Bis(*N*-acetyl-DL-leucinate)copper(II) Complexes and Their Amine Adducts

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A compound of the type Cu(AcLeu)$_2$ and its amine adducts of the type Cu(AcLeu)$_2$B$_n$ (AcLeu=*N*-acetyl-DL-leucinato ion; n=2 and B=pyridine, 3- and 4-methylpyridine, *N*-methylpiperazine, morpholine, and piperidine; n=1 and B=1,10-phenanthroline, 2,2′-bipyridyl, piperazine, and pyridazine) were prepared and investigated by means of electronic, infrared and EPR spectroscopy and magnetic moment measurements. The results suggest a tetragonal configuration for the Cu(AcLeu)$_2$ complex and the amine adducts with CuO$_4$ and CuO$_2$N$_2$ chromophores, respectively. For the green Cu(AcLeu)$_2$·pid complex a binuclear configuration similar to that observed for the bis(acetato)copper(II) monohydrate complex is suggested. The amino acid in all the complexes is found to coordinate toward the carboxylato group. In the assignment of the way in which the carboxylato group coordinates, in addition to the difference between their antisymmetric and symmetric stretching frequencies, we also pay special attention to the position of the symmetric stretch, which is directly connected with the oxygen atom linked to the metal ion.

The amino acids containing terminal *N*-acetyl residues are of great interest not only because they are present in protein, albumin, mosaic virus, ovalbumin, cytochrome C, and other natural proteins and peptides, but also because it is possible that an acetylamino acid might be the starting unit in the biosynthesis of some peptide chains which grow the stepwise addition of acylamino residues to the acetylated N-terminal amino acid.[1)]

Being interested in the donor properties of amino acids as models for metal-protein interaction, we have paid particular attention to the interaction of some transition metal ions with simple *N*-protected amino acids containing a peptide group, as the *N*-acetyl and *N*-benzoyl derivatives of the glycine, alanine and valine.[2)]

In this paper we have now investigated the coordination properties of the *N*-acetyl-DL-leucine (hereafter abbreviated as AcLeuH) with the copper(II) ion and the effect of additional ligands, such as saturated and aromatic heterocyclic amines, on the amino acid coordination.

Experimental

All the reagents used were of the best chemical grade.

Preparation of the Compounds. The *Cu(AcLeu)$_2$* complex, which was used as starting material for the adduct preparations, was obtained by adding a copper(II) perchlorate hexahydrate (2×10^{-2} mol) solution in anhydrous ethanol (10 ml) to a *N*-acetyl-DL-leucine (4×10^{-2} mol) solution (50 ml) neutralized with a stoichiometric amount of potassium hydroxide. From the cooled solution (4—5 °C) the potassium perchlorate precipitated was filtered off and the green solution was slowly concentrated (20 ml). A blue solid compound separated by cooling after 24 h. *Cu(AcLeu)$_2$B$_n$* (n=1 and B=bpy, phen pid; n=2 and B=py, Mepipz, morph, pipd) complexes were prepared by adding an excess of amine to a methanolic Cu(AcLeu)$_2$ solution. Solid compounds precipitated from the concentrated solutions on adding diethyl ether and on cooling. *Cu(AcLeu)$_2$B$_2$* (B=3-pic and 4-pic) complexes were prepared in ethanol as reported above. *Cu(AcLeu)$_2$·pipz* complex instantaneously precipitated on mixing Cu(AcLeu)$_2$ (1.5×10^{-3} mol) and piperazine (3×10^{-3} mol) in ethanol.

Physical Measurements. The IR spectra of the compounds in KBr or Nujol (4000—250 cm^{-1}) were recorded with a Perkin-Elmer 180 spectrophotometer. The room temperature spectra of the solid compounds were recorded as mull transmission spectra with a Shimadzu MPS 50L spectrophotometer. The room temperature magnetic moments were measured with the Gouy method, using Ni(en)$_3$S$_2$O$_3$ as calibrant and correcting for diamagnetism with the appropriate Pascal constant. The EPR spectra were recorded on a JEOL PE-3X spectrometer. Quartz sample tubes were employed for polycrystalline samples. Spectra were calibrated with 2,2′-diphenyl-1-picrylhydrazyl (DPPH, g=2.0036) as a field marker.

Analyses. Nitrogen, carbon, and hydrogen were analyzed by Mr. Giuseppe Pistoni, using a Perkin-Elmer 240 Elemental Analyser.

Results and Discussion

The analytical results are reported in Table 1. The room temperature EPR spectrum of the bis(*N*-acetyl-DL-leucinato)copper(II) complex (Table 2 and Fig. 1), which is of axial type, shows g values of a typical isolated compound having a CuO$_4$ chromophore.[3,4)] The broad EPR line excludes the possibility of exchange interaction between copper ions.[5)] Its room temperature electronic spectrum (Table 1 and Fig. 2) also strongly resembles those reported for tetragonal copper(II)–oxygen systems.[4)] By correlating the g values and the electronic spectrum, which shows two d-d bands at 12990 and 16950 cm^{-1} tentatively assigned to the $d_{xy}\rightarrow d_{x^2-y^2}$ and $d_{xz,\,yz}\rightarrow d_{x^2-y^2}$ transitions,[4)] respectively, values of the molecular orbital coefficients ($k_{\parallel}=0.58$, $k_{\perp}=0.61$) are obtained. Since $k_{\perp}>k_{\parallel}$, this indicates the presence of more π bonding of the d_{xy} orbitals than of the d_{xz}, d_{yz} orbital. A tetragonal distortion in our complex greater than that found for some copper(II)–oxygen systems[4)] may be suggested from the comparison of their g and k values and d-d band positions.

All the amine adducts, which have "normal" magnetic moments, show EPR spectra (Table 2) of axial type, except the pipd adduct which presents a rhombic spectrum. For these adducts the observed EPR line shapes are quite similar to each other and indicate a normal elongated tetragonal structure, while for the pipd adduct they indicate a rhombically-distorted

Table 1. Conventional chemical analysis

		C, %		H, %		N, %	
		calcd	found	calcd	found	calcd	found
$Cu(AcLeu)_2$	blue	47.55	47.75	5.99	6.02	6.94	6.47
$Cu(AcLeu)_2(py)_2$	blue	55.13	54.82	6.77	7.08	9.91	9.95
$Cu(AcLeu)_2(3pic)_2$	blue	56.57	57.24	7.13	6.80	9.43	10.03
$Cu(AcLeu)_2(4pic)_2$	blue	56.57	57.20	7.13	7.02	9.43	9.62
$Cu(AcLeu)_2 \cdot pid$	green	49.20	48.65	6.61	6.25	11.49	11.20
$Cu(AcLeu)_2 \cdot bpy$	blue	55.33	55.19	6.43	6.52	9.93	10.04
$Cu(AcLeu)_2 \cdot phen$	blue	57.16	56.83	6.17	6.23	9.53	9.65
$Cu(AcLeu)_2 \cdot pipz$	lilac	48.59	47.97	7.76	7.86	11.35	11.24
$Cu(AcLeu)_2(Mepipz)_2$	blue	50.77	51.31	9.04	8.62	13.75	13.82
$Cu(AcLeu)_2(morph)_2$	lilac	49.49	50.04	7.97	8.53	9.63	9.95
$Cu(AcLeu)_2(pipd)_2$	blue	53.98	54.28	8.72	8.93	9.69	9.88

Abbreviations: AcLeu = N-Acetyl-DL-leucinato ion; py = pyridine; 3- or 4-pic = 3- or 4-methylpyridine; pid = pyridazine; bpy = 2,2′-bipyridyl; phen = 1,10-phenanthroline; pipz = piperazine; Mepipz = N-methylpiperazine; morph = morpholine; pipd = piperidine.

Table 2. Electronic spectra, magnetic moments, and EPR spectra of the solid complexes

	d-d bands/cm^{-1}			μ_{eff}/B.M.	$g_\parallel$	$g_\perp$	g_0		
$Cu(AcLeu)_2$	12990	16950		1.78	2.297	2.051	2.133		
$Cu(AcLeu)_2(py)_2$	13330 sh	16670		1.89	2.202	2.048	2.098		
$Cu(AcLeu)_2(3pic)_2$	13330 sh	16000		1.80	2.238	2.041	2.107		
$Cu(AcLeu)_2(4pic)_2$	13330 sh	16390		1.85	2.203	2.059	2.107		
$Cu(AcLeu)_2 \cdot bpy$	14290 sh	16670	23810 sh	1.83	2.257	2.053	2.121		
$Cu(AcLeu)_2 \cdot phen$	14290 sh	17390		1.80	2.234	2.055	2.115		
$Cu(AcLeu)_2 \cdot pipz$	15390 sh	19420		1.78	2.222	2.050	2.107		
$Cu(AcLeu)_2(Mepipz)_2$	13160 sh	15630		1.86	2.223	2.051	2.108		
$Cu(AcLeu)_2(morph)_2$	14820 sh	17860		1.77	2.249	2.053	2.118		
					g_3	g_2	g_1	g_0	
$Cu(AcLeu)_2(pipd)_2$	9520 sh	14290		1.85	2.201	2.133	2.048	2.127	
					Monomer		Dimer		D
					$g_\parallel$	$g_\perp$	$g_\parallel$	$g_\perp$	cm^{-1}
$Cu(AcLeu)_2 \cdot pid$	13510		24390 sh	1.38	2.234	2.066	2.40	2.09	0.39

a) $\lambda = -825\ cm^{-1}$.

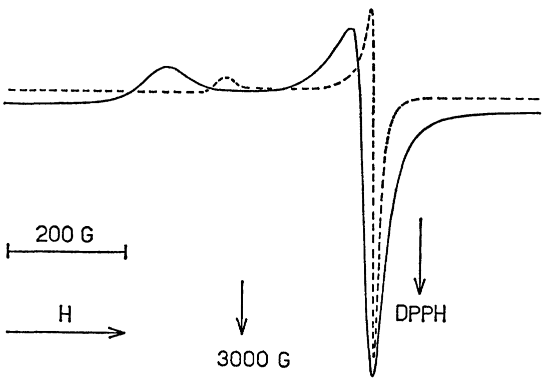

Fig. 1. EPR spectra of the $Cu(AcLeu)_2$ (——) and $Cu(AcLeu)_2 \cdot pipz$ (······) complexes.

tetragonal configuration. Their g values are lower than those found for the bis(N-acetyl-DL-leucinato)-copper(II) complex, suggesting a chromophore change from CuO_4 to CuO_2N_2 as a consequence of the amine coordination.[4,6] From the shape and positions of the d-d bands (Table 2) a tetragonal distortion in the aliphatic heterocyclic amine adducts greater than in the aromatic heterocyclic amine adducts may be generally proposed, in agreement with the pK_a values of the former amines greater than those of the latter.

A correlation between EPR and electronic spectra[7] gives an approximate measure (k_0^2=0.45—0.58) of the degree of covalency for the copper(II)–ligand bondings, which are strictly similar to those reported for copper(II) complexes of other amino acids with an essentially CuO_2N_2 chromophore.[7]

The narrow EPR line in the pipz adduct (Fig. 1) ($\Delta H_\parallel = 20$ G; $\Delta H_\perp = 5$ G) is suggestive of a fairly strong spin exchange interaction through the piperazine molecules "bridging" two copper(II) ions.[5,8]

The "anomalous" room temperature magnetic moment and the EPR spectrum (Fig. 3) of the green $Cu(AcLeu)_2 \cdot pid$ complex are indicative of a binuclear structure.[9,10] In particular the EPR spectrum shows zero field splitting of 0.39 cm^{-1} and the presence of magnetically dilute copper(II) impurities. Its room temperature electronic spectrum (Fig. 2) are also strictly similar to those of the dimeric carboxylates.[9,11,12] It also presents a band at 24390 cm^{-1}, which is considered characteristic of dimeric carboxylate and similar

Table 3. Relevant IR bands (cm^{-1}) of the solid complexes

	ν(NH)	$\nu(\mathrm{OCO})_{as}$	$\nu(\mathrm{OCO})_{s}$	$\Delta\nu$
AcLeuH	3380 vs	1694 vs	1238 vs	456
AcLeuNa	3285 s	1590 vs	1403 s	187
AcLeuK	3278 s	1590 vs	1390 s	200
$\mathrm{Cu(AcLeu)_2}$	3250 m	1580 vs	1390 vs	190
$\mathrm{Cu(AcLeu)_2(py)_2}$	3282 s 3250 m	1600 vs	1390 vs	210
$\mathrm{Cu(AcLeu)_2(3pic)_2}$	3328 m 3293 m 3245 m	1615 vs	1368 vs	247
$\mathrm{Cu(AcLeu)_2(4pic)_2}$	3300 m 3245 m	1590 vs	1373 vs	217
$\mathrm{Cu(AcLeu)_2 \cdot bpy}$	3242 m	1600 vs	1400 vs	200
$\mathrm{Cu(AcLeu)_2 \cdot phen}$	3250 s	1590 vs	1393 vs	197
$\mathrm{Cu(AcLeu)_2 \cdot pipz}$	3240 s (3195 mb)a)	1586 vs	1396 vs	190
$\mathrm{Cu(AcLeu)_2(Mepipz)_2}$	3275 s (3135 mb)a)	1580 vs	1382 vs	198
$\mathrm{Cu(AcLeu)_2(morph)_2}$	3240 s (3188 s)a)	1582 vs	1390 vs	192
$\mathrm{Cu(AcLeu)_2(pipd)_2}$	3275 s (3230 m)a)	1588 vs	1390 vs	198
$\mathrm{Cu(AcLeu)_2 \cdot pid}$	3252 s	1614 vs	1410 vs	204

a) ν(NH) of the saturated heterocyclic amines.

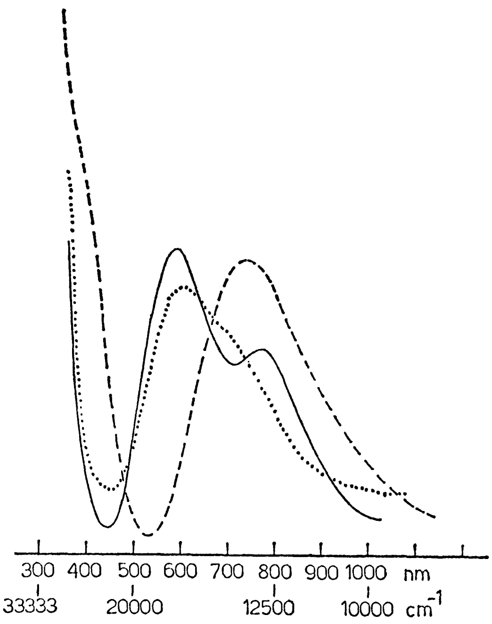

Fig. 2. Exemplifying electronic spectra of the $\mathrm{Cu(AcLeu)_2}$ (——), $\mathrm{Cu(AcLeu)_2 \cdot pid}$ (----), and $\mathrm{Cu(AcLeu)_2(pyridines)_2}$ (······) complexes.

complexes.[9,11,12]

The electronic spectrum (14140 cm^{-1}, $\varepsilon = 188$ l·mol^{-1}·cm^{-1}) of the green methanolic solution of the $\mathrm{Cu(AcLeu)_2}$ complex is very different to that of the solid state complex. The blue $\mathrm{Cu(AcLeu)_2B_2}$ (B= py, 3pic, 4pic, morph, Mepipz, pipd) adducts in methanolic solution ($1 \div 3 \cdot 10^{-2}$ mol·dm^{-3}) also give rise to green solutions, which show electronic spectra (14100—14600 cm^{-1} and $\varepsilon = 75 \div 90$ l·mol^{-1}·cm^{-1}) different to those of the solid state complexes. The color of the solutions and the position of the d-d bands suggest the presence of binuclear species due to a dissociation equilibrium involving the solvent molecules of this type:

$$2\mathrm{Cu(AcLeu)_2B_2} + 2\mathrm{Solv} — [\mathrm{Cu(AcLeu)_2 \cdot Solv}]_2 + 4\mathrm{B}$$

Fig. 3. EPR spectrum of the $\mathrm{Cu(AcLeu)_2 \cdot pid}$ complexes.

This may be confirmed as an amine excess addition in the methanolic adduct solutions results in a blue shift of the d-d band (15350—15870 cm^{-1}) and generally in a decrease of the molar extinction (57—80 l·mol^{-1}·cm^{-1}). The lower d-d band positions of the blue solution complexes than those of the solid complexes (16000—17800 cm^{-1}) indicate that they are different and a lower tetragonal distortion in the former than in the latter complexes, being probably four amines entered in the coordination sphere around the metal ion.

The assignments of the more relevant infrared bands (Table 3) for emphasizing the amino acid coordination are made by comparing the amino acid, its sodium and potassium salts and their deuterated analogues. The coordination sites of the amino acid may be securely evidentiated, as the IR spectra of the complexes are very similar in shape and position to those of the sodium and potassium *N*-acetyl-DL-leucinato salts (Table 3).

This suggests that the carboxylato group is the only group of the ligand involved in the coordination of the metal ion, confirming the previous results obtained from the electronic spectra.

Trends in positions of and separation ($\Delta\nu$) between antisymmetric and symmetric carboxylate stretching bands provide a useful observation for assigning its coordination type. In fact a large splitting of the carboxylate stretching frequencies is often an indication of a monodentate coordination, as the CO bonds become inequivalent, and a small splitting is indicative of bidentate coordination or bidentate "bridging" coordination.[10,13] In bidentate coordination $\Delta\nu$ values consistent with the above considerations may be obtained only in the absence of any strong hydrogen bonding effects.[13,14]

For the assignment of bidentate or monodentate coordination of our complexes we have also taken into consideration the position of the symmetric stretching band of the carboxylato group, as this band is directly connected with the oxygen atom certainly linked to the metal ion. Values of $\nu(OCO)_s$ at the same or lower energies than those found for the alkali metal salts are considered indicative of the presence of "symmetric" or "asymmetric" bidentate coordination of the carboxylato group, while values greater than 1410 cm^{-1} may be associated with a bridging bidentate behaviour of the carboxylato group, as has been experimentally found in some polynuclear complexes.[10] This also agrees with a greater double bond character of the symmetric CO bond when the carboxylato group links two metal ions, acting as "bridging" bidentate ligand, than when it links one metal ion, acting as a simple bidentate ligand.

By considering the $\Delta\nu$ values and the $\nu(OCO)_s$ position we may suggest the presence of "bridging" bidentate carboxylato groups in the $Cu(AcLeu)_2 \cdot pid$ complex and "asymmetric" bidentate groups in all the other complexes. These conclusions are also in agreement with the EPR and electronic results, and confirm the presence of an essentially CuO_2N_2 chromophore in the amine adducts.

The coordination of the amines is confirmed by the shift to lower frequencies of the $\nu(NH)_B$ (Table 3), with respect to the free amines,[15,16] in the saturated heterocyclic amine adducts, and by the shifts of the bands in the 800—500 cm^{-1} region, with respect to the free amines,[17–19] in the aromatic amine adducts.

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