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Synthesis and characterization of copper–ibuprofenate complexes with 2,2′-bipyridine and 1,10-phenanthrolines and their hydrolytic activities in phosphate diester cleavage

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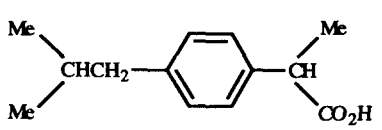
Abstract—A synthetic investigation of copper(II) ibuprofenate (Ibup) addition compounds with 2,2′-bipyridine (bpy), 1,10-phenanthroline (phen) and 2,9-dimethyl-1,10-phenanthroline (dmph) has led to the isolation of dinuclear adducts of the forms $[Cu(Ibup)_2(bpy)]_2 \cdot 4H_2O$ (**1**) and $[Cu(Ibup)_2(phen)]_2$ (**2**) and a mononuclear adduct $Cu(Ibup)_2(dmph)$ (**3**). Spectroscopic data for adducts **1** and **2** are consistent with a dinuclear structure with two CuN_2O_2+O chromophors. Each copper is coordinated with two ibuprofenate bridges, a terminal diimine molecule and a monodentate ibuprofenate group complete five-coordination at each metal atom. Spectroscopic data for adduct **3** are consistent with a mononuclear structure having a very distorted square-pyramidal CuN_2O_2+O chromophore. The Cu^{II} atom is coordinated to two nitrogen atoms from a chelating dmph ligand, two carboxylic oxygens of a bidentate ibuprofenate ion and an oxygen atom of a monodentate carboxylic group of a second ibuprofenate ion. The reduction of adduct (**3**) by ascorbic acid produced stable red copper(I) complex of the form $[Cu(dmph)_2]$ (Ibup) (**4**). Spectral data of this adduct indicated that the cation has distorted tetrahedral geometry about the copper atom. The effect of **1** and **2** on the rate of hydrolysis of bis(*p*-nitrophenyl) phosphate (BNPP) have been examined in aqueous methanol solution at 70°C and pH 7.4. Copyright © 1996 Elsevier Science Ltd

Keywords: copper complexes; ibuprofen; diimines; hydrolysis; phosphate.

It has been suggested that copper(II) complexes of anti-inflammatory drugs are often more active and desirable drugs than the parent ligands themselves [1]. Ibuprofen [2-(4-isobutylphenyl)propionic acid], [Scheme 1] is a non-steroidal anti-inflammatory drug and has been used for many years in the treatment of inflammatory diseases. Physical studies of copper(II) ibuprofenate [2] have shown that it contains dinuclear units with bridging carboxylates, similar to the familiar copper acetate and many other copper(II) carboxylates [3]. It is well known that many copper(II) carboxylates form dinuclear adducts with basic ligands [3,4]; however, with certain bases many copper(II) carboxylates also form mononuclear adducts [3b,4–8]. Several studies from our laboratories and others have been designed to investigate the factors which influence the adoption of either dinuclear or mononuclear complexes for copper(II) carboxylate adducts [3a,4–10]. In general, it has been found that by increasing the acidity of the alkyl (or aryl) carboxylate ligands, such as through halogenation of alkyl groups and/or by increasing the basicity of the other ligands, the tendency towards formation of mononuclear complexes increases [2b,4–10].



Scheme 1.

Our interest in copper(II) carboxylate complexes with nitrogen-donor ligands evolves from their biological implications [1,4,7,11]. As an example, the imidazole and carboxylate groups are the ligating moieties found in proteins and in many naturally occurring mixed-ligand complexes [12]. In addition, mononuclear and dinuclear copper(II) carboxylates and their nitrogen-donor adducts have been found

to have a variety of pharmacological effects, such as antitumour [1,13], superoxide dismutase [14], catecholase [4,7], cytotoxicity and antiviral activities [11]. Chelators such as 2,2′-bipyridine and 1,10-phenanthroline have potential antitumour activity and their activity may be increased through their chelation to the copper ion [15]. A complex between the chelating agent 1,10-phenanthroline and copper(II) is able to induce the degradation of DNA in the presence of reducing agents[16] and 2,2′-bipyridine complexes of copper(II) have been used as non-enzymatic catalysts for the hydrolytic cleavage of phosphodiester backbone of DNA and RNA [17,18]. There has been interest in developing metal complexes which can promote hydrolysis of phosphate esters as model systems for metallo-phosphatase enzymes and as catalysts for the detoxification of man-made phosphorus(V) toxins of some pesticides and chemical weapons [17,18]. In addition, the development of new artificial photosynthetic assemblies capable of harvesting solar energy is of great interest in inorganic photochemistry [19]. Cuprous diimine chromophores have received considerable attention since these chromophores display metal-to-ligand charge transfer (MLCT) bands in the visible region [20]. Recently, light excitation into these bands leads to room-temperature emission in argon dichloromethane solution and the photo-driven energy transfer from cuprous phenanthroline derivatives has been demonstrated [21]. As part of an ongoing investigation into the biological and photochemical activities of copper compounds, this article reports the synthesis and spectroscopic characterization of ternary complexes of copper(II) ibuprofenate with 2,2′-bipyridine, 1,10-phenanthroline and 2,9-dimethyl-1,10-phenanthroline and examines the activities of the first two complexes for the hydrolysis of bis(*p*-nitrophenyl)phosphate. In addition, the reduction of copper(II) ibuprofenate adduct of 2,9-dimethyl-1,10-phenanthroline to bis(2,9-dimethyl-1,10-phenanthroline) copper(I) ibuprofenate is also reported.

EXPERIMENTAL

Materials

2,2′-Bipyridine (bpy), 1,10-phenanthroline(phen) and 2,9-dimethyl-1,10-phenanthroline (dmph) were purchased from Aldrich; sodium bis(*p*-nitrophenyl)phosphate (BNPP) and biological buffer HEPES [N-(2-hydroxyethyl) piperazine-N′-ethanesulfonic acid] were from Sigma and used without further purification. Tetrakis(μ-ibuprofenato) dicopper(II), $[Cu_2(Ibup)_4]$ (Ibup = ibuprofenate ion), was prepared as described previously [2b] and recrystallized from anhydrous diethylether: dichloromethane (1 : 1).

Preparation of complexes

$[Cu(Ibup)_2(bpy)]_2 \cdot 4H_2O$ (**1**). A solution of 2,2′-biypridine (0.164 g, 1.05 mmol) in methanol (50 cm^3) was added to Cu_2 $(Ibup)_4$ (0.496, 0.524 mmol). The mixture was stirred at room temperature for 2 h. The blue solution was filtered and left in the hood to evaporate. The bluish-green precipitate that formed was recrystallized from chloroform and air dried. Yield 0.58 g (83%). Found: C 65.0; H, 7.0; N, 4.1. Calc. for $C_{72}H_{92}N_4O_{12}Cu_2$: C, 64.9; H, 6.9; N, 4.2%.

$[Cu(Ibup)_2(phen)]_2$ (**2**). A solution of 1,10-phenanthroline (0.133 g, 0.68 mmol) in methanol (50 cm^3) was added to $Cu_2(Ibup)_2$ (0.319 g, 0.337 mmol). The mixture was stirred at room temperature for 2 h. The bluish-green solution was filtered and left in the hood to evaporate. The sky-blue precipitate that formed was recrystallized from chloroform and air dried. Yield 0.38 g (86%). Found: C 70.0; H, 6.6; N, 4.2. Calc. for $C_{76}H_{84}N_4O_8Cu_2$: C, 69.8; H, 6.4; N, 4.3%.

$Cu(Ibup)_2(dmph)$ (**3**). A solution of 2,9-dimethyl-1,10-phenanthroline (0.176 g, 0.845 mmol) in methanol (50 cm^3) was added to $Cu_2(Ibup)_4$ (0.398 g, 0.420 mmol). The solution was protected from the light and stirred at room temperature for 3 h. The green solution was filtered and left in the hood to evaporate. The green precipitate that formed was recrystallized from chloroform and air dried. Yield 0.37 g (65%). Found: C, 70.1; H, 6.9; N, 4.0. Calc. for $C_{40}H_{46}N_2O_4Cu$: C, 70.4; H, 6.8; N, 4.1%.

$[Cu(dmph)_2]Ibup$ (**4**). Solid ascorbic acid (0.053 g, 0.30 mmol) was added to the green solution of **3** (0.2 g, 0.29 mmol) in acetonitrile (15 cm^3). The red solution which formed was stirred for 15 min, filtered and left in the hood to evaporate. The red oily product was dissolved in dichloromethane (20 cm^3) and filtered. The red filtrate was concentrated by slow evaporation to *ca* 2 cm^3 then anhydrous diethylether was added to the solution with stirring until the red precipitate formed. The complex was filtered under reduced pressure, washed several times with anhydrous diethyether and dried *in vacuo*. Yield 0.045 g (45%). Found: C, 71.2; H, 6.1; N, 8.4. Calc. for $C_{41}H_{41}N_4O_2Cu$: C, 71.9; H, 6.0; N, 8.2%.

Physical measurements

Elemental analyses for C, H and N were performed by Galbraith Laboratories, Knoxville, Tennessee, U.S.A. Room-temperature (298 K) magnetic susceptibility measurements of powdered and solution samples were determined as described previously [4,6]. Electronic data of dichloromethane solutions were obtained with a Bausch and Lomb Spectronic 2000. IR spectra of Nujol or hexachlorobutadiene mulls sealed between polyethylene sheets were obtained in the 4000–200 cm^{-1} region with a Perkin–Elmer model 843 IR spectrophotometer. X-band ESR spectra of polycrystalline material and of methanol/toluene solu-

tions were obtained at room temperature and 77 K with an ESPIT-330 Vol. 501 spectrometer. Diphenylpicrylhydrazide (DPPH, $g = 2.0036$) was used as the calibrating field marker. A Varian 360A-60MHz spectrometer was used to obtain NMR spectra and chemical shifts were referenced to $SiMe_4$.

Kinetics

All kinetic studies were performed at 70°C and pH 7.4 with temperature compensation probe. The Sigma biological buffer HEPES (5 mmol dm^{-3}) was used to maintain a constant pH at 7.4. The pH of the buffer solutions was adjusted with NaOH or HNO_3 and checked at 70°C. Kinetic measurements were performed with the use of Bausch and Lomb 2000 UV–vis spectrophotometer equipped with a thermostated cell compartment.

The hydrolysis of sodium bis(*p*-nitrophenyl) phosphate (BNPP) by copper(II) complexes was monitored spectrophotometrically by following the production of *p*-nitrophenolate at 400 nm ($\varepsilon = 14\,000$ M^{-1} cm^{-1}, pH = 7.4) [17a]. The reactions were carried out under pseudo-first-order conditions with an excess copper(II) complex over BNPP concentrations. In a typical kinetic experiment, 1.5 cm^3 (2×10^{-3} M) of copper(II) complex dissolved in methanol and 1.5 cm^3 (1×10^{-4} M) of BNPP dissolved in HEPES buffer (pH 7.4) were combined in a 1 cm quartz cell and the absorbance changes at 400 nm were recorded at 70°C against the reference cell under identical conditions, except copper(II) complex was omitted. The final concentrations in the cell were (1×10^{-3} M) copper(II) complex and (5×10^{-5} M) BNPP.

First-order rate constants, k_{obs} (s^{-1}), were calculated from the slope of the linear plots of absorbance against time by converting to concentration units and dividing by the initial BNPP concentration. All experiments were run in triplicate and the first-order rate constants represent the average of these experiments.

RESULTS AND DISCUSSION

Magnetic and spectroscopic characterization

The ESR parameters, g and A, for frozen solutions and solid-state spectra of complexes studied are given in Table 1. The room-temperature ESR spectra of solid state samples of **1, 2** and **3** are anisotropic and contain $g_\parallel$ and $g_\perp$ components. Two of the four copper(II) hyperfine components in the $g_\parallel$ region for complex **3** are partially resolved. These spectra are of axial type ($g_\parallel > g_\perp > 2.040$), suggesting for all compounds $d_{x^2-y^2}$ (or d_{xy}) ground state, characteristic of a square-planar, square-based pyramidal or octahedral stereochemistry [22].

Frozen-solution ESR spectra of complexes **1** and **2** in 3.0 kG region exhibit a resolved structure with $g_\parallel > g_\perp$ (Table 1) and a representative frozen solution spectrum is that of **1** shown in Fig. 1. In addition to the hyperfine structure of copper(II) in the $g_\parallel$ region, the $g_\perp$ regions of these spectra exhibit ^{14}N-super-hyperfine structure consisting of five lines. This structure is attributed to the presence of two nitrogen atoms in the plane of the copper(II) ion. The spectral parameters for the complexes are comparable to those previously reported complexes that have square-based CuN_2O_2 of tetragonally elongated CuN_2O_2+O or $CuN_2O_2+O_2$ chromophore, including those reported for copper(II) carboxylates with α,α'-diimine [4–7, 23]. In these complexes the copper(II) ion is bonded to two unidentate nitrogen donors (e.g. imidazoles) or one bidentate chelate α,α'-diimine ligand and one oxygen atom from each of the two carboxylate anions. The second oxygen atom of each carboxylate ligand is in a weakly pseudo-axial position [5,7,9,11,24].

In addition to the above signals expected for $\Delta M_s = 1$ allowed transition of magnetic dilute copper(II) complexes $S = \frac{1}{2}$, the ESR spectra for complexes **1** and **2** in the full ESR region show another three weak signals at about 1200, 2230 and 3830 G and a representative spectrum is that of **2** shown in Fig. 2(a). These signals are attributed to the spin-

Table 1. ESR data for copper(II) ibuprofenates

Compound	State (temperature)	g_0^a	$g_\parallel$	$g_\perp$	$A_\parallel Cu$ ($\times 10^4$ cm^{-1})	$A_\perp N$ ($\times 10^4$ cm^{-1})
1	Solid (room)	2.128	2.255	2.064	—	—
	Frozen (77 K)	2.134	2.277	2.063	221	14
2	Solid (room)	2.122	2.243	2.061	—	—
	Frozen (77 K)	2.141	2.286	2.069	222	14
3	Solid (room)	2.172	2.362	2.082	—	—
	Frozen (77 K)	2.169	2.337	$g_x = 2.035$ $g_y = 2.134$	167	—

[a] g_0 values are calculated from the equation $g_0 = \frac{1}{3}(g_\parallel + 2g_\perp)$.

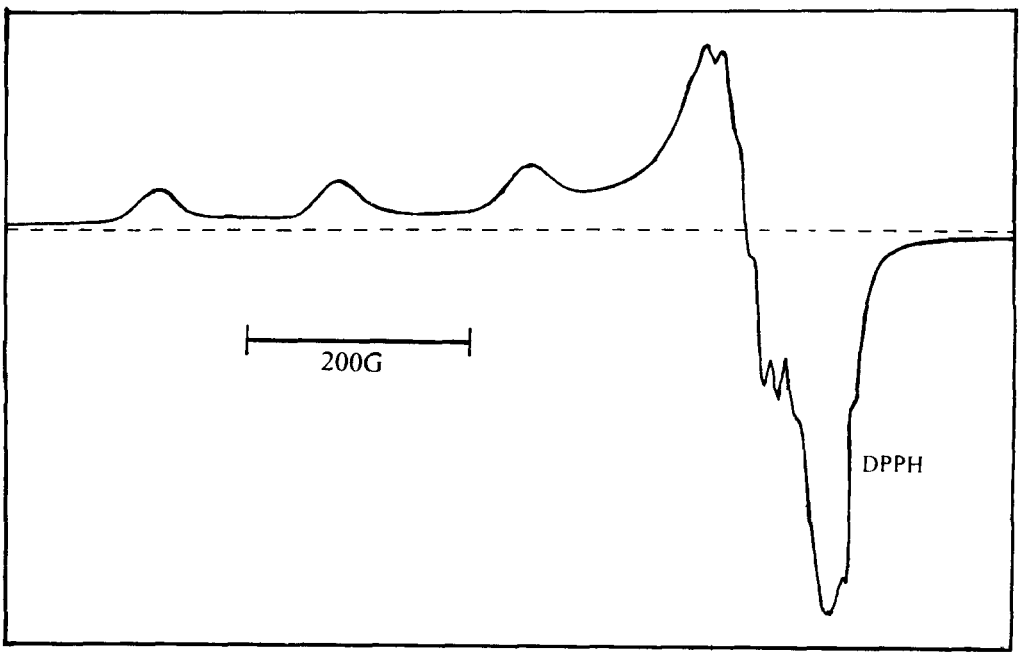


Fig. 1. Frozen-solution ESR spectrum of compound **1**.

triplet state with $S = 1$. The signals at 2230 and 3830 G are devoid of any hyperfine structure, they are assigned to the $\Delta M_s = 1$ transitions Hxy_1 and Hxy_2 [24a]. The weak signal at 1200 G showed a resolved seven-line hyperfine structure ($A = 100 \times 10^{-4}$ cm^{-1}) and is attributed to the half-field $\Delta M_s = 2$ forbidden transition in dinuclear copper(II) complexes [25]. The positions and the assignment of these signals are comparable with those found for dicopper(II) complexes having an acetate ion-bridged ligand [25] and with those reported recently for ternary dinuclear copper(II) complexes of 4-aminobenzoic acid with 4,7-disubstituted phenanthrolines [26]. In these complexes each copper atom is coordinated with two 4-aminobenzoate bridges, a terminal diimine molecule and the fifth coordination position is occupied by a water molecule. In addition, the hyperfine coupling constant observed, 100×10^{-4} cm^{-1}, is about one half of that of mononuclear copper(II) units of axial symmetry (Table 1) and is comparable to those of the spin-triplet states of magnetically coupled dicopper(II,II) complexes [25,27]. Based on these ESR spectral properties along with other spectral data, dinuclear structure are proposed for these complexes of the type $[Cu(Ibup)_2(diimine)]_2$ (diimine = bpy or phen) in the solid state and the dinuclearity of these complexes is, at least partially, preserved in methanolic solutions with the monomeric units being bridged by two ibuprofenato ligands. In addition, spectral parameters for complexes **1** and **2** are comparable to those of previously reported for other dinuclear copper(II) carboxylates with diimines [26,28], such as $[Cu(4\text{-aminobenzoate})_2(H_2O)(phen)]_2(NO_3)_2$ [26] and $[Cu(acetate)_2(OClO_3)(bpy)]_2$ [28]. X-ray analysis of these complexes showed that the geometry at each copper(II) atom is distorted square-pyramidal. The basal coordination sites are occupied by the nitrogen atoms of a chelating diimine and two oxygen atoms of bridging carboxylates and the apical position is occupied by an oxygen atom of a monodentate ligand (water or perchlorato group). The dinuclear structure is stabilized by diimine–diimine stacking interactions. The structure of complex **1** or **2** (Scheme 2) can be described in the same manner, except ibuprofenato groups replaced both the bridging 4-aminobenzoato or acetato groups and the terminal monodentate ligands (water or perchlorato group).

The frozen-solution ESR spectrum of complex **3** [Fig. 2(b)] is clearly of rhombic type (Table 1), suggesting a distortion from square symmetry in solution. No signals due to a triplet state were observed in the spectrum of this compound, which is consistent with its mononuclear structure. The lowest g value (2.035) lies between the values obtainable in rhombic spectra for distorted square-based pyramidal or for distorted trigonal-bipyramidal geometry [22]. The structure deviation from square symmetry is attributed to the presence of methyl groups in the 2 and 9 positions on the phenanthroline moiety, close to the coordinated nitrogens to copper(II). In addition, the absence of the ^{14}N superhyperfine splitting may be attributed to the deviation from square symmetry. The ESR and other spectral parameters for complex **3** (Scheme 3) are comparable to those of ternary mononuclear copper(II) complexes of 2,5-dimethoxycinnamic acid or 3,5-disubstituted salicylates and 2,9-dimethyl-1,10-phennthroline [11, 23]. The crystal structure of the ternary complex of 2,5-dimethoxycinnamic acid have

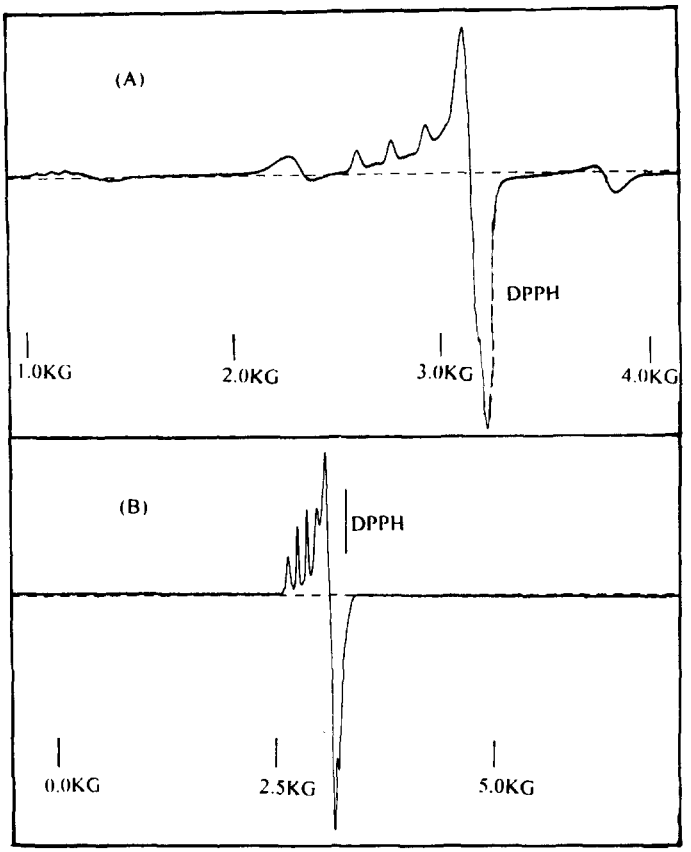
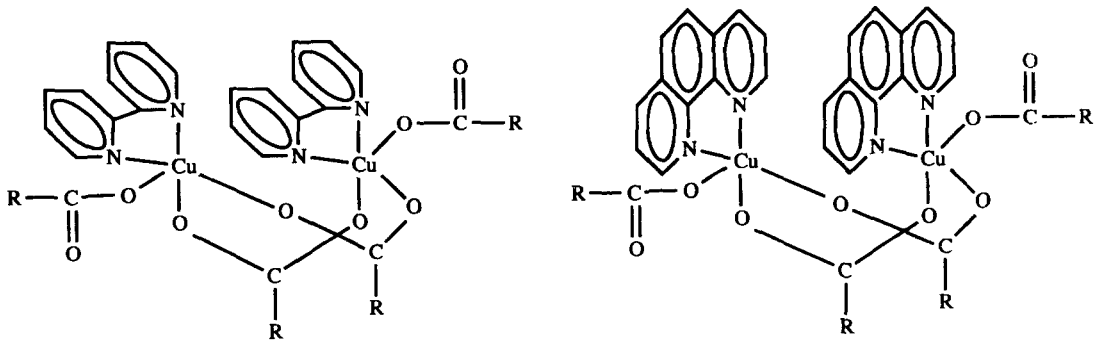
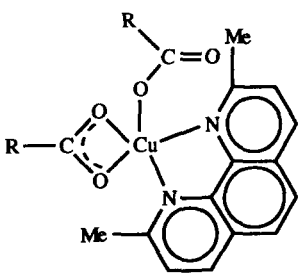


Fig. 2. Frozen-solution ESR spectra of compound (a) **2** and (b) **3**.



RCOO = ibuprofenate anion

Scheme 2.



RCOO = ibuprofenate anion

Scheme 3.

been determined [23]. The copper(II) ion in this complex is five-coordinated and complexes by two nitrogen atoms from 2,9-dimethyl-1,10-phenanthroline, two carboxylic oxygens of a bidentate cinnamic acid and one oxygen atom of a monodentate carboxyl group of a second cinnamic acid molecule. The geometry of the complex has been described as a very distorted square pyramid or trigonal bipyramid.

Inspection of the ESR parameters (Table 1) shows that $A_{\perp}$ values for complexes **1** and **2** are greater than $A_{\parallel}$ for complex **3**, while $g_{\parallel}$ values in the former complexes are smaller. These results are consistent with the presence of a stronger equatorial ligand-field in complexes **1** and **2** with an in-plane CuN_2O_2 chro-

mophore, compared with complex **3** with a very distorted an in-plane CuN_2O_2 chromophore.

The magnetic moments and electronic and IR spectral data are summarized in Table 2. Complexes **1** and **2** exhibit magnetic moments values at room temperature a little lower than normally found in magnetically dilute copper(II) ion complexes, as found in complex **3**. This is attributed to the presence of weak antiferromagnetic coupling in complexes **1** and **2**, which are proposed to have dinuclear structure as shown from spectral data. Facilities to carry out detailed magnetic properties with temperature variation were not available to us. However, it is worth noting that dinuclear copper(II) complexes with doubly bridged carboxylate groups, including those of 2,2′-bipyridine as a secondary ligand, are known to be weakly antiferromagnetically coupled [26–30]. Their $-2J$ values are much less than those found in the familiar tetracarboxylato-ligand complexes of the type $Cu_2(O_2CR)_4L_2$. This decrease has been attributed [30] to the decrease in the number of bridging carboxylato groups by which the superexchange interaction is mediated [26–30].

The electronic spectra for complexes **1** and **2** obtained in CH_2Cl_2 solutions exhibit one very broad absorption band near 675 nm and shoulder near 400 nm (Table 2). The broad band is assigned to the copper(II) *d–d* transitions. The position of this band fall within the range expected for a distorted-tetragonal copper(II) environment with an in-plane CuN_2O_2 chromophore [4–7], including those reported for copper(II) carboxylates with α,α^--diimine [11, 23, 27, 28]. The shoulder near 400 nm is assigned to the charge-transfer band, as expected when π–π interactions between aromatic system are present [36].

The electronic spectrum of complex **3** in CH_2Cl_2 solution exhibits a very broad *d–d* band at 820 nm, similar to that seen for mononuclear copper(II) carboxylates with 2,9-dimethyl-1,10-phenanthroline [11, 23]. The copper(II) ion is five-coordinated, contains the CuN_2O_2+O chromophore and complexes by a chelating 2,9-dimethyl-1,10-phanenthroline, one bidentate and one monodentate carboxylate groups. The low energy of the *d–d* electronic transitions is due to the presence of a pronounced distortion from planar symmetry in this complex and it is consistent with the ESR spectral data.

In the solid-state IR spectra, complexes **1** and **2** possess similar spectra for the ν_{as}(COO) and ν_s(COO) bands (Table 2), supporting similar structures. Two ν_{as}(COO) and two ν_s(COO) are observed, indicating the presence of two types of ibuprofenate groups. The bands at 1610 and 1395–1380 cm^{-1} with large separation, $\Delta\nu$ [ν_{as}(COO) − ν_s(COO)] value of 230–215 cm^{-1}, are assigned to the stretching modes of the monodentate carboxyl group. The positions and separation between them are comparable to those associated with a monodentate coordination of carboxylate group [31]. The bands at 1595 and *ca* 1420–1415 cm^{-1} with $\Delta\nu$ value of 175–180 cm^{-1} are assigned to the "bridging" bidentate carboxylate ligand. The positions and separation between these frequencies are similar to those associated with classical carboxylate bridges (Cu—O—C—O—Cu), including those of $Cu_2(Ibup)_4$ [2, 8, 31]. These IR spectral results are consistent with the proposed structures of these complexes in which two ibuprofenate are bridging two copper atoms and one ibuprofenate is coordinated as a monodentate ligand to each copper atom. In addition to bands of carboxyl groups in complex **1**, bands due to water molecules were observed at 3530–3460 cm^{-1}. When this complex was heated at 110°C for *ca* 10–15 min these bands only disappeared from the IR spectra, while the rest of the spectrum retained its features. This observation indicated that water molecules in this complex are not coordinated, but are present as lattice molecules which were lost on heating.

Solid-state IR spectra for complex **3** exhibit two ν_{as}(COO) and two ν_s(COO) stretching bands (Table 2), indicating the presence of two types of ibuprofenate ligands. The 1610 and 1380 cm^{-1} ($\Delta\nu$ = 230 cm^{-1}) pair observed in the solid-state are assigned to the carboxylate group that acts as a monodentate ligand and the 1600 and 1410 cm^{-1} ($\Delta\nu$ = 190 cm^{-1}) pair are assigned to the other carboxylate that acts as

Table 2. Magnetic moments and electronic and IR spectral data for copper-ibuprofenate complexes

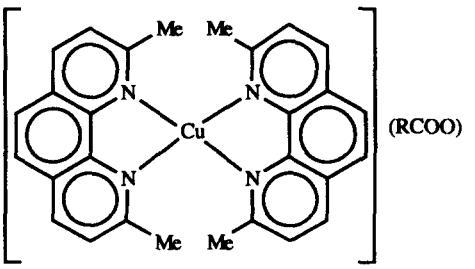
Compound	μ_{eff} (BM) (298 K) Solution	Solid	λ_{max} (nm) (ε = $dm^3\ mol^{-1}\ cm^{-1}$)[a]	ν_{asym} (CO_2) (cm^{-1})	ν_{sym} (CO_2) (cm^{-1})	$\Delta\nu$ (cm^{-1})
1	1.85	1.80	675(180)	1595	1420	175
			sh. 390(170)[b]	1610	1395	215
2	1.84	1.80	680(170)	1595	1415	180
			sh. 400(155)[b]	1610	1380	230
3	1.90	1.87	820(120)	1600	1410	190
				1610	1380	230
4	Diamagnetic		456(6400)	1585	1380	205

[a] ε is per dimer unit for complex **1** and **2**.
[b] sh. is shoulder.

asymmetric bidentate ligand [31]. These results are consistent with the proposed mononuclear structure containing CuN_2O_2+O chromophore, as discussed in the above spectral properties.

In conclusion, all physical measurements carried out in this study suggest that complexes **1** and **2** have essentially identical dinuclear structures of the type $[Cu(Ibup)_2(diimine)]_2$, in which a dinuclear structure results from the bridging of two ibuprofenate molecules by bidentate carboxylic groups (Scheme 2). In these adducts intermolecular stacking which is usually connected with π–π interactions between the diimine ligands (bpy or phen) may be important in determining the dinuclear structure. The steric hindrance caused by the presence of methyl groups in the 2 and 9 positions on the diimine (dmph) aromatic rings close to the coordination sites, which resulted in a pronounced distortion in the sphere of coordination, complex **3**, precludes the possibility of obtaining an intermolecular stack between diimine ligands and then obtaining the dinuclear structure; instead only mononuclear complex of the type $Cu(Ibup)_2(dmph)$ was obtained (Scheme 3).

Complex **4**, bis(2,9-dimethyl-1,10-phenanthroline) copper(I) ibuprofenate, which was obtained by the reduction of complex **3** was identified by UV–vis, IR and NMR spectral data, in addition to its elemental analyses. Its electronic spectrum obtained in CH_2Cl_2 solution exhibited the metal-to-ligand charge-transfer (MLCT) at 456 nm ($\varepsilon = 6400\ M^{-1}\ cm^{-1}$). The position of this band and its molar absorptivity are comparable with those previously reported for the $Cu(dmph)_2^+$ cation [20, 32]. Examination of the ^1H NMR spectrum, especially the methyl groups of the ligand (dmph), showed an upfield change in the chemical shift of the six proton at *ca* 2.4 ppm compared with those of the free ligand at *ca* 2.8 ppm. This shift was ascribed to an aromatic ring current effect [32] exhibited by cations of the type $[(2,9\text{-dialkyl-1,10-phenanthroline})_2Cu]^+$. The structure of these cations are known to have the distorted tetrahedral geometry about the copper atom [20,32]. The other protons of dmph ligand were not resolved, but relatively broad signals were observed between 7 and 9 ppm. An IR spectrum of the complex revealed peaks of coordinated dmph ligands at 1635, 1505, 1362, 855, 730 and 550 cm^{-1} and peaks of the carboxyl group of ibuprofenate ion at 1585 and 1380 cm^{-1}. The positions of these peaks are comparable with those recently reported for $CuCl(dmph)_2$ [32a] and $(dmph)_2$ Cu(butyrate) [32b]. Collectively, these spectral data suggest that complex **4** has structure of the type $[(dmph)_2Cu](Ibup)$ (Scheme 4).



RCOO = ibuprofenate anion

Scheme 4.

Hydrolysis of BNPP

Since the hydrolysed product *p*-nitrophenolate anion shows a characteristic band at 400 nm ($\varepsilon = 14\,000\ M^{-1}\ cm^{-1}$, at pH 7.4) [17a], the hydrolysis of BNPP [bis(*p*-nitrophenyl)phosphate] by copper(II) complexes **1** and **2** can be easily followed spectrophotometrically. The change in absorbance at 400 nm versus time of the reaction with complexes **1** and **2** was obtained and the pseudo-first-order rate constants, k_{obs}, for the two complexes were found to be $1.0\times10^{-5}\ s^{-1}$ and $0.7\times10^{-5}\ s^{-1}$, respectively. These values showed rate enhancement of *ca* 3.6×10^3 and 2.6×10^3 in the presence of 1 mM of complex **1** or **2**, respectively, compared with the rate constant of the uncatalysed reaction (k_{unc}) of *ca* $2.75\times10^{-9}\ s^{-1}$ at 70°C and pH 7.4 [17d]. It was not possible to obtain kinetic data for complex **3** due to its reduction to copper(I) diimine adduct at 70°C in aqueous methanol solution. This was judged by the disappearance of the copper(II) *d*–*d* transition band at 820 nm and the appearance of an intense metal-to-ligand charge-transfer band at 456 nm characteristic of the copper(I) diimine adduct, **4**.

BNPP has been used as a model for hydrolytic cleavage of the phosphodiester backbone of DNA and RNA [18a,b]. Several possible mechanisms for the hydrolysis of phosphate diesters, including BNPP, by transition-metal complexes have been proposed [17, 18]. In these mechanisms the metal ions supply electrophilic acceptor sites for the phosphodiester's P—O^- followed by an external nucleophilic (H_2O or OH^-) attack or an intramolecular metal hydroxide attack at P=O, which then facilitates the hydrolysis of *p*-nitrophenolate groups. In addition, cooperation between metal ions and carboxyl groups of the ibuprofenate ions which may make a nucleophilic attack at phosphodiester cannot be ruled out in the hydrolysis of BNPP in the presence of complex **1** or **2**. Detailed kinetic studies and the potential application of these new complexes in the hydrolysis of biological phosphoric ester is being investigated.

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