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Metal Complexes of 2,4-Diamino-5-(3′,4′,5′-trimethoxybenzyl)pyrimidine, (Trimethoprim).
Part II. Synthesis, Magnetic Characterization and X-ray Structure of $[Cu_2(O_2CCH_3)_4(Trimethoprim)_2]\cdot 2C_6H_6\cdot CH_3OH$

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*The reaction of $[Cu_2(O_2CCH_3)_4\cdot 2H_2O]$ with trimethoprim is reported. In methanol a green solution was obtained, which, on adding benzene, yielded tetrakis(μ-acetato)bis(trimethoprim)dicopper(II) dibenzene methanol solvate. The compound crystallizes with four molecules per unit cell in the monoclinic space group C2/c, with a = 24.109(5), b = 15.256(3), c = 16.532(3) Å, β = 116.89(2) for λ(Mo-Kα) = 0.71073 Å. The copper atoms are bridged by four acetate groups to form the binuclear molecule $[Cu_2(O_2CCH_3)_4(TMP)_2$**$]\cdot 2C_6H_6\cdot CH_3OH$. The TMP ligand acts as a donor molecule through one pyrimidinic nitrogen atom.*

Introduction

As part of our program to investigate the interaction of pyrimidine-derived ligands with metal ions [1], we describe here the complex of the 2,4-diamino-5-(3′,4′,5′-trimethoxybenzyl)pyrimidine ligand with copper(II) acetate, isolated as tetrakis(μ-acetato)bis(2,4-diamine-5-(3′,4′,5′-trimethoxybenzyl)pyrimidinecopper(II)) and characterized by elemental analyses, magnetic susceptibilities, ESR measurements, and IR and X-Ray analyses.

Experimental

Nitrogen, carbon and hydrogen were analysed with a Perkin-Elmer 240 Elemental Analyser.

Magnetic susceptibilities were carried out at room temperature with $Hg[Co(SCN)_4]$ as calibrant and corrected for diamagnetism with the appropriate Pascal constants.

X-band ESR spectra of polycrystalline samples were obtained using a Varian E109 spectrometer. The magnetic parameters were derived by standardization with diphenylpicrylhydrazyl.

Infrared spectra were recorded with a Beckman 4250 spectrophotometer in KBr phase.

Preparation of $[Cu_2(O_2CCH_3)_4(TMP)_2]\cdot 2C_6H_6\cdot CH_3OH$

To a solution of 1.000 g (3.45 mmol) of TMP in 70 ml of methanol was added a solution of 0.688 g (3.45 mmol) of copper(II) acetate monohydrate in 130 ml of the same solvent. The resulting green solution was stirred for two hours. Suitable crystals for X-ray analysis were obtained by adding benzene (100 ml) and after the solution had stood for some days. *Anal.* Calcd. for $C_{49}H_{64}Cu_2N_8O_{15}$: C, 52.0; H, 5.70; N, 9.90. Found: C, 51.7; H, 5.67; N, 9.63. M.P. 205–206 °C. μ_{eff} = 1.35 B.M.

Crystal Data

$C_{49}H_{64}Cu_2N_8O_{15}$, M = 1132.18, monoclinic, space group C2/*c*, a = 24.109(5), b = 15.256(3), c = 16.532(3) Å, β = 116.89(2)°, V = 5423 Å^3, $Z = 4$, $D_c = 1.387$ g cm^{-3}, μ(Mo-$K\alpha$) = 8.54 cm^{-1}.

Diffracted intensities were collected on a Nonius CAD-4 automatic diffractometer, by the ω-scan technique using graphite monochromated Mo-$K\alpha$ radiation (λ = 0.71073 Å). The standard CAD-4 centering, indexing and data collection programs were used. The unit cell parameters and the orientation matrix

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**TMP = 2,4-diamino-5-(3′,4′,5′-trimethoxybenzyl)pyrimidine.

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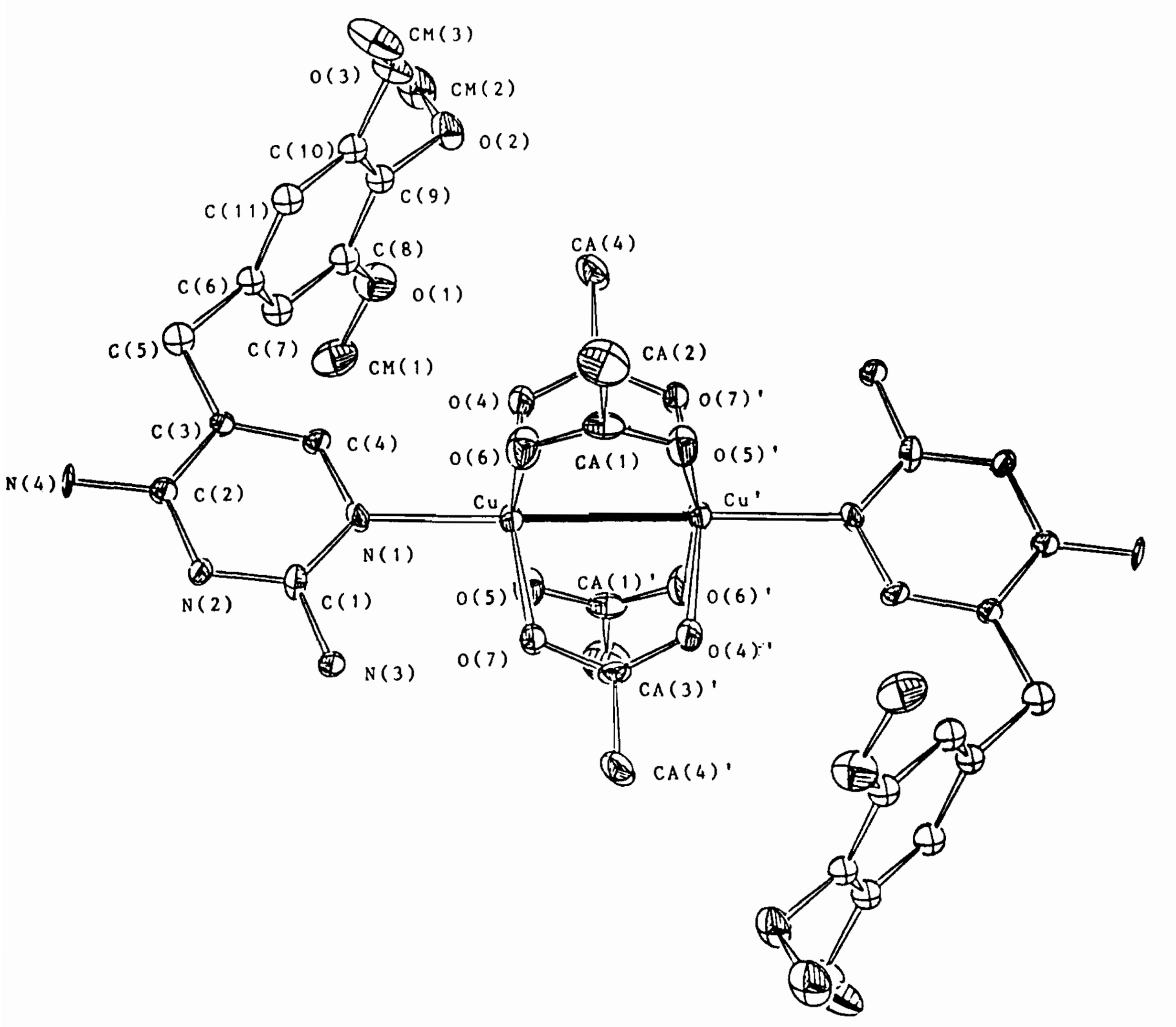

Fig. 1. ORTEP diagram of $Cu_2(O_2CCH_3)_4(TMP)_2$.

were obtained from least-squares fitting of 25 reflections having $16.9 < 2\theta < 20.0$. 4412 independent reflections were collected by exploring the ±h, +k, +l region of the reciprocal space in the 2θ range 3–47°; scan width was taken as $\Delta\omega = 1.00 + 0.35\tan\theta$. No crystal decay was observed by periodically re-measuring three standard reflections during the data collection. Three orientation standards were checked after every 200 reflections; if the standard deviation of the *h, k. l* values for any orientation reflection exceeded 0.10 a new orientation matrix was calculated by re-centering 22 reference reflections. Lorentz, polarization and absorption corrections were applied, the latter by an empirical method based on a set of ψ scans of reflections having χ values near to 90° [2].

All the non-hydrogen atoms were located by the usual Patterson and Fourier methods and the structure refinement was carried out on F_o values, the minimized function being $\Sigma w(F_o - k|F_c|)^2$. The contribution of hydrogen atoms in their calculated position was included in the last cycles of the full-matrix least-squares refinement which led to final values for R and R_w of 0.054 and 0.057 respectively for 1931 reflections having $I \geqslant 2\sigma(I)$. Individual weights were assigned according to the formula $w = \sigma^{-2}(F_o)$, where $\sigma(F_o) = \sigma(F_o^2)/2F_o$, $\sigma(F_o^2) = (\sigma^2(I) + (i\ I)^2)^{1/2}/Lp$ and i an 'ignorance factor' equal to 0.04. Scattering factors and anomalous dispersion factors were taken from ref. [3].

All the computations were carried out on a PDP 11/34 computer using the Nonius Structure Determination Package (SDP).

Results and Discussion

Crystals of the complex $[Cu_2(O_2CCH_3)_4(TMP)_2]\cdot 2C_6H_6\cdot CH_3OH$ consist of a packing of $[Cu_2(O_2$-

TABLE I. Positional Parameters of Non-hydrogen Atoms.

Atom	*x*	*y*	*z*
Cu	0.49123(4)	0.08615(6)	0.48343(6)
O1	0.2919(2)	0.1241(4)	0.0463(4)
O2	0.2057(3)	0.0459(4)	0.0864(4)
O3	0.1764(2)	0.1123(4)	0.2100(3)
O4	0.4105(2)	0.0486(3)	0.3861(4)
O5	0.5299(2)	0.0615(6)	0.4035(3)
O6	0.4549(2)	0.0816(4)	0.5683(3)
O7	0.5758(2)	0.0937(4)	0.5879(3)
N1	0.4734(3)	0.2243(4)	0.4507(4)
N2	0.4944(3)	0.3782(4)	0.4726(4)
N3	0.5702(3)	0.2778(4)	0.5528(5)
N4	0.4204(3)	0.4817(4)	0.3982(5)
C1	0.5108(3)	0.2936(5)	0.4904(5)
C2	0.4361(3)	0.3962(5)	0.4092(5)
C3	0.3952(3)	0.3280(5)	0.3594(5)
C4	0.4170(3)	0.2448(5)	0.3842(5)
C5	0.3316(3)	0.3499(5)	0.2824(5)
C6	0.2974(3)	0.2696(5)	0.2280(5)
C7	0.3110(3)	0.2378(5)	0.1614(5)
C8	0.2809(3)	0.1620(5)	0.1125(5)
C9	0.2354(3)	0.1226(5)	0.1307(5)
C10	0.2209(3)	0.1559(5)	0.1963(5)
C11	0.2522(3)	0.2292(5)	0.2462(5)
CM1	0.3333(4)	0.1666(7)	0.0202(6)
CM2	0.1655(4)	0.0564(6)	−0.0082(6)
CM3	0.1652(4)	0.1368(8)	0.2826(7)
CA1	0.4513(3)	0.0117(6)	0.6055(5)
CA2	0.4182(4)	0.0169(8)	0.6650(7)
CA3	0.3925(3)	−0.0282(5)	0.3698(5)
CA4	0.3288(4)	−0.0461(6)	0.2946(6)
CB1	0.2614(5)	0.1634(8)	0.5312(7)
CB2	0.3055(5)	0.2083(8)	0.5159(7)
CB3	0.2955(5)	0.2943(8)	0.4850(7)
CB4	0.0301(5)	0.137(1)	0.3359(8)
CB5	0.0163(5)	0.2182(9)	0.2969(9)
CB6	−0.0113(8)	0.068(1)	0.210(2)
CS	0.500	0.222(2)	0.250
OS	0.470(1)	0.298(2)	0.203(2)

$CCH_3)_4(TMP)_2]$ molecules with benzene and methanol molecules clathrated in the molar ratio 1:2:1 (Fig. 1). The $[Cu_2(O_2CCH_3)_4(TMP)_2]$ and the benzene molecules lie on crystallographic inversion centers so that only one half molecule is crystallographically independent. The methanol molecules, lying on a two-fold axis, are packed in a disordered way. Shortest contacts within the packing are the intramolecular N(3)···O(7) (2.86 Å) and the intermolecular N(4)···O(3) (2.97 Å), N(3)···O(3) (3.18 Å) interactions, the latter indicative of a weak hydrogen bonding pattern.

A large number of copper(II) carboxylates with stoichiometry $[Cu(O_2CR)_2L]$ is reported, where L is a donor molecule such as water or pyridine [4–10]. It is well known that many compounds of this type are magnetically non diluted, and are better formulated as $[Cu_2(O_2CR)_4L_2]$, with interaction between the two copper atoms, held together by bridging carboxylate groups. The coordination geometry around each copper atom in the $[Cu_2(O_2CCH_3)_4(TMP)_2]\cdot 2C_6H_6\cdot CH_3OH$ complex closely resembles that found in the above cited complexes.

The four bidentate acetate groups bridge two copper atoms which are in a distorted octahedral environment with the carboxylic oxygens at the equatorial sites of the octahedron and the apical positions occupied by the pyrimidinic nitrogen atom N(1) of the trimethoprim ligand and by the centrosymmetrically related copper atom. Each metal atom is displaced from the plane of the four equatorial oxygens by 0.23 Å towards the N(1) atom and away from the other copper atom. The Cu′–Cu–N(1) linkage is effectively linear (177.4(2)°). For comparison a list of structural parameters for $[Cu_2(O_2CCH_3)_4(TMP)_2]\cdot 2C_6H_6\cdot CH_3OH$ and other binuclear carboxylates is given in Table III.

Although the geometry of the tetra-μ-acetato-dicopper moiety is similar to that of the other

TABLE II. Relevant Interatomic Distances (A) and Angles (°) with Estimated Standard Deviations in Parentheses.

a) *within the* $Cu_2(O_2CCH_3)_4$ *moiety*			
Cu–Cu′	2.679(1)	CA(1)–O(6)	1.254(10)
Cu–O(4)	1.968(5)	CA(1)–O(5)′	1.241(9)
Cu–O(5)	1.966(6)	CA(1)–CA(2)	1.521(12)
Cu–O(6)	1.961(6)	CA(3)–O(4)	1.235(8)
Cu–O(7)	1.992(5)	CA(3)–O(7)′	1.260(8)
Cu–N(1)	2.170(5)	CA(3)–CA(4)	1.501(10)
Cu–O (average)	1.972	C–O(average)	1.247
		C–C(average)	1.511
Cu–O(6)–CA(1)	122.3(6)	O(4)–Cu–O(5)	89.4(2)
O(6)–CA(1)–O(5)′	126.5(8)	O(4)–Cu–O(6)	88.8(3)
CA(1)–O(5)′–Cu′	124.4(5)	O(4)–Cu–O(7)	166.4(2)
Cu–O(4)–CA(3)	125.0(5)	O(5)–Cu–O(6)	166.8(2)

(continued overleaf)

TABLE II. *(continued)*

O(4)–CA(3)–O(7)'	124.5(7)	O(5)–Cu–O(7)	89.1(2)
CA(3)–O(7)'–Cu'	124.1(5)	O(6)–Cu–O(7)	89.7(2)
mean O–C–O	125.5	Cu'–Cu–N(1)	177.4(2)
O(6)–CA(1)–CA(2)	116.5(9)	Cu'–Cu–O(4)	83.6(2)
O(5)'–CA(1)–CA(2)	116.5(9)	Cu'–Cu–O(5)	82.6(2)
O(4)'–CA(3)–CA(4)	118.6(7)	Cu'–Cu–O(6)	84.2(2)
O(7) –CA(3)–CA(4)	116.9(7)	Cu'–Cu–O(7)	82.8(2)
b) *within the trimethoprim ligand*			
C(1)–N(1)	1.352(8)	C(8)–C(9)	1.398(10)
C(1)–N(2)	1.343(8)	C(9)–C(10)	1.378(10)
C(1)–N(3)	1.356(8)	C(10)–C(11)	1.392(9)
N(2)–C(2)	1.349(8)	C(11)–C(6)	1.399(9)
C(2)–C(3)	1.413(9)	C(8)–O(1)	1.358(9)
C(2)–N(4)	1.348(8)	O(1)–CM(1)	1.418(10)
C(3)–C(4)	1.364(9)	C(9)–O(2)	1.395(8)
C(4)–N(1)	1.342(8)	O(2)–CM(2)	1.428(9)
C(3)–C(5)	1.522(9)	C(10)–O(3)	1.365(8)
C(5)–C(6)	1.522(10)	O(3)–CM(3)	1.396(11)
C(6)–C(7)	1.371(9)		
C(7)–C(8)	1.410(9)		
Cu–N(1)–C(1)	128.6(6)	C(5)–C(6)–C(7)	119.9(7)
Cu–N(1)–C(4)	116.4(4)	C(5)–C(6)–C(11)	119.5(7)
N(1)–C(1)–N(3)	118.4(6)	C(6)–C(7)–C(8)	120.2(7)
N(2)–C(1)–N(3)	116.2(6)	C(7)–C(8)–C(9)	118.6(8)
C(1)–N(2)–C(2)	117.8(6)	C(8)–C(9)–C(10)	120.9(7)
N(2)–C(2)–C(3)	120.7(6)	C(9)–C(10)–C(11)	120.0(7)
N(2)–C(2)–N(4)	115.6(6)	C(11)–C(6)–C(7)	120.6(7)
C(3)–C(2)–N(4)	123.7(6)	C(7)–C(8)–O(1)	124.9(7)
C(2)–C(3)–C(4)	115.9(6)	C(9)–C(8)–O(1)	116.5(7)
C(2)–C(3)–C(5)	119.9(6)	C(8)–C(9)–O(2)	120.9(7)
C(4)–C(3)–C(5)	124.1(6)	C(10)–C(9)–O(2)	118.1(7)
C(3)–C(4)–N(1)	124.9(6)	C(9)–C(10)–O(3)	116.6(7)
C(4)–N(1)–C(1)	115.0(6)	C(11)–C(10)–O(3)	123.4(7)
C(3)–C(5)–C(6)	112.9(6)		

TABLE III. Individual and Mean Structural Parameters for Binuclear Copper(II) Acetates, $[Cu_2(O_2CCH_3)_4L_2]$.

L[a]	Cu–Cu (A)	Cu–O (A)	Cu–L (A)	C–O (A)	Cu–Cu–L (°)	O–C–O (°)	Cu–O–C (°)	Bridge length (A)	Ref.
H_2O	2.614(2)	1.967	2.162(2)	1.260	–	124.9	122.8	6.45	11
	2.616(1)	1.969	2.156(4)	1.260	–	124.8	123.1	6.46	12
py[b]	2.645(3)	1.96	2.186(8)	1.25	–	125.6	–	6.42	7
py[c]	2.630(3)	1.98	2.122(9) 2.129(11)	1.24	–	125	124	6.44	4
Quin	2.642	1.93	2.17	1.24	–	130	–	6.34	13
NCS^-	2.643(3)	2.03	2.08(2)	1.24	–	126	123	6.54	14
TMP	2.679(1)	1.972	2.170(5)	1.247	177.35	125.5	123.6	6.43	This work

[a] Ligand abbreviations: py = pyridine, Quin = quinoline, TMP = trimethoprim. [b] Orthorhombic form. [c] Monoclinic form.

acetates, the metal–metal bond length, 2.679(1) Å, is the longest observed in this class of compounds. The four acetate groups are all planar; the coordination planes Cu–O(6)–CA(1)–O(5)'–Cu'–O(6)'–CA(1)'–O(5) and Cu–O(4)–CA(3)–O(7)'–Cu'–O(4)'–CA(3)'–O(7) are nearly perpendicular, the dihedral angle being 89.7°. A small but significant lengthening of the Cu–O(7) distance, 1.992(5) Å,

TABLE IV. Least-squares Planes. The equation of the plane is in the form Ax + By + Cz + D = 0, where A, B, C, D are constants and x, y, z are orthogonalized coordinates.

a) Equation of planes through selected groups of atoms

Plane	Atoms	A	B	C	D
1	N(1), C(1), N(2), C(2), C(3), C(4)	0.7307	0.0044	−0.6827	1.3846
2	C(6), C(7), C(8), C(9), C(10), C(11)	−0.4420	0.5843	−0.6806	−2.2946
3	O(4), O(5), O(6), O(7)	−0.0496	0.9813	−0.1857	−0.6730

b) Distances (A × 10^3) of selected atoms from planes

Plane	
1	N(1) −29(7), C(1) 18(8), N(2) 12(7), C(2) −30(7), C(3) 17(8), C(4) 12(8), Cu −233(1), N(3) 95(7), N(4) −131(7), C(5) 94(9)
2	C(6) −5(7), C(7) 14(8), C(8) −11(8), C(9) 0(8), C(10) 10(8), C(11) −7(8), C(5) − 21(8), O(1) −24(8), O(2) −70(6), O(3) 2(5)
3	O(4) −5(5), O(5) 5(5), O(6) 5(6), O(7) −5(5), Cu 230(1)

c) Dihedral angle (°) between planes

Plane 1 Plane 2 81.7

TABLE V. Infrared Carbon–Oxygen Stretching Frequencies (cm^{-1}).

Compound	$\nu_{as}(CO_2)$	$\nu_s(CO_2)$	$\Delta\nu$	Ref.
CH_3COONa	1578	1414	164	15
$[Cu_2(CH_3COO)_4]$	1591	1420	171	15
$[Cu_2(CH_3COO)_4(H_2O)_2]$	1603	1418	185	15
$[Cu_2(CH_3COO)_4(TMP)_2]\cdot 2C_6H_6\cdot CH_3OH$	1618	1420	198	This work

with respect to the remaining three Cu–O(4,5,6) (1.965 Å, average), is probably related to the intramolecular hydrogen bonding in which O(7) is involved, (H(N3)···O(7) 2.10 Å). As far as the trimethoprim ligand is concerned, the coordination to the copper atom occurs as already observed in $[CoCl_2(TMP)_2]$, [1] *via* its pyrimidinic nitrogen atom N(1). The Cu–N(1) distance, 2.170(5) Å, is comparable with that of 2.186(8) Å, found in the orthorhombic form of monopyridinecopper(II) acetate (Table III). Again, as in $[CoCl_2(TMP)_2]$, the main features of the trimethoprim ligand are unaltered with respect to the free molecule, with the exception of those related with the conformational freedom degrees around C(3)–C(5) and C(5)–C(6) bonds and those of the methoxy groups. The magnetic moment of $[Cu_2(O_2CCH_3)_4(TMP)_2]\cdot 2C_6H_6\cdot CH_3OH$ measured at room temperature (1.35 B.M.) is lower than the spin only value of 1.73 B.M., and also lower than the value of 1.8 to 2.22 B.M. usually found for mononuclear copper(II) compounds.

The ESR spectrum of polycrystalline $[Cu_2(O_2CCH_3)_4(TMP)_2]\cdot 2C_6H_6\cdot CH_3OH$ sample affords complementary information to the susceptibility results in that it confirms the binuclear structure. Using X-band radiation at room temperature three transitions are seen. Using these measured positions and the available literature methods [5, 8, 15, 17], we find D = 0.36 cm^{-1}, $g_\parallel$ = 2.41, $g_\perp$ = 2.09. These values agree with those found for binuclear

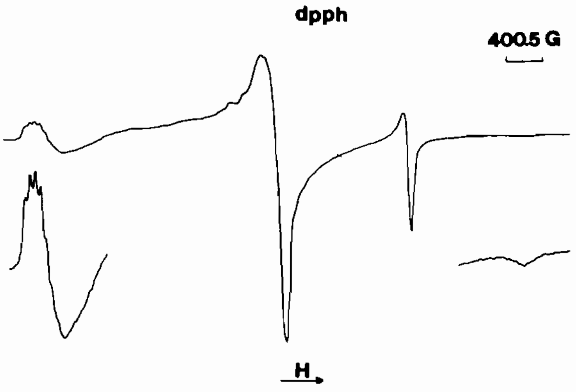

Fig. 2. ESR spectrum of polycrystalline $Cu_2(O_2CCH_3)_4(TMP)_2\cdot 2C_6H_6\cdot CH_3OH$ at 123 K.

copper(II) carboxylate complexes having a populated spin triplet state. The resonance at *ca.* 3000 G is due to non-dimeric (doublet species) copper(II); the absorptions at the highest and lowest magnetic fields are associated with the parallel direction. At 123 K (Fig. 2), the seven-line hyperfine splitting from the two equivalent copper nuclei ($A_{\parallel} = 55$ G) is visible on the lower field line.

IR carboxylate bands have been assigned based on data available in the literature [15, 16, 19]. The mode of coordination of carboxylate groups has often been deduced from the magnitude of the observed separation (Δ) between $\nu_{as}(CO_2)$ and $\nu_s(CO_2)$. For binuclear copper(II) carboxylates $\nu_{as}(CO_2)$ bands are found at higher frequencies than for the free ion. The values of the $\nu_{as}(CO_2)$ and $\nu_s(CO_2)$ stretching vibrations of our complex and of other similar compounds are listed in Table V.

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