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Infrared Spectra of the Copper(II) Complexes of Amino Acids with Hydrophobic Residues

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SUMMARY. The infrared spectra of the bis-chelated Cu(II) complexes of the amino acids glycine, alanine, leucine, isoleuceine, valine and phenylalanine, which posses different kind of pharmacologic activity, were recorded and analyzed in relation to its structural peculiarities. Some comparisons between the recorded spectra are also presented and the characteristics of the carboxylate motions as well as those of the metal-to-ligand vibrations are discussed in detail.

RESUMEN. "Espectros de Infrarrojo de los Complejos de Cobre(II) de Aminoácidos con Residuos Hidrofóbicos". Los espectros de infrarrojo de los complejos de Cu(II), bisquelados con los aminoácidos glicina, alanina, leucina, isoleucina, valina y fenilalanina, conocidos por presentar diferentes tipos de actividad farmacológica, fueron registrados y analizados en base a sus peculiaridades estructurales. Asimismo, se presentan algunas comparaciones entre los espectros obtenidos y las características de las vibraciones asociadas a los grupos carboxilato y a las uniones metal-ligando se discuten en detalle.

INTRODUCTION

As a part of a research project devoted to the synthesis and characterization of copper complexes with pharmacologic activity, we are investigating some general physicochemical properties of Cu(II) complexes of different amino acids. As it is known, many of these complexes posses an effective anti rheumatic and or anti-inflammatory activity [1-5]. Within this project, we have now initiated the study of the vibrational spectra of complexes of this type. In this paper we present the first results of this investigation belonging to complexes of general stoichiometry $Cu(aa)_2$ or $Cu(aa)_2.nH_2O$, where *aa* is an amino acid containing a hydrophobic residue: glycine (gly), alanine (ala), valine (val), leucine (leu), isoleucine (ile) and phenylalanine (phe), which formulas are depicted in Figure 1.

KEY WORDS: Cu(II), Amino Acid Complexes, Infrared Spectra.
PALABRAS CLAVE: Cu(II), Complejos con Aminoácidos, Espectros de Infrarrojo.

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EXPERIMENTAL

Amino acids (L-form) were purchased from Sigma, basic copper carbonate, copper sulfate and copper chloride were from Merck. All these chemicals were used as supplied. The investigated complexes were obtained from aqueous solutions, following well known synthetic procedures [6]. The infrared spectra were recorded with a Bruker FTIR model 113 v instrument, with the powdered samples dispersed either in KBr or polyethylene pellets.

NH_2-CHR-COOH

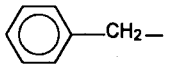
Glycine (gly)	R=H–
Alanine (ala)	R=CH_3–
Valine (val)	R=$(CH_3)_2$-CH–
Leucine (leu)	R=$(CH_3)_2$-CH-CH_2–
Isoleucine (ile)	R=C_2H_5-CH-CH_3–
Phenylalanine (phe)	R= 

Figure 1. Formulas of the amino acids used as ligands.

RESULTS AND DISCUSSION

Structural characteristics of the complexes

Structural characteristics of most of the investigated complexes are known. Only for the L-valine complex structural data are missing. In Table 1 the available structural information [7-11] is summarized.

$Cu(gly)_2.H_2O$	orthorhombic, sp.group $P2_12_12_1$, Z = 4. Amino acid arrangement: *cis*. Cu-environment: roughly octahedral; $CuN_2O_2O'O''$ (O'= oxygen atom from the water molecule; O" = weak interaction with an adjacent carboxyl oxygen) [7].
$Cu(ala)_2$	monoclinic, sp.group $P2_1$, Z = 2. Amino acid arrangement: *trans*. Cu-environment: roughly octahedral; $CuN_2O_2O_2'$ (O'= weak interaction with carboxyl oxygens of neighbouring complexes)[8].
$Cu(leu)_2$	monoclinic, sp.group $P2_1$, Z = 2. Amino acid arrangement: *trans*. Cu-environment: roughly octahedral, similar as above [9].
$Cu(ile)_2.H_2O$	orthorhombic, sp. group $P2_12_12_1$, Z = 4. Amino acid arrangement: *cis*. Cu-environment: square pyramidal; CuN_2O_2O' (O'= oxygen atom from the water molecule) [10].
$Cu(phe)_2$	monoclinic, sp.group $P2_1$, Z = 2. Amino acid arrangement: *trans*. Cu-environment: roughly octahedral, similar to that in $Cu(ala)_2$ [11].

Table 1. Structural characteristics of the investigated complexes.

Interestingly, the two monohydrated complexes, $Cu(gly)_2.H_2O$ and $Cu(ile)_2.H_2O$, belong to the same orthorhombic space group and present the amino acids in cis conformation. The three remaining complexes are monoclinic, space group $P2_1$, with the amino acids in trans conformation.

Infrared spectra

The spectra of all the investigated compounds are very complex and present a great number of bands in all the spectral ranges. Therefore, it seems very difficult to attempt a detailed assignment of them. Notwithstanding, the most important and characteristic bands could be identified and different comparisons between all the investigated compounds could be made. Some general conclusions on the vibrational behaviour could also be derived from these comparisons.

The infrared spectrum of the most simple complex of this series, $Cu(gly)_2.H_2O$, has been widely studied [12-15] and so may be useful as a starting point for the analysis of the behaviour of the other, most complex, compounds.

In Table 2 we compare the most important and characteristic bands of $Cu(gly)_2.H_2O$ and $Cu(ile)_2.H_2O$, the two complexes which present the ligands in a cis arrangement. The assignment is based on the arguments advanced by Percy for the bisglycinate complex [15]. The metal-to ligand vibrations for the two complexes are found in totally similar ranges, in agreement with the practically equal CuO_2N_2 environments in both species [7,10].

The assignments proposed for the complexes with L-leucine and L-valine are shown in Table 3. The similarity of the most characteristic absorption bands clearly

$Cu(gly)_2.H_2O$	$Cu(ile)_2.H_2O$	Assignment
3335 m/3265 vs	3307s/3220 m	((N-H)
1604 vs	1623 vs	NH_2-sciss
1580 vs	1589 vs	ν(C=O)
1390 vs	1391 s	ν(C-O)
1320 s	1335 s	CH_2-wag + ν(C-CO_2)
1120 s	1112 w	NH_2-wag +ν(C-CO_2)
1060/1037 s	1065 w	ν(C-N)
668 m	668 m	CO_2-rock + NH_2-rock
476 m	468 m	N_{as}(Cu-N) + CO_2-wag
456 m	428 w	ν_s(Cu-N) + CO_2-wag
379 s	343 w	ν_{as}(Cu-O)
333 s	315 s	ν_s(Cu-O)
280 s	276/267m	Cu-ligand bend
202 s		ν(Cu . . .O=)

Table 2. Comparison of the most characteristic IR bands (in cm^{-1}) of $Cu(gly)_2.H_2O$ and $Cu(Ile)_2.H_2O$. *vs:* very strong; *s:* strong; *m:* medium; *w:* weak

$Cu(val)_2$	$Cu(leu)_2$	Assignment
3300sh/3272 vs	3390m3290 vs	ν(N-H)
1615 vs	1620 s	NH_2-sciss
1584 vs	1595 vs	ν(C=O)
1390 s	1390 s	ν(C-O)
1330 m	1330 m	CH_2-wag + ν(C-CO_2)
1133 m	1140w1133w	NH_2-wag + ν(C-CO_2)
1030 w	–	ν(C-N)
667 w	670 w	CO_2-rock + NH_2-rock
459 w	470 vw	ν(Cu-N) + CO_2-wag
315 s	322 m	ν(Cu-O)
214 m	220 s,br	Cu-ligand bend

Table 3. Comparison of the most characteristic IR bands (in cm^{-1}) of $Cu(val)_2$ and $Cu(leu)_2$. *vs:* very strong; *s:* strong; *m:* medium; *w:* weak; *vw:* very weak; *br:* broad.

points to similar coordination characteristics in both complexes, suggesting that the structure of the L-valine complex should be closely related to that of L-leucine.

The most important IR bands of the L-alanine and L-phenylalanine complexes are compared in Table 4. The spectrum of this last complex shows additional complexities due to the presence of the typical vibrations related to the phenyl-ring. But, as it can be seen from the data presented in Table 4, most of the characteristic bands appear in the same ranges as those of the L-alanine complex.

Another aspect which has been analyzed is the displacement of the characteristic carboxylic bands after coordination. The "free" amino acids exist as zwitterions in the crystalline state; thus, one expects two vibrations for the COO- moiety present in these systems ν(s(COO⁻ and $\nu_{as}(COO^-)$ respectively). The first one is usually of medium intensity, whereas the second is strong and broad. After coordination, one should expect a lowering of the frequency of one of these bands, due to the generation of the Cu-O-bond and the increase of the other, because a C-O double bond is partially reconstructed.

As it can be seen from the data presented in Table 5, the band which is assigned to the $\nu_s(COO^-)$ vibration in the "free" acid suffers a small shift to lower frequencies in all cases, in agreement with the participation of one C-O bond in metal binding. However, interestingly, the other vibration is not always reinforced after complex formation. In fact it also suffers a small frequency decrease in three of the investigated complexes, whereas in the other three a rather small increment was observed. This behaviour can be explained by the fact that this C=O group participates in hydrogen bonding with water molecules or is involved in weak secondary bonds to the metal of the neighboring complex. Both interactions produce, obviously, a weakening of this C=O bond *(cf.* also [16]).

Another aspect which should be especially emphasized is the position of the Cu-ligand vibrations. The identification of bands related to these modes, by comparison of the spectra of the complexes with those of the corresponding free ligands, is not always easy because most of the amino acids present a great number of strong bands in this region. This important part of the spectral pattern for the investigated complexes is depicted schematically in Figure 2.

Cu(ala)2	Cu(phe)2	Assignment
3293m3245 vs	3315s3235vs	ν(N-H)
1620 vs,br	1625 vs,br	ν(C=O) + NH_2-sciss
1400vs1394sh	1398vs1393sh	ν(C-O)
1297 vs	1312 vs	CH_2-wag + ν(C-CO_2)
1116 vs	1102 vs	NH_2-wag + ν(C-CO_2)
1070 s	1076 s	ν(C-N)
780s768s	782 m	CO2-rock + NH_2-rock
475(?) vw	404s396w	ν(Cu-N) + CO_2-wag
322 m	341s324 w	ν(Cu-O)
211 s	206 s	Cu-ligand bend

Table 4. Comparison of the most characteristic IR band (in cm^{-1}) of $Cu(ala)_2$ and $Cu(phe)_2$. *vs:* very strong; *s:* strong; m: medium; *w:* weak; *br:* broad.

Acid/Complex	$\nu_{as}(COO^-)$	$\nu_s(COO^-)$
glycine	1608	1412
$Cu(gly)_2.H_2O$	1580	1390
L-isoleucine	1602	1418
$Cu(ile)_2.H_2O$	1589	1391
L-Valine	1586	1425
$Cu(val)_2$	1584	1390
L-leucine	1583	1407
$Cu(leu)_2$	1595	1390
L-alanine	1605	1413
$Cu(ala)_2$	1620	1400
L-phenylalanine	1564	1411
$Cu(phe)_2$	1625	1398

Table 5. Comparison of the carboxylate vibrations (in cm^{-1}) in the "free" amino acids and in its Cu(II) complexes.

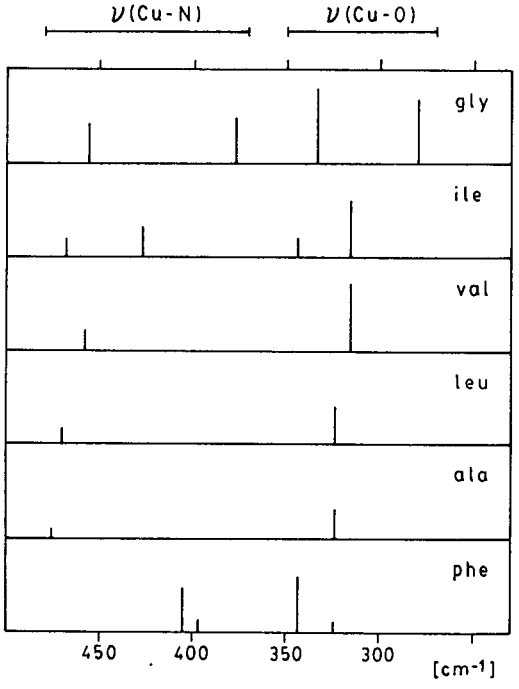


Figure 2. Schematic representation of the metal-to-ligand vibrations of the investigated complexes.

In the case of the cis-isomers the appearance of two bands for each of the metal-to-ligand vibrations is expected, whereas for the trans isomers only one band for each of these modes is predicted [16, 17]. This expectations are clearly fulfilled in the investigated cases.

All of these vibrations are found to lie in similar spectral ranges, in agreement with the fact that the Cu-N and Cu-O bond lengths of all of them are very similar. Only in the case of the $Cu(phe)_2$ complex, the ν(Cu-N) mode is found at a somewhat lower frequency than in the other trans-complexes. Interestingly, in this case, both ligand-to-metal bands present a clear doublet structure. This behaviour can be probably related to a peculiar crystal field effect in this structure.

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