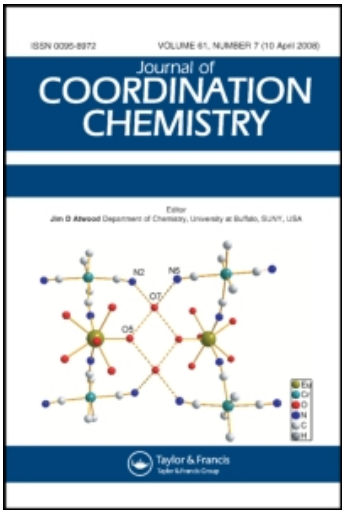

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

Co(II) and Cu(II) complexes of 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine

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First published on: 13 September 2007

To cite this Article Ajibade, P. A. , Kolawole, G. A. , O'brien, P. , Raftery, J. and Helliwell, M.(2008) 'Co(II) and Cu(II) complexes of 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine', Journal of Coordination Chemistry, 61: 3, 328 — 340, First published on: 13 September 2007 (iFirst)
To link to this Article: DOI: 10.1080/00958970701338770
URL: http://dx.doi.org/10.1080/00958970701338770

Journal of Coordination Chemistry
Vol. 61, No. 3, 10 February 2008, 328–340

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Co(II) and Cu(II) complexes of 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine

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(*Received 28 August 2006; in final form 1 March 2007*)

The Co(II) and Cu(II) complexes of 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine (trimethoprim) were synthesized and characterized by elemental analysis, UV-Vis and IR spectroscopy, magnetic susceptibility measurements, EPR (Cu complexes) and single crystal X-ray studies. The molecular structures of the compounds consist of dimeric metal ions in distorted octahedral environments, bridged with four acetate ions and each metal ion coordinated to one trimethoprim through the pyrimidinyl nitrogen atom.

Keywords: Cobalt; Copper; Molecular structure; Malaria; Trimethoprim; Metal complexes

1. Introduction

Trimethoprim (TMP) is a substituted 2,4-diaminopyrimidine. The pyrimidine ring system, present in nucleic acids, several vitamins and coenzymes, provides potential binding sites for metal ions and plays a significant role in many biological systems [1]. Trimethoprim is a well-known drug which exhibits antibacterial and antiprotozoal activities and is widely used in medicine [2]. It is used as an antibacterial agent and an inhibitor in chemotherapeutic treatment due to its antifolate effect by interaction with dihydrofolate coenzymes [3, 4] and is commonly administered in combination with a sulfonamide. Both drugs block the folic acid metabolism and produce synergistic antibacterial activity [5]. Trimethoprim is weakly bactericidal and resistance has emerged due to intensive use and misuse [6]. Resistance to major antibacterial [7] and antiparasitic drugs [8] necessitates drugs with novel properties, modes of action, or both. Metal complexes capable of enhancing biological activity has become a vibrant and growing area of research over the last few decades resulting in a variety of exciting and invaluable drugs such as *cis*-platin and related complexes [9, 10]. Research is being conducted in fields such as cancer, [11] arthritis [12] and cardiovascular medicine, although until recently this has been restricted predominantly to organic drugs. In the

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Journal of Coordination Chemistry
ISSN 0095-8972 print/ISSN 1029-0389 online © 2008 Taylor & Francis
DOI: 10.1080/00958970701338770

search for novel drugs against drug-resistant bacterial and parasitic organisms, the modification of current drugs by coordination to a metal center has attracted considerable attention [13–15].

Trimethoprim has seven potential binding sites for metal ions. Studies on the interaction of trimethoprim as ligands with metal ions have received some attention. The complexes of Co(II) [16], Cu(II) [17, 18], Rh(II) [19], Cd(II) [20, 21], and Ni(II) [22] have been reported. In these complexes, results of X-ray diffraction studies showed that the metal ions were coordinated to trimethoprim through the pyrimidinyl N(1). The interactions of Ag(I), Zn(II), Cd(II), Hg(II), and Ni(II) with trimethoprim have also been reported [23, 24]. The authors concluded, based on the IR spectra of the complexes, that coordination occurred between the metal ions and one of the NH_2 groups on the pyrimidine ring system of the trimethoprim. As part of our ongoing studies [22, 25] on the use of metal complexes as potential chemotherapeutic agents, we present in this work the synthesis and characterization of Co(II) and Cu(II) complexes of trimethoprim.

2. Experimental

2.1. *Materials and instrumentation*

All reagents, metal salts, and trimethoprim were used as obtained from Aldrich. Elemental analyses were performed at the Micro-analytical laboratory of the School of Chemistry, The University of Manchester, UK. IR spectra were obtained as KBr discs on a Perkin-Elmer Paragon 1000 FTIR spectrophotometer equipped with CsI windows (4000–250 cm^{-1}). UV-Vis spectra were obtained on a Perkin-Elmer Lambda 20 spectrophotometer. Magnetic susceptibility measurements were carried out at room temperature using a Sherwood Scientific magnetic susceptibility balance. Diamagnetic corrections were made using Pascal's constants [26].

2.2. *Preparation of cobalt(II) complex of trimethoprim, $\{[Co_2(TMP)_2(OCOCH_3)_4] \cdot 2C_6H_5CH_3 \cdot (CH_3OH)\}$ (I)*

Complex **I** was synthesized by dissolving trimethoprim (0.586 g, 2 mmol) in 35 mL of methanol followed by slow addition of $Co(CH_3COO)_2 \cdot 4H_2O$ (0.498 g, 2 mmol) in 65 mL of methanol. The resulting pink solution was refluxed for 3 h, layered with 65 mL of toluene and covered with cotton wool to undergo slow evaporation at room temperature. Pink crystals were formed after a week. The complex is formulated as $\{[Co_2(TMP)_2(OCOCH_3)_4] \cdot 2C_6H_5CH_3 \cdot (CH_3OH)\}$; molar mass, 1150.99. Anal. Calcd for $C_{51}H_{68}N_8O_{15}Co_2$ (%): C, 53.23; H, 5.91; N, 9.74; Co, 10.24. Found: C, 53.53; H, 5.85; N, 9.82; Co, 10.16.

2.3. *Preparation of copper(II) complex of trimethoprim, $\{[Cu_2(TMP)_2(OCOCH_3)_4] \cdot 2C_6H_5CH_3 \cdot (CH_3OH)\}$ (II)*

1.465 g (5 mmol) of trimethoprim was dissolved in 60 mL of methanol followed by slow addition of $Cu_2(CH_3COO)_4 \cdot 2H_2O$ in 100 mL of methanol. The resulting green solution

was refluxed for 1 h, layered with 120 mL of toluene, and transferred into the refrigerator. Green crystals, consisting of two polymorphs of the same composition, $\{[Cu_2(TMP)_2(OCOCH_3)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ formed after three days. Molar mass, 1160.21. Anal. Calcd for $C_{51}H_{68}N_8O_{15}Cu_2$ (%): C, 52.74; H, 5.86; N, 9.65; Cu, 10.94. Found: C, 52.34; H, 5.91; N, 9.68; Cu, 10.87.

2.4. *X-ray crystallography*

The data sets for the single crystal X-ray studies were collected with Mo-Kα radiation at 100° K on a Bruker SMART APEX CCD diffractometer equipped with an Oxford Cryosystems low temperature device. A semi-empirical absorption correction was applied using SADABS [27] in one case (the $C2/c$ polymorph of **II**). The structures were solved by direct methods using SHELXS-97 and completed by iterative cycles ΔF syntheses, using the SHELXTL package [27]. Hydrogen atoms were included in calculated or difference map positions, except for the disordered solvent molecules and the structures were refined using full-matrix least-squares refinement against F^2 [27]. The crystal data are summarized in table 1.

3. Results and discussion

Dimeric Co(II) and Cu(II) complexes of trimethoprim, **I** and **II**, are synthesized by reaction between the metal acetate and trimethoprim in methanol. The complexes are air stable and crystallized with incorporation of two molecules of toluene and one of methanol in the crystal lattice; two polymorphs of **II** were obtained from the same recrystallization condition. In the synthesis of the copper complexes, attempts were made for templating trimethoprim and pyrimethamine on the copper ions in the hope that the presence of two different drugs on the metal ions might vary the antiplasmodial activities of the resulting complexes, but only **II** was formed i.e. without the incorporation of pyrimethamine. The analytical and spectroscopic data are consistent with the proposed formulation of the complexes. The crystal structure of **I** and one polymorph of **II** were found to be isomorphous. The structure of the other polymorph of **II** is also reported. The structures of **I** and both polymorphs of **II** are very similar and therefore will be discussed together.

3.1. *Description of the crystal structures of I and II*

The isomorphous structures, $\{[M_2(TMP)_2(OCOCH_3)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ (M = Co, Cu) crystallize in the space group $C2/c$ and the atom-numbering scheme used is shown in figure 1 and selected geometric parameters are shown in table 2; the second polymorph of **II**, also with the formulation $\{[Cu_2(TMP)_2(OCOCH_3)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$, crystallizes in the space group $P2_1/c$ and is shown in figure 2. Selected bond distances and angles are given in table 3. The structures of **I** and **II** in the polymorph with the space group $C2/c$ contain an inversion center lying on the midpoint between the two metal atoms, so that only half of the molecule is crystallographically independent; there is one ordered and one

Table 1. Summary of crystal data and structure refinement.

Compound	$\{[Co_2(TMP)_2(OCOCH_3)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$	$\{[Cu_2(TMP)_2(OCOCH_3)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$; polymorph **1**	$\{[Cu_2(TMP)_2(OCOCH_3)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$; polymorph **2**
Formula	$C_{51}H_{68}Co_2N_8O_{15}$	$C_{51}H_{68}Cu_2N_8O_{15}$	$C_{51}H_{68}Cu_2N_8O_{15}$
Formula weight	1150.99	1160.21	1160.21
Temperature (K)	100(2)	100(2)	100(2)
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$C2/c$	$C2/c$	$P2_1/c$
a (Å)	24.313(4)	24.182(3)	22.299(3)
b (Å)	15.321(3)	15.2339(16)	15.2270(17)
c (Å)	16.323(3)	16.2306(17)	16.2410(18)
β (°)	116.526(2)	116.5020(10)	104.0990(18)
Volume (A^3)	5440.1(17)	5350.9(10)	5348.5(10)
Z	4	4	4
D_{Calcd} ($Mg\,m^{-3}$)	1.405	1.440	1.431
Absorption coefficient (mm^{-1})	0.683	0.870	0.870
$F(000)$	2416	2432	2432
Crystal size (mm^3)	$0.30\times0.20\times0.05$	$0.50\times0.50\times0.30$	$0.30\times0.20\times0.20$
θ range (°)	1.63–26.90°.	1.63—26.37	1.64–28.29
Limiting indices	$-30\le h\le30$, $-18\le k\le19$, $-20\le l\le20$	$-30\le h\le30$, $-18\le k\le19$, $-20\le l\le20$	$-29\le h\le29$, $-20\le k\le19$, $-21\le l\le21$
Reflections collected	21241	20828	45633
Independent reflection	5825 [$R_{int}=0.094$]	5464 [$R_{int}=0.0239$]	12713 [$R_{int}=0.0523$]
Data/restraints/parameters	5825/102/384	5464/1/384	12713/62/728
Goodness-of-fit on F^2	0.903	1.042	1.063
Final R indices [$I>2\sigma(I)$]	$R_1=0.0519$, $wR_2=0.1250$	$R_1=0.0394$, $wR_2=0.1035$	$R_1=0.0442$, $wR_2=0.1195$
R indices (all data)	$R_1=0.1094$, $wR_2=0.1415$	$R_1=0.0454$, $wR_2=0.1071$	$R_1=0.0597$, $wR_2=0.1254$
Largest diff. peak and hole ($e\,Å^{-3}$)	0.546 and −0.572	0.786 and −0.343	0.907 and −0.849

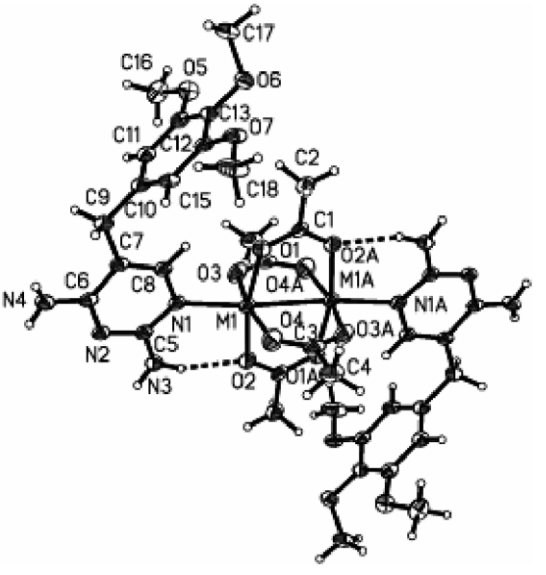

Figure 1. X-ray crystal structure of $\{[M_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ (M = Co, Cu) in the space group $C2/c$, with ellipsoids drawn at the 50% probability level and intramolecular hydrogen bonding contacts shown with dashed lines. The toluene and methanol solvent molecules have been omitted for clarity.

Table 2. Selected bond lengths (Å) and angles (°) for $\{[M_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$, M = Co, Cu in the space group $C2/c$.

	M=Co	M=Cu		M=Co	M=Cu
M(1)–O(3)	1.970(3)	1.9640(18)	O(3)–M(1)–O(4)	166.85(14)	166.83(8)
M (1)–O(4)	1.970(3)	1.9645(19)	O(3)–M(1)–O(1)	89.61(13)	89.59(8)
M(1)–O(1)	1.977(3)	1.9731(16)	O(4)–M(1)–O(1)	89.15(13)	89.01(9)
M(1)–O(2)	1.994(3)	1.9858(17)	O(3)–M(1)–O(2)	89.11(13)	89.08(8)
M(1)–N(1)	2.185(4)	2.179(2)	O(4)–M(1)–O(2)	89.20(13)	89.29(9)
M(1)–M(1)#1	2.6893(12)	2.6745(6)	O(1)–M(1)–O(2)	167.19(14)	166.78(7)
			O(3)–M(1)–N(1)	94.28(13)	94.34(8)
			O(4)–M(1)–N(1)	98.85(14)	98.81(8)
			O(1)–M(1)–N(1)	92.15(12)	92.44(7)
			O(2)–M(1)–N(1)	100.66(12)	100.78(7)
			O(3)–M(1)–M(1)#1	82.41(10)	82.36(6)
			O(4)–M(1)–M(1)#1	84.44(10)	84.47(6)
			O(1)–M(1)–M(1)#1	83.48(10)	83.15(5)
			O(2)–M(1)–M(1)#1	83.72(10)	83.64(5)
			N(1)–M(1)–M(1)#1	174.52(9)	174.48(5)

Symmetry transformation: #1: $-x, -y+2, -z$.

disordered toluene and one disordered methanol for each dimer unit. In the $P2_1/c$ polymorph of **II**, the asymmetric unit contains the whole dimeric complex, together with one ordered and one disordered toluene, and an ordered methanol; generally geometric parameters are the same within experimental error as those of the $C2/c$ polymorph of **II** although the $P2_1/c$ polymorph is slightly more ordered. In all three crystal structures the metal atoms are in a distorted octahedral environment in which each is bonded to trimethoprim, acting as a monodentate ligand through pyrimidine

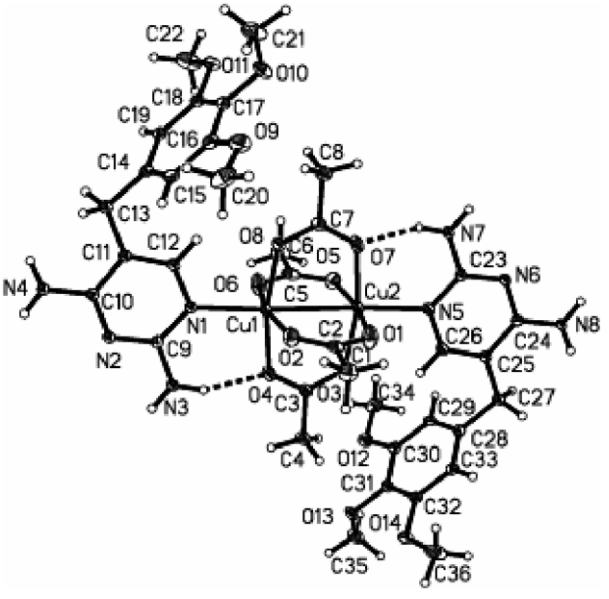

Figure 2. X-ray crystal structure of $\{[Cu_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ in the space group $P2_1/c$, with ellipsoids drawn at the 50% probability level and intramolecular hydrogen bonding contacts shown with dashed lines. The toluene and methanol solvent molecules have been omitted for clarity.

Table 3. Selected bond lengths (Å) and angles (°) for $\{[Cu_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$, in the space group $P2_1/c$.

Cu(1)–O(6)	1.9658(17)	O(6)–Cu(1)–O(2)	166.16(7)
Cu(1)–O(2)	1.9661(16)	O(6)–Cu(1)–O(8)	89.16(8)
Cu(1)–O(8)	1.9700(16)	O(2)–Cu(1)–O(8)	89.72(7)
Cu(1)–O(4)	1.9813(17)	O(6)–Cu(1)–O(4)	89.14(8)
Cu(1)–N(1)	2.1812(18)	O(2)–Cu(1)–O(4)	88.79(7)
Cu(1)–Cu(2)	2.6756(5)	O(8)–Cu(1)–O(4)	166.75(7)
Cu(2)–O(5)	1.9669(17)	O(6)–Cu(1)–N(1)	98.77(7)
Cu(2)–O(1)	1.9672(17)	O(2)–Cu(1)–N(1)	95.06(7)
Cu(2)–O(3)	1.9742(16)	O(8)–Cu(1)–N(1)	92.41(7)
Cu(2)–O(7)	1.9816(17)	O(4)–Cu(1)–N(1)	100.84(7)
Cu(2)–N(5)	2.1818(18)	O(6)–Cu(1)–Cu(2)	84.14(5)
		O(2)–Cu(1)–Cu(2)	82.03(5)
		O(8)–Cu(1)–Cu(2)	83.11(5)
		O(4)–Cu(1)–Cu(2)	83.64(5)
		N(1)–Cu(1)–Cu(2)	174.65(5)
		O(5)–Cu(2)–O(1)	167.59(7)
		O(5)–Cu(2)–O(3)	89.50(7)
		O(1)–Cu(2)–O(3)	88.76(8)
		O(5)–Cu(2)–O(7)	89.51(8)
		O(1)–Cu(2)–O(7)	89.34(8)
		O(3)–Cu(2)–O(7)	166.61(7)
		O(5)–Cu(2)–N(5)	93.46(7)
		O(1)–Cu(2)–N(5)	98.89(7)
		O(3)–Cu(2)–N(5)	92.59(7)
		O(7)–Cu(2)–N(5)	100.79(7)
		O(5)–Cu(2)–Cu(1)	82.81(5)
		O(1)–Cu(2)–Cu(1)	84.79(5)
		O(3)–Cu(2)–Cu(1)	83.11(5)
		O(7)–Cu(2)–Cu(1)	83.52(5)
		N(5)–Cu(2)–Cu(1)	174.31(5)

Table 4. Hydrogen bonding contacts.

D–H···A	d(D–H)	d(H···A)	d(D···A)	∠(DHA)
(a) {[$Co_2(TMP)_2(CH_3COO)_4$]·2$C_6H_5CH_3$·(CH_3OH)}				
N(3)–H(1N)···O(2)	1.16(6)	1.72(6)	2.863(5)	167(4)
N(4)–H(3N)···N(2)#1	0.87(5)	2.24(5)	3.084(5)	163(5)
N(3)–H(2N)···O(7)#2	1.05(6)	2.17(6)	3.075(4)	143(4)
N(4)–H(4N)···O(7)#3	0.84(5)	2.32(5)	3.003(5)	138(4)
(b) {[$Cu_2(TMP)_2(CH_3COO)_4$]·2$C_6H_5CH_3$·(CH_3OH)} in the space group $C2/c$				
N(3)–H(1N)···O(2)	0.83(3)	2.05(3)	2.855(3)	161(3)
N(4)–H(3N)···N(2)#1	0.79(3)	2.28(3)	3.065(3)	177(3)
N(3)–H(2N)···O(7)#2	0.84(3)	2.28(3)	3.061(3)	156(3)
N(4)–H(4N)···O(7)#3	0.77(3)	2.34(3)	2.980(3)	141(3)
(c) {[$Cu_2(TMP)_2(CH_3COO)_4$]·2$C_6H_5CH_3$·(CH_3OH)} in the space group $P2_1/c$				
N(3)–H(3A)···O(14)#1	0.88	2.27	3.053(2)	148.0
N(3)–H(3B)···O(4)	0.88	2.02	2.849(2)	156.7
N(4)–H(4D)···N(6)#2	0.88	2.18	3.050(3)	171.0
N(4)–H(4E)···O(11)#3	0.88	2.26	2.990(2)	139.7
N(7)–H(7A)···O(7)	0.88	2.04	2.859(2)	155.1
N(7)–H(7B)···O(11)#4	0.88	2.27	3.065(2)	149.9
N(8)–H(8D)···N(2)#5	0.88	2.20	3.066(2)	167.6
N(8)–H(8E)···O(14)#6	0.88	2.24	2.960(2)	138.4
O(15)–H(15A)···O(5)	0.84	2.25	2.994(3)	148.2
O(15)–H(15A)···N(5)	0.84	2.58	3.196(3)	130.7

Symmetry transformations used to generate equivalent atoms:
(a, b) #1: $-x, -y+1, -z$; #2: $x-1/2, -y+3/2, z-1/2$; #3: $-x+1/2, y-1/2, -z+1/2$.
(c) #1: $-x+2, y-1/2, -z+3/2$; #2: $x, y-1, z$; #3: $-x+1, y-1/2, -z+3/2$; #4: $-x+1, y+1/2, -z+3/2$; #5: $x, y+1, z$; #6: $-x+2, y+1/2, -z+3/2$.

(at the N1 position for the $C2/c$ polymorph and the N1 and N5 positions for the $P2_1/c$ polymorph) and two bridging acetate ligands. The Co–Co bond length of 2.6893(12) Å in **I** is at the extreme of normal bond lengths obtained for acetate-bridged crystals; the Cu–Cu bond length of the $C2/c$ and $P2_1/c$ polymorphs of **II** of 2.6745(6) and 2.6756(5) Å, respectively, are in the range of those reported in the literature but slightly shorter than for the copper trimethoprim complex reported by Naldini *et al.* [17]. In each complex, one M–O bond length at each metal atom site is significantly longer than the other three (tables 2 and 3), this probably arising because that particular oxygen atom forms a strong intramolecular hydrogen bond with a TMP nitrogen atom. These hydrogen bonding contacts are N(3)–H(1N)···O(2) for the structures of **I** and **II** in the space group $C2/c$ and N(3)–H(3B)···O(4) and N(7)–H(7A)···O(7) for the $P2_1/c$ polymorph of **II**, illustrated in figures 1 and 2, respectively. Table 4 shows these hydrogen bonding contacts and the additional intermolecular contacts for all three crystal structures.

The packing diagrams viewed approximately down c, for the $C2/c$ and $P2_1/c$ polymorphs are shown in figures 3 and 4, respectively; these illustrate that the intermolecular hydrogen bonding interactions lead to sheets of molecules lying in the *ab* plane. Figure 5 shows a plot of the $P2_1/c$ polymorph of **II** viewed down the a axis, where the toluene solvent molecule can be seen in pockets between the hydrogen bonded sheets; the methanols, also found between the sheets, are hydrogen bonded to an acetate oxygen and TMP nitrogen atom. Similar features are seen in the packing arrangement of the of the $C2/c$ polymorph. Overall the main difference between the $C2/c$ and $P2_1/c$ polymorph is the slightly greater degree of order in the latter.

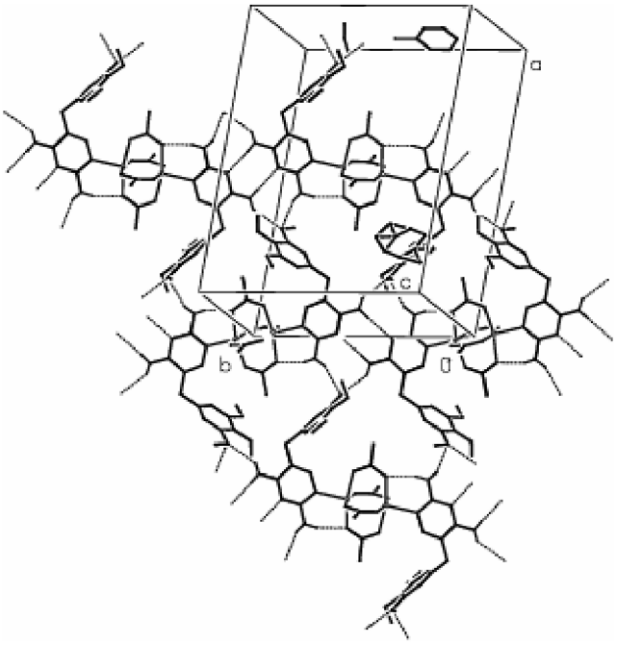

Figure 3. Crystal packing for $\{[M_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ (M = Co, Cu) in the space group $C2/c$ showing the hydrogen bonded sheets of molecules in the *ab* plane. Only those H atoms involved in hydrogen bonding have been included.

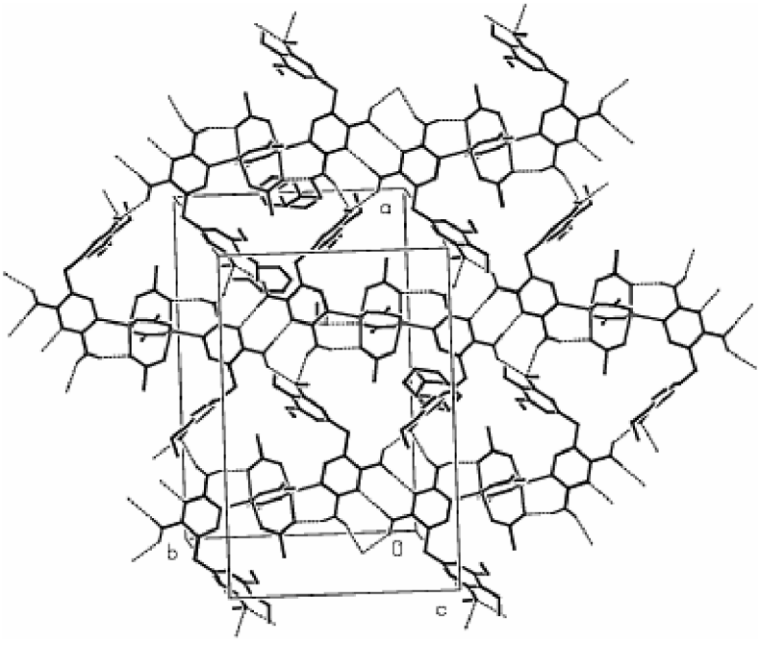

Figure 4. Crystal packing for $\{[Cu_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ in the space group $P2_1/c$ showing the hydrogen bonded sheets of molecules in the *ab* plane. Only those H atoms involved in hydrogen bonding have been included.

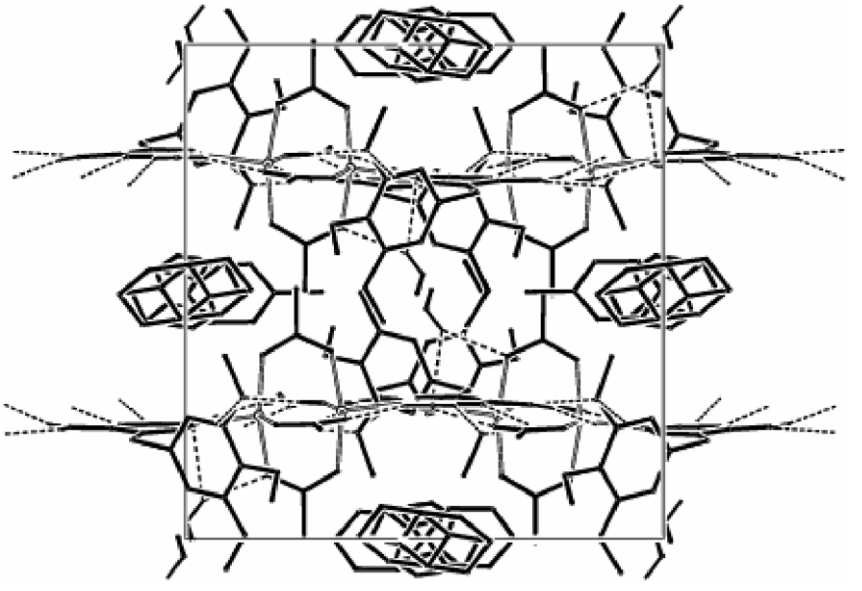

Figure 5. Crystal packing for $\{[Cu_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ in the space group $P2_1/c$ showing the toluene and methanol solvent molecule positioned between the hydrogen bonded sheets of molecules. Only those H atoms involved in hydrogen bonding have been included.

The structures of the copper complexes are typically of copper(II) carboxylates with empirical formula $[Cu(O_2CR)_2L]$ where L is an adduct such as water or pyridine [28]. Many compounds of this type are magnetically non-dilute, and are better formulated as $[Cu_2(O_2CR)_4L_2]$, with interaction between the two copper atoms, held together by bridging carboxylate groups.

3.2. *Electronic spectra and magnetic properties of the complexes*

The electronic spectrum of the Co(II) complex is shown in figure 6. Three weak bands, typical of Co(II) octahedral complexes, are observed [29]. A band in the near infrared region at 10,030 cm^{-1} (997 nm) is assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, the second band occurs at 15,105 cm^{-1}, due to $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and a more intense band at 18,656 cm^{-1} is assigned to $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$. The fine structure around this band is probably due to spin–orbit coupling or overlap due to the many metal centres within the crystal lattice [30].

The electronic spectrum of one of the Cu complexes is shown in figure 7. A single broad band around 14,286 cm^{-1} (700 nm) is observed, characteristic of Cu^{2+} with six-coordinate geometry [28], in agreement with the X-ray diffraction data. A survey of copper(II) electronic spectroscopy presents difficulty because of the lack of correlation of spectra to structure. Since the ground state in an octahedral field is the Jahn–Teller unstable ^2E_g, very few regular octahedral copper(II) complexes exist. The single crystal X-ray of the complex reported here shows a distorted octahedron. The shoulder at about 26,316 cm^{-1} (380 nm) is typical of dimeric copper(II) complexes [31] in agreement

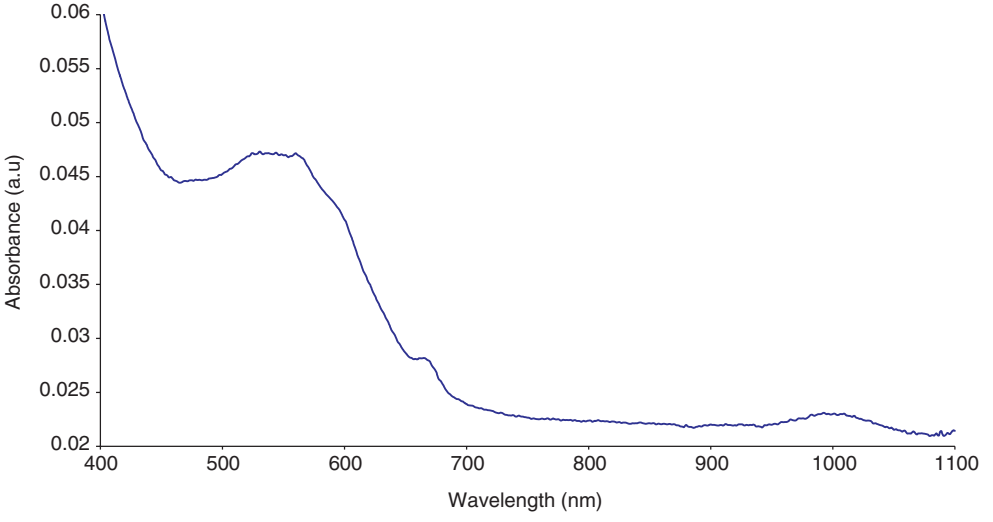

Figure 6. Solution spectrum of in DMF.

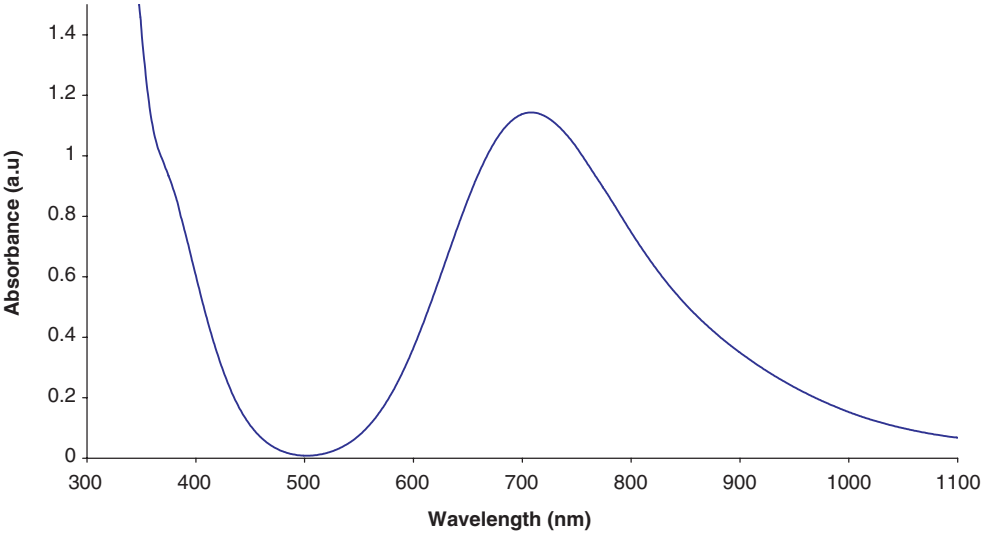

Figure 7. Solution spectrum of $\{[Cu_2(TMP)_2(CH_3COO)_4]\cdot 2C_6H_5CH_3\cdot(CH_3OH)\}$ in DMF.

with the X-ray structural data. The distortion does not seem to be prominent because the band at 700 nm does not appear to be particularly unsymmetrical.

The room temperature magnetic moments for the Cu complexes were sub-normal at 1.27 B.M. for $C_{51}H_{60}Cu_2N_8O_{15}$, 1.32 B.M. for $C_{52}H_{62}Cu_2N_8O_{15}$ and 1.30 for $C_{51}H_{74}Cu_2N_8O_{15}$. These values are much lower than the spin-only moment for magnetically dilute copper(II) complexes. The lower magnetic moment can be attributed to the dimeric structure in which two copper atoms interact

anti-ferromagnetically to produce a low-lying singlet (diamagnetic) and an excited, but thermally accessible, triplet (paramagnetic) level [28]. In spite of a continuous flow of work on this type of compounds, there is still no general agreement as to the actual mechanism of the interaction or on possible correlations to relevant properties of the carboxylate and axial ligands [32]. The most common interpretation assumes that the singlet and triplet levels arise from a single interaction between unpaired spins of the copper atoms [33] in the form of δ overlap of the copper $d_{x^2-y^2}$ orbital [34].

Using X-band radiation at room temperature, three bands could be observed from the typical EPR spectrum of the copper complexes with $g_1 = 2.34$, $g_2 = g_3 = 2.06$, $D = 1.159\,cm^{-1}$, $E = 0.0412\,cm^{-1}$. These values are in agreement with binuclear copper(II) complexes [35–37]. Thus, the result complements the magnetic moments to support the binuclear nature of the complex as confirmed from the X-ray crystal structure.

3.3. *Infrared spectra for the complexes*

A comparison of the infrared spectrum of free trimethoprim with those of the complexes showed that the absorption bands in the region 3467–3174 cm^{-1} experienced only very slight changes in the complexes which might be attributed to NH_2 on the drug not being involved in direct bond formation with the metal. The mode of coordination of the carboxylate groups can be deduced from the magnitude of the observed separation (Δ) between $\nu_{as}(CO_2^-)$ and $\nu_s(CO_2^-)$. In binuclear complexes, the $\nu_{as}(CO_2^-)$ bands are expected to be at higher frequencies than that of the free ligand. The $\nu_{as}(CO_2^-)$ band occurs at 1667 cm^{-1} for $C_{51}H_{60}Cu_2N_8O_{15}$ and $C_{52}H_{62}Cu_2N_8O_{15}$ complexes compared to 1578 cm^{-1} for CH_3COONa and 1618 cm^{-1} for a reported Cu(II) complex of trimethoprim [17]. The $\nu_s(CO_2^-)$ for $C_{51}H_{60}Cu_2N_8O_{15}$ and $C_{52}H_{62}Cu_2N_8O_{15}$ also occur at 1462 cm^{-1} in both complexes compared to 1414 cm^{-1} for CH_3COONa. A very sharp band at 681 cm^{-1} is assigned to Cu–N while the band at 404 cm^{-1} is assigned to Cu–O. Other Cu–O bands occur at 469 and 343 cm^{-1}. The multiple bands in the region 625–534 cm^{-1} can be attributed to the N–Cu–O interactions.

4. Conclusions

We report cobalt(II) and copper(II) complexes of trimethoprim and their characterization. The structures were elucidated by single crystal X-ray diffraction. The complexes are octahedral with each metal ion coordinated to one trimethoprim acting as a monodentate ligand through the pyrimidinyl N atom. The octahedral geometry around the metal ions was completed by two acetate ions bridging the two metal ions. Further information about the complexes was obtained from IR, electronic spectra and magnetic susceptibility measurements, all supporting the dimeric nature of the complexes confirmed by single crystal X-ray data.

Supplementary material

CCDC 285445-285448 contain the supplementary crystallographic data for this article. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif or from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336-033; Email: deposit@ccdc.cam.ac.uk).

Acknowledgements

The authors are grateful to the National Research Foundation (South Africa) and the Royal Society (UK) for financial support. PAA thanks the University of Ado Ekiti (Nigeria) for a study leave.

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