	3689(1)	1812(2)	8538(1)	52(1)
O(w)	4136(1)	−1735(3)	8715(1)	59(1)
C(1)	4774(1)	1799(4)	10209(1)	49(1)
C(2)	5003(1)	1876(4)	10581(1)	57(1)
C(3)	4886(1)	1461(4)	11439(1)	63(1)
C(4)	4552(1)	962(4)	11379(1)	54(1)
C(5)	4339(1)	857(3)	10716(1)	42(1)
C(6)	3985(1)	213(3)	10572(1)	42(1)
C(7)	3818(1)	−368(3)	11079(1)	51(1)
C(8)	3494(1)	−1030(4)	10876(2)	58(1)
C(9)	3339(1)	−1135(4)	10171(2)	59(1)
C(10)	3514(1)	−521(4)	9692(1)	55(1)
C(11)	4407(1)	2021(4)	8087(1)	49(1)
O(2)	4277(1)	747(3)	7712(1)	68(1)
C(12)	4602(1)	3533(6)	7821(1)	66(1)
O(3)	4566(1)	3559(3)	7073(1)	65(1)
C(13)	4272(1)	4263(4)	6672(1)	51(1)
C(14)	4004(1)	4926(4)	6932(1)	61(1)
C(15)	3711(1)	5562(4)	6489(2)	59(1)
C(16)	3690(1)	5517(4)	5774(1)	53(1)
Cl(1)	3313(1)	6237(1)	5209(1)	72(1)
C(17)	3956(1)	4901(3)	5504(1)	52(1)
C(18)	4253(1)	4286(3)	5940(1)	49(1)
C(19)	4545(1)	3667(5)	5653(2)	59(1)
C(20)	3629(1)	3510(3)	8412(1)	43(1)
O(5)	3786(1)	4803(3)	8718(1)	59(1)
C(21)	3328(1)	3790(3)	7793(1)	51(1)
O(6)	3240(1)	5656(3)	7648(1)	58(1)
C(22)	3028(1)	6476(4)	8007(1)	51(1)
C(23)	2921(1)	5675(5)	8558(2)	64(1)
C(24)	2697(1)	6590(5)	8873(2)	73(1)
C(25)	2589(1)	8300(5)	8644(2)	73(1)
Cl(2)	2304(1)	9445(2)	9042(1)	114(1)
C(26)	2699(1)	9130(5)	8103(2)	66(1)
C(27)	2923(1)	8240(4)	7774(1)	53(1)
C(28)	3052(1)	9093(5)	7190(2)	68(1)

ference map were 0.738 and −0.561 e $Å^{-3}$. The largest shift/e.s.d. in the final cycle was 0.004. Positional and U_{eq} thermal parameters are given in Table 2.

3. Results and discussion

Synthesis of the complexes was achieved via two methods.

(i) Template reaction of $CuCl_2 \cdot 4H_2O$, NaOH, bipy and the ligand results in the formation of the cationic complex, e.g.

$$C_6H_3(CH_3)Cl\text{-}OCH_2COOH + NaOH + CuCl_2 + 2(NH_4C_5\text{-}C_5H_4N) \rightarrow [Cu[C_6H_3(CH_3)Cl\text{-}OCH_2COO](NH_4C_5\text{-}C_5H_4N)_2]Cl \qquad (1)$$

The compounds are 1:1 electrolytes in DMF or DMSO solutions.

(ii) Reaction of the mononuclear complexes with bipy results in the formation of the mononuclear neutral compound, e.g.

$$C_6H_3(CH_3)Cl\text{-}OCH_2COOH + NaOCH_3 \rightarrow C_6H_3(CH_3)Cl\text{-}OCH_2COONa \qquad (2)$$

$$2C_6H_3(CH_3)Cl\text{-}OCH_2COONa + CuCl_2 \rightarrow Cu[C_6H_3(CH_3)Cl\text{-}OCH_2COO]_2(H_2O)_2 \qquad (3)$$

$$Cu[C_6H_3(CH_3)Cl\text{-}OCH_2COO]_2(H_2O)_2 + NH_4C_5\text{-}C_5H_4N \rightarrow Cu[C_6H_3(CH_3)Cl\text{-}OCH_2COO]_2(NH_4C_5\text{-}C_5H_4N)(H_2O) \qquad (4)$$

The complexes are blue crystalline solids, soluble in DMF, DMSO and no electrolytes.

3.1. Description of the structure Cu[$C_6H_3(CH_3)Cl$-$OCH_2COO]_2(NH_4C_5$-$C_5H_4N)(H_2O)$ (1)

In **1** the carboxylate group of MCPA behaves as a unidentate ligand. An ORTEP diagram of **1** is given in Fig. 1, and selected bond distances and angles in Table 3. In this complex the copper atom is five-coordinate and could be described as having a distorted square pyramidal geometry. The changes in bond lengths described by the tetragonality index [40]

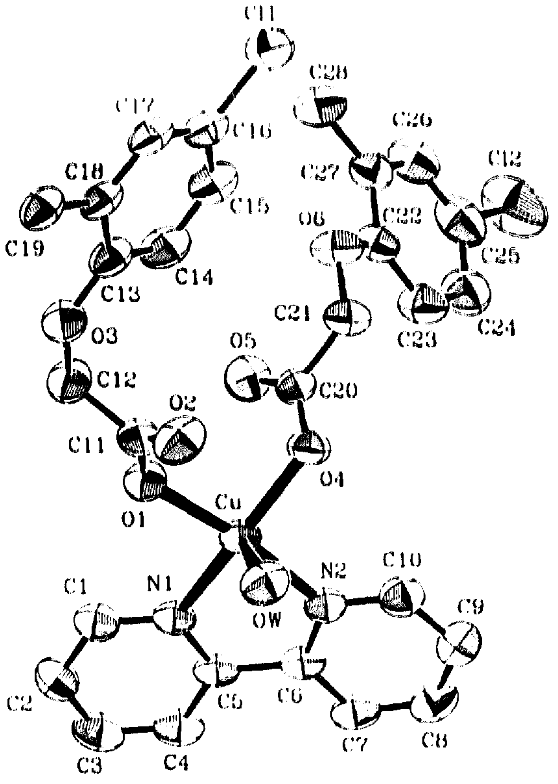


Fig. 1. ORTEP view of **1** with 50% thermal ellipsoids showing the atom-labelling scheme.

Table 3
Selected bond distances (Å) and angles (°) of 1

Bond distances (Å)			
Cu–O(1)	1.940(2)	Cu–O(W)	2.369(2)
Cu–O(4)	1.945(2)	Cu···O(2) (separation)	3.246(3)
Cu–N(2)	1.994(2)	Cu···O(5) (separation)	3.008(3)
Cu–N(1)	2.013(2)		
Angles (°)			
O(4)–Cu–O(1)	95.66(8)	N(2)–Cu–N(1)	80.63(8)
O(1)–Cu–N(2)	171.03(7)	O(4)–Cu–O(W)	92.47(8)
O(4)–Cu–N(2)	92.31(8)	O(1)–Cu–O(W)	91.31(9)
O(1)–Cu–N(1)	90.46(8)	N(2)–Cu–O(W)	92.45(9)
O(4)–Cu–N(1)	158.22(8)	N(1)–Cu–O(W)	108.30(8)

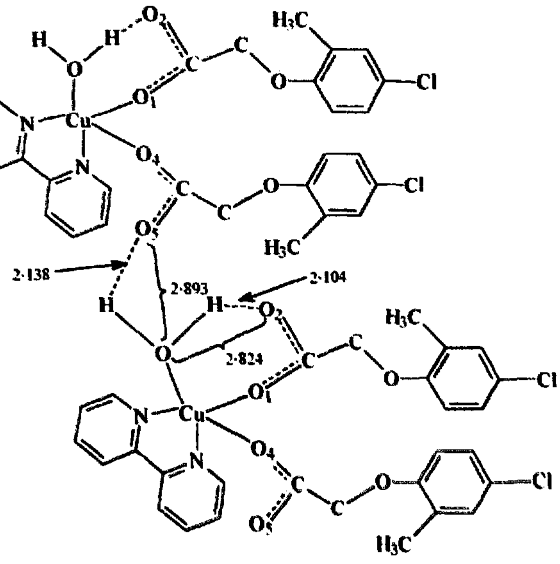
$T^5 = 0.83$ and the in-plane angular distortions described by the trigonality index [41] $\tau = (171.0 - 158.2)/60 = 0.21$ (where $\tau = (\varphi_1 - \varphi_2)/60$, φ_1, φ_2 are the largest angles in the coordination sphere, $\tau = 0$ is a perfect square pyramid, $\tau = 1$ is a perfect trigonal bipyramid) show the distortion away from the regular square-based pyramidal geometry [42–47]. The two nitrogen atoms N(1) and N(2) (Cu–N(1) = 2.013(2) and Cu–N(2) = 1.994(2) Å) of the bipyridine molecule and the carboxylate oxygen atoms O(1) and O(4) (Cu–O(1) = 1.940(2) and Cu–O(4) = 1.945(2) Å) occupy *cis* positions in the basal plane, while the water oxygen is 2.369(2) Å away. The uncoordinated carboxylato-oxygen atoms O(2) and O(5) (Cu···O(2) = 3.246(3) and Cu···O(5) = 3.008(3) Å) lie below and above the basal plane of the pyramid, respectively (1.834 and 2.025 Å). The ligand atoms which form this basal plane of the pyramid are not strictly coplanar. Atoms N(2), O(1) and O(4) are 0.165, 0.150 and 0.023 Å above the plane towards the apex, while N(1) lies 0.307 Å below the basal plane.

The Cu–O(W) distance of 2.369(2) Å is about 0.1 Å longer than the distances observed for the methoxyacetato (2.24 Å) [7], maleato (2.26 Å) [43] or 2,4-DP (2.236 Å) [37] analogues. This difference may be assigned to the hydrogen-bond network which is extensive in the present compound. There is intramolecular and intermolecular hydrogen bond interaction. The intramolecular interaction is between the water molecule and the uncoordinated O(2) atom at a distance H(W)···O(2) = 2.104 Å, while the intermolecular interaction is between the water molecule and the uncoordinated carboxylato oxygen atom, O(5), of a neighbouring molecule at a distance H(W)···O(5)′ = 2.138 Å giving a polymer chain. The oxygen atom O(W) lies 2.824 and 2.893 Å away from O(2) and O(5)′, respectively (Scheme 2).

The copper atom (Cu) is displaced 0.21 Å toward the water ligand. The *trans* N–Cu–O system of the basal plane gives angles of O(4)–Cu–N(2) = 92.3(1)° and O(1)–Cu–N(1) = 90.5(1)°.

3.2. Powder ESR spectra (4 K)

The polycrystalline ESR spectra of cationic complexes are rhombic [50,51] with $g_1 = 2.004$–2.017, $g_2 = 2.090$–2.103 and $g_3 = 2.165$–2.243. The lowest g value only slightly above 2.00 is consistent with an approximate d_{z^2} ground state for the CuN_2O chromophore with a distorted trigonal–bipyramidal stereochemistry.



Scheme 2.

The X-band ESR spectra of polycrystalline samples of **1** and **3** indicate the presence of magnetic exchange (Fig. 2). Using the approach employed by Wasserman et al. [48] for the spectra of randomly oriented organic triplets, we assign the pair of bands at 2560 and 3620 Gauss as the $\Delta m = 1$ transitions H_{xy1} and H_{xy2}. Setting $E = 0$ and using the equations

$$H_{xy1}^2 = \left(\frac{g_e}{g_\perp}\right)^2 H_0(H_0 - D)$$

$$H_{xy2}^2 = \left(\frac{g_e}{g_\perp}\right)^2 H_0(H_0 + D)$$

$$H_{z1} = (g_e/g_z)|H_0 - D|$$

$$H_{z2} = (g_e/g_z)(H_0 + D)$$

we obtain $g_\perp = 2.195$ and the zero-field splitting parameter $D = 0.106$ cm^{-1} (Table 4). We were unable to detect the corresponding $g_\parallel$ H_{z1} and H_{z2} lines. The band at lowest field at ~1600 Gauss ($g = 4.15$, $A = 73 \times 10^{-4}$ cm^{-1}) may be assigned to the $\Delta m = 2$ transition between the $|-1>$ and $|+1>$ levels. 'Half-field' transitions have been observed in a series of double bridged dinuclear Cu(II) compounds [49–51], while similar copper nuclear hyperfine splitting on the 'half-field' band has been observed for the complex $Cu(2,4\text{-}DP)_2(bipy)(H_2O)$ diluted in diamagnetic host [37]. The isotropic signal with $g_\parallel = 2.302$ and $g_\perp = 2.072$ may be assigned to mononuclear species with $S = 1/2$. The Cu···Cu distance (7.28 Å) is in the range, up to 11 Å, in which a magnetic exchange has been observed [40,42,45,51] and the value of $\mu_{eff} = 1.65$ BM is indicative of this.

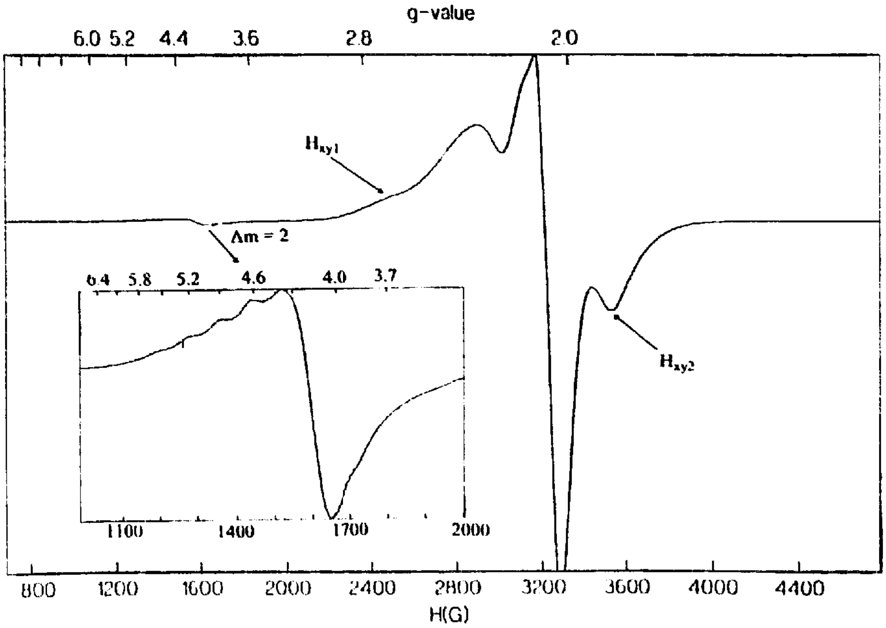


Fig. 2. X-band powder ESR spectrum of **1** at 4 K. Inset: enlargement of the ESR signal at 1600 Gauss.

Table 4
Spin-Hamiltonian parameters in solid state of the Cu(II) complexes

Compound	g_1	$g_\perp$	g_2	$g_\parallel$	g_3	D (cm^{-1})
Cu(2,4-DP)$_2$(bipy)(H$_2$O) $S=1$		2.196				0.108
Cu(2,4-DP)$_2$(bipy)(H$_2$O) $S=1/2$		2.072		2.302		
Cu(MCPA)$_2$(bipy)(H$_2$O) $S=1$		2.195				0.106
Cu(MCPA)$_2$(bipy)(H$_2$O) $S=1/2$		2.072		2.302		
Cu(2,4,5-T)$_2$(bipy)(H$_2$O)	2.048		2.091		2.262	
Cu(2,4-D)$_2$(bipy)(H$_2$O)		2.071		2.201		
Cu(2,3-D)$_2$(bipy)(H$_2$O)		2.072		2.200		
[Cu(2,4-DP)(bipy)$_2$]Cl	2.017		2.103		2.243	
[Cu(2,4-D)(bipy)$_2$]Cl	2.004		2.090		2.165	

3.3. Electrochemical studies

For the neutral complexes the cyclic voltammogram of **3** in the range +1.5 to −1.5 V is shown in Fig. 3, while similar voltammograms were recorded for this series of compounds. The complete scan in this range shows two cathodic waves at −0.55 and −1.20 V and two anodic waves at 0.25 and 0.60 V. The two one-electron waves at −0.55 and −1.20 V suggest a reduction of the mononuclear species in two steps.

The reduction at −0.55 V is followed by a disproportionation [33].

In a second scan two new reduction waves at 0.00 and −0.40 V were observed. These waves may be assigned to copper ion processes, as has been confirmed using Cu(ClO$_4$)$_2$ in DMF [33].

Scanning in the range 1.5 to −1.0 V, the wave at 0.25 V assigned to Cu^0→Cu^{II} disappears, confirming that the disproportionation process starts above −1.0 V, while a couple of not reversible anodic and cathodic waves appear at 0.11 and 0.70 and −0.40 and 0.01 V, respectively.

Considering all the above processes, the complete pattern in the range +1.5 to −1.5 V could be described by the following equations.

$$[\mathrm{Cu^{II}}] + e^- \xrightarrow{-0.55} [\mathrm{Cu^{I}}] + e^- \xrightarrow{-1.25} [\mathrm{Cu^{0}}]$$

$$2[\mathrm{Cu^{I}}] \xrightarrow{\mathrm{dispr}} [\mathrm{Cu^{II}}] + [\mathrm{Cu^{0}}]$$

$$[\mathrm{Cu^{0}}] \xrightarrow{0.25} [\mathrm{Cu^{II}}] + 2e$$

$$[\mathrm{Cu^{0}}] \xrightarrow{0.60} [\mathrm{Cu^{I}}] + e^-$$

$$[\mathrm{Cu^{II}}] + e^- \xrightarrow{0.01} [\mathrm{Cu^{I}}] \xrightarrow{-0.40} [\mathrm{Cu^{0}}]$$

In the range 1.5 to −1.0 V only the processes

$$[\mathrm{Cu^{II}}] + e \xrightarrow{0.01} [\mathrm{Cu^{I}}] \xrightarrow{-0.40} [\mathrm{Cu^{0}}]$$

$$[\mathrm{Cu^{0}}] - e^- \xrightarrow{0.70} [\mathrm{Cu^{I}}] - e^- \xrightarrow{0.11} [\mathrm{Cu^{II}}]$$

were detected.

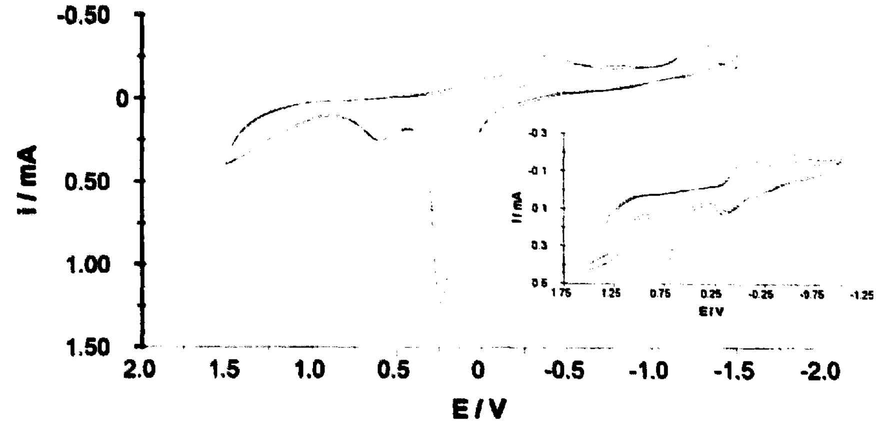


Fig. 3. Cyclic voltammograms of $Cu(2,4\text{-}D)_2(bipy)(H_2O)$ in DMF in the range 1.5 to − 1.5 V. Inset: cyclic voltammogram in the range 1.5 to − 1.0 V.

Table 5
Antimicrobial activity of the copper complexes

Complex	*Escherichia coli*	*Bacillus subtilis*	*Staphylococcus aureus*	*Proteus bulgaris*
$Cu(2,4\text{-}DP)_2 \cdot 2MeOH$	800 [a]	800	1600	1600
$Cu(MCPA)_2 \cdot 2MeOH$	800	800	800	800
$Cu(2,4,5\text{-}T)_2 \cdot 2MeOH$	800	800	1600	1600
$Cu_2(2,4\text{-}D)_4 \cdot 2MeOH$	400	400	800	800
$Cu_2(2,3\text{-}D)_4 \cdot 2MeOH$	400	400	800	800
$Cu(2,4\text{-}DP)_2(bipy)(H_2O)$	400	800	800	800
$Cu(MCPA)_2(bipy)(H_2O)$	400	800	800	400
$Cu(2,4,5\text{-}T)_2(bipy)(H_2O)$	400	800	800	800
$Cu(2,4\text{-}D)_2(bipy)(H_2O)$	400	400	400	400
$Cu(2,3\text{-}D)_2(bipy)(H_2O)$	400	400	400	400
$[Cu(2,4\text{-}DP)(bipy)_2]Cl$	200	200	400	200
$[Cu(MCPA)(bipy)_2]Cl$	100	200	200	200
$[Cu(2,4,5\text{-}T)(bipy)_2]Cl$	200	400	400	400
$[Cu(2,4\text{-}D)(bipy)_2]Cl$	200	200	400	200
$[Cu(2,3\text{-}D)(bipy)_2]Cl$	200	200	400	200
$[Cu(bipy)_2Cl]Cl$	200	100	100	100

[a] MIC in $\mu g\ ml^{-1}$.

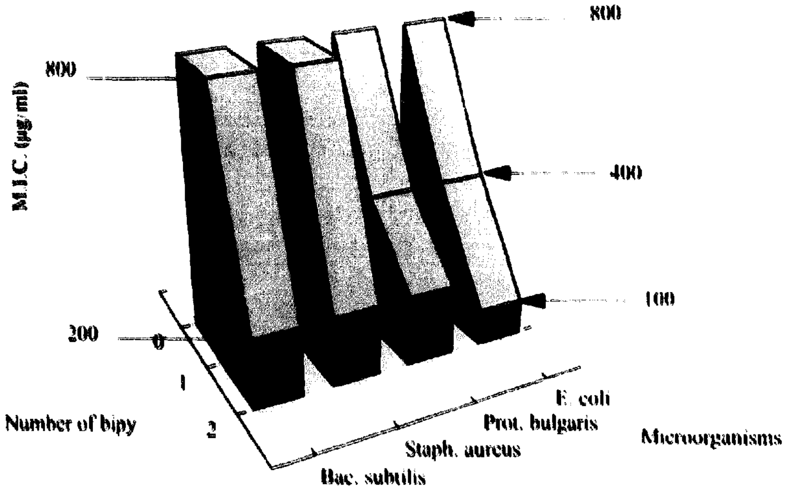


Fig. 4. Antimicrobial efficiency of the MCPA complexes against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Proteus bulgaris* microorganisms.

3.4. Antimicrobial activity

The efficiency of the complexes against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Proteus bulgaris* is given in Table 5, while in Fig. 4 the efficiency of MCPA complexes is presented schematically. A certain dependence as to an increasing effect could be observed in connection with the number of bipy molecules in the complexes. The presence of one coordinated bipy molecule increases the efficiency about 50%, except for the dinuclear complexes $Cu_2(2,4\text{-}D)_4 \cdot 2MeOH$ and $Cu_2(2,3\text{-}D)_4 \cdot 2MeOH$ which show similar behaviour against *Escherichia coli* and *Bacillus subtilis*, while the presence of two bipy increases the efficiency dramatically by 4–8 times. The antimicrobial activity of bipy itself has a healing action ($MIC = 400\ \mu g\ ml^{-1}$) against all the tested microbial species. While the position of the chlorides in the phenyl ring and the size of the chain do not affect the efficiency of the complexes, it seems that there is a structural relation. The dinuclear complexes $Cu_2(2,4\text{-}D)_4 \cdot 2MeOH$ and $Cu_2(2,3\text{-}D)_4 \cdot 2MeOH$ are more active than mononuclear complexes $Cu(2,4\text{-}DP)_2 \cdot 2MeOH$, $Cu(MCPA)_2 \cdot 2MeOH$ and $Cu(2,4,5\text{-}T)_2 \cdot 2MeOH$. This is in agreement with other dinuclear carboxylato complexes [52].

It is noticeable that the most efficient compounds are those of the type $[CuL(bipy)_2]Cl$, but we do not know whether there is a relation between the efficiency and the charge of the complex. The best inhibition is given by $[Cu(MCPA)(bipy)_2]Cl$ ($MIC = 100\ \mu g\ ml^{-1}$) against *Escherichia coli*.

4. Supplementary material

Tables giving crystal data and details of the structure determination (1S), anisotropic thermal parameters of the non-H atoms (2S), positional and isotropic thermal parameters of the hydrogen atoms (3S) and bond lengths, bond angles (4S) (5 pages), observed and calculated structure factors (19 pages) and a stereoview packing diagram are available from the authors on request.

Acknowledgements

The author V. Tangoulis thanks Mrs A. Athanassiou for financial support.

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