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Mini-Review

An analysis of the carboxylate stretching vibrations in some Cu(II) complexes of amino acids

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ABSTRACT

The behavior of the stretching vibrations of the carboxylate groups in twenty one Cu(II) complexes of amino acids (aa) of general composition $Cu(aa)_2$ or $Cu(aa)_2 \cdot nH_2O$ is analyzed on the basis of previously reported vibrational spectroscopic data and on the structural characteristics of these complexes. Some general trends are pointed out and discussed. In all cases, the spectroscopic results are consistent with the monodentate binding of the COO^- groups with the metal center. Brief comments on the spectroscopic behavior of the carboxylate groups in a series of polymeric Cu(II) complexes of dipeptides are also presented.

KEYWORDS: copper(II), amino acids, dipeptides, carboxylate, stretching vibrations

1. INTRODUCTION

Besides iron and zinc, copper is the most ubiquitous transition metal present in living organisms, and is involved in a large number of important functions and processes. Copper metalloenzymes are present in oxidases, and they participate in electron transport, in oxygenation and dismutation reactions and even in oxygen transport in the case of arthropods and molusks [1-4].

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During the past years substantial efforts have been made to understand the intricate and specific mechanisms related to different aspects of copper absorption and transport. But knowledge on the molecular aspects of copper trafficking within the body began to emerge only recently. The recent discovery of Wilson and Menkes disease genes and the identification of copper chaperones led to unprecedented advances in our understanding of these mechanisms [5-7].

Besides, copper compounds, and in particular Cu(II) coordination compounds, present important pharmacological interest as several of them show various clinical effects, including anti-inflammatory, antiulcer, anticonvulsant and even anti-tumoral activity [8-12]. In this context, copper complexes of most of the simplest amino acids show a special relevance, as they are even useful for copper supplementation in human and veterinary medicine [12, 13].

Due to the above-mentioned importance of these complexes, since the last fifteen years we have been investigating their vibrational-spectroscopic behavior and in this paper we discuss, in particular some general trends observed in the spectroscopic behavior of the carboxylate groups involved as ligands in these species. Although the behavior of these groups in a variety of complex compounds has been discussed by different authors, and some general trends which relate the

wavenumbers of the COO^- stretching vibrations or its energy differences with bonding characteristics are relatively well established [14-18], a systematic analysis of their behavior in Cu(II) amino acid complexes has not so far been attempted. Besides, such an analysis may be of interest for a deeper understanding of the spectroscopic characteristics of these important and relevant bioinorganic systems.

2. Structural data and discussion of the spectroscopic results

The most relevant structural characteristics of the investigated Cu(II) complexes of amino acids are summarized in Table 1 [19-39]. In the case of the valine complex, although structural data for a complex of stoichiometry $Cu(Val)_2 \cdot H_2O$ has been reported, the spectroscopic investigation [40] was performed on an anhydrous complex of unknown structure. Also for $Cu(Trp)_2$ no structural information is so far available.

In all cases, the primary bonding between the metal center and the amino acids occurs in the way schematized in Fig. 1 for the case of the Cu(II)/L-alanine complex [20], generating the characteristic CuN_2O_2 environment (in this case, *in trans* arrangement). The glutamato and aspartato complexes are the only exceptions, as only one direct Cu(II)/amino acid bond occurs in them [28, 29].

In Table 2 the positions of the carboxylate stretching vibrations of the "free" amino acids are compared with those found in the respective cupric complexes. As the "free" amino acids exist as zwitterions in the crystalline state [42, 43], one expects two stretching modes for the COO^- moieties present in these systems, a symmetric and an antisymmetric stretching vibration [43]. The first one is generally seen as a medium intensity band in the IR spectra, whereas the second one is usually very strong and broad. After coordination, one may expect a lowering of the frequency of one of these bands due to the generation of the Cu-O bond and an increase of the other, because a C-O double bond is partially reconstructed.

A thorough analysis of the data presented in Table 2 immediately shows that the mentioned expectations are not entirely fulfilled. 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, the other vibration ($\nu_{as}(COO^-)$ for the free acid) is not always reinforced after complex formation. In fact, in most of the investigated complexes it suffers a small frequency decrease whereas in some other cases a very small increment of the frequency could be observed. This behavior can be explained by the fact that this C=O group participates in hydrogen bonding and/or is involved in weak secondary bonds to the metal center of a neighboring complex (cf. again Table 1). Both interactions obviously produce a weakening of this C=O bond. Some additional comments on peculiar aspects detected during the spectroscopic analysis can be explained, as follows:

a) In the case of the complexes of the six amino acids with hydrophobic residues (glycine, isoleucine, valine, leucine, alanine, and phenylalanine) the first four show the two COO^- stretching vibrations as strong and well-defined IR bands. In the two remaining complexes the ν(C=O) band appears somewhat broadened and partially superimposed by the $\delta_{sciss.}(NH_2)$ band, whereas ν(C-O) presents a weak shoulder on the lower energy-side [40]. As it can be seen from the data presented in Table 2, in the cases of the complexes with Gly, Ile and Val, both carboxylate vibrations suffer a shift to lower frequencies after complex formation. It is interesting to mention that also the Zn(II) complexes of these amino acids behave in a very similar way [52].

b) For the Cu(II) complexes of amino acids containing hydroxyl residues (serine, tyrosine, threonine), it must be mentioned that in the case of the threonine complex it was difficult to locate the stretching vibration of the terminal C=O group, because it appears partially overlapped by the $\delta_{sciss.}(NH_2)$ mode. On the contrary, the ν(C-O) band could be clearly identified as a relatively strong IR band in all cases [44]. Also in these three complexes, both carboxylate stretching vibrations are displaced to lower frequencies after complex formation.

Table 1. Structural characteristics of the investigated Cu(II) complexes of amino acids.

Composition	**Description**	**Ref.**
$Cu(Gly)_2 \cdot H_2O$	Orthorhombic, sp. group $P2_12_12_1$, Z = 4. Amino acid arrangement: *cis*. Cu-environment: roughly octahedral $CuN_2O_2O'O''$ (O' = O-atom from the water molecule; O" = weak interaction with an adjacent carboxyl oxygen)	[19]
$Cu(Ala)_2$	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 neighboring complexes)	[20]
$Cu(Leu)_2$	Monoclinic, sp. group: $P2_1$, Z = 2. Amino acid arrangement: *trans*. Cu-environment: roughly octahedral, similar as above	[21]
$Cu(Ile)_2 \cdot H_2O$	Orthorhombic, sp. group $P2_12_12_1$, Z = 4. Amino acid arrangement: *cis*. Cu-environment: square pyramidal CuN_2O_2O' (O' = O-atom from the water molecule)	[22]
$Cu(Phe)_2$	Monoclinic, sp. group $P2_1$, Z = 2. Amino acid arrangement: *trans*. Cu-environment: roughly octahedral, similar to that in $Cu(Ala)_2$	[23]
$Cu(Val)_2$	Structure unknown. Probably similar to that of $Cu(Ala)_2$	(cf. text)
$Cu(Ser)_2$	Monoclinic, sp. group $P2_1$, Z = 2. Amino acid arrangements: *cis*. Cu-environment: square pyramidal CuN_2O_2O' (O' = weak interaction with a carboxylic O-atom from a neighboring complex)	[24]
$Cu(Thr)_2 \cdot H_2O$	Monoclinic, sp. group $P2_1$, Z = 2. Amino acid arrangements: *trans*. Cu-environment: strongly distorted elongated octahedral environment $CuN_2O_2O_2'$ (O' = carboxylate O-atoms of a pair of symmetry related ligand molecules)	[25, 26]
$Cu(Tyr)_2$	Orthorhombic, sp. group $P2_12_12_1$, Z = 4. Amino acid arrangement: *trans*. Cu-environment: square pyramidal CuN_2O_2O' (O' = weak interaction with an adjacent carboxyl oxygen)	[27]
$Cu(Glu)_2 \cdot 2H_2O$	Orthorhombic, sp. group $P2_12_12_1$, Z = 4. Cu-environment: strongly distorted octahedron $CuNOO'O_3''$ (O' = O-atom from a water molecule; O" = carboxylic O-atoms from two adjacent glutamate moieties)	[28]
$Cu(Asp)_2 \cdot 2H_2O$	Monoclinic, sp. group C2, Z = 4. Cu-environment: distorted tetragonal pyramid $CuNOO_2'O''$ (O' = O-atoms from two water molecules; O" = O-atom from a terminal COO^- group of another Asp molecule)	[29]
$Cu(Asn)_2$	Monoclinic, sp. group $P2_1$, Z = 2. Amino acid arrangement: *trans*. Cu-environment: distorted octahedron $CuN_2O_2O_2'$ (O' = amide O-atoms of two adjacent ligand molecules)	[30]

Table 1 continued..

$Cu(Gln)_2$	Monoclinic, sp. group C2, Z = 4. Amino acid arrangement and Cu-environment: similar as above	[31]
$Cu(Met)_2$	Monoclinic, sp. group $P2_1$, Z = 4. Amino acid arrangement: *trans*. Cu-environment: distorted octahedron $CuN_2O_2O_2$' (O' = carboxylic O-atoms from two neighboring ligands)	[32]
$Cu(Se\text{-}met)_2$	Isostructural with $Cu(met)_2$	[33]
$Cu(Trp)_2$	Structure unknown. Amino acid arrangement probably *trans* and Cu-environment probably a distorted octahedra $CuN_2O_2O_2$' Involving O-atoms from two neighboring ligand molecules (O')	[34]
$[Cu(Pro)_2]_2 \cdot 5H_2O$	Monoclinic, sp. group $P2_1$, Z = 2. Two chemically different complex moieties. One is pyramidal CuN_2O_2O' (O' = water O-atom), the other distorted octahedral $CuN_2O_2O_2$' (O' = water O-atoms)	[35]
$Cu(His)_2 \cdot 1.5H_2O$	Monoclinic, sp. group $P2_1$, Z = 2. Cu-environment: distorted square pyramidal CuN_2O_2N' (N' = N-atom of an imidazole moiety)	[36]
$[Cu(Arg)_2(H_2O)]CO_3 \cdot H_2O$	Monoclinic, sp. group $P2_1$, Z = 2. Cu-environment: square pyramidal. Amino acid arrangement: *trans*. Apical H_2O molecule	[37]
$[Cu(Lys)_2Cl_2] \cdot 2H_2O$	Monoclinic, sp. group $P2_1$, Z = 2. Cu-environment distorted octahedron $CuN_2O_2Cl_2$ involving the α-amino nitrogens	[38]
$[Cu(Orn)_2Cl_2] \cdot 2H_2O$	Monoclinic, sp. group $P2_1/c$, Z = 2. Cu-environment similar as above	[39]

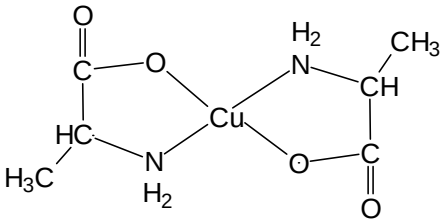

Fig. 1. Schematic structure of *bis* (L-alaninato)copper(II) (Adapted from [20]).

c) The complexes of glutamic and aspartic acid present some interesting features as the spectral behavior of the carboxylate motions clearly reflects the structural differences marked in Table 1. The $\nu_{as}(COO^-)$ vibration of the "free" acids appears clearly splitted, in agreement with the presence of two structurally non-equivalent carboxylate groups. For the corresponding $\nu_s(COO^-)$ vibration two bands are observed in the case of glutamic acid, whereas in aspartic acid, the two non-equivalent groups generate a unique band [45]. After complex formation, in both cases one of the vibrations suffer a small shift to lower energies as expected; but the other vibration shows a different behavior in both complexes. In the case of $Cu(Glu)_2 \cdot 2H_2O$ the bands are also displaced to lower wavenumbers, in agreement with the participation of the carboxylate groups in secondary interactions with the metal centers. As such secondary bonds are not established in the case of $Cu(Asp)_2 \cdot 2H_2O$, the corresponding vibrations are shifted to higher energies (cf. [45] and Tables 1 and 2).

d) The spectra of the complexes of L-methionine and L-selenomethionine are comparable [33, 46]

Table 2. Comparison of the two carboxylate stretching vibrations (in cm^{-1}) in the "free" amino acids and in the corresponding Cu(II) complexes (values obtained from IR-spectra). (Δ is the energy difference between the two stretching vibrations in the complexes).

Acid/complex	**$\nu_{as}(COO^-)$**	**$\nu_s(COO^-)$**	**Δ**	**Ref.**
Glycine	1608	1412		[40]
$Cu(Gly)_2 \cdot H_2O$	1580	1390	190	[40]
L-alanine	1605	1413		[40]
$Cu(Ala)_2$	1620	1400	220	[40]
L-leucine	1583	1407		[40]
$Cu(Leu)_2$	1595	1390	205	[40]
L-isoleucine	1602	1418		[40]
$Cu(Ile)_2 \cdot H_2O$	1589	1391	198	[40]
L- valine	1586	1425		[40]
$Cu(Val)_2$	1584	1390	194	[40]
L-phenylalanine	1564	1411		[40]
$Cu(Phe)_2$	1625	1398	227	[40]
L-serine	1597	1412		[44]
$Cu(Ser)_2$	1597	1398	199	[44]
L-threonine	1626	1417		[44]
$Cu(Thr)_2 \cdot H_2O$	(1579)	1404	175	[44]
L-tyrosine	1590	1436		[44]
$Cu(Tyr)_2$	1586	1425	161	[44]
L-glutamic acid	1662, 1644	1434, 1419		[45]
$Cu(Glu) \cdot 2H_2O$	1626, 1573	1407, 1392	219,181	[45]
L-aspartic acid	1592, 1550	1418		[45]
$Cu(Asp) \cdot 2H_2O$	1629, 1592	1410	219,182	[45]
L-tryptophan	1589	1412		[34]
$Cu(Trp)_2$	1578	1385	193	[34]
L-methionine	1583	1409		[46]
$Cu(Met)_2$	1569	1404	165	[46]
L-Semethionine	1583	1406		[33]
$Cu(Semet)_2$	1616	1403	213	[33]
L-asparagine	1613	1498		[47]
$Cu(Asn)_2$	1637	1414	223	[47]
L-glutamine	1587	1451		[47]
$Cu(Gln)_2$	1620	1427	193	[47]
L-proline	1624	1408		[48]

Table 2 continued..

$[Cu(Pro)_2]_2 \cdot 5H_2O$	1610	1375	235	[48]
L-histidine	1590	1414		[49]
$Cu(His)_2 \cdot 1.5H_2O$	1598	1401	197	[49]
L-arginine	1620	1417		[37]
$Cu[(Arg)_2(H_2O)]CO_3 \cdot H_2O$	1605	1360	245	[37]
L-lysine·HCl	1580	1420		[50]
$[Cu(Lys)_2Cl_2] \cdot 2H_2O$	1660	1394	266	[50]
L-ornithine·HCl		cf. text		
$[Cu(Orn)_2Cl_2] \cdot 2H_2O$	1589	1401	190	[51]

in agreement with the fact that they are isostructural [33]. Notwithstanding, the behavior of the carboxylate motions (cf. Table 2) suggests that in $Cu(Semet)_2$ the secondary apical interactions may be relatively weaker than in $Cu(Met)_2$ [33].

e) It is worth commenting that different Cu(II) complexes of L-cysteine, the other biologically important sulfur-containing amino acid, are known. In this cage-like cluster complexes copper is present as Cu(II) and bonding occurs via the thiol groups of the amino acid, without participation of carboxylate groups [53].

f) In the case of the amino acids containing amide residues (glutamine and asparagine) the carboxylate vibrations behave in the normally expected way, i.e. one of the vibrations is reinforced and the other weakened after complexation in agreement with the fact that this group is not involved in secondary bonds to the metal center [47].

g) For the arginine complex, the situation is not entirely clear, because the expected shift to higher frequencies of one of the carboxylate stretchings is not clearly evident, essentially due to the fact that this spectral region is very complex and this band is partially coupled with an NH_2 bending mode [37]. The situation is even more complex to analyze in the case of $Cu(His)_2 \cdot 1.5H_2O$, as the two L-histidine ligands are structurally very different. One of them binds in the normal way, i.e., through one carboxylate O-atom and the amino N-atom; whereas the other is tridentate, using the imidazole N-atom, the amino N-atom and one carboxylate O-atom, which occupies the apical position [36, 49]. Finally, in the case of the L-proline complex, $[Cu(Pro)_2]_2 \cdot 5H_2O$, the shift to lower frequencies of the non-bonded carboxylate O-atom is surely caused by its involvement in H-bonding [35].

h) In the case of the $[Cu(Lys)_2Cl_2] \cdot 2H_2O$ complex, a comparison with the data of L-lysine·HCl shows the expected trend, i.e., one of the stretching vibrations is reinforced and the other diminishes in energy [50]. In the case of the analogous ornithine complex [51], this comparison was not possible, as the FTIR spectrum of L-ornithine·HCl presents a great number of bands in the spectral range between 1600 and 1400 cm^{-1} and no detailed assignment for the carboxylate stretching vibrations has so far been attempted [54, 55].

Another parameter which can be analyzed on the basis of the reviewed spectroscopic data is the frequency separation, Δ, between the two stretching vibrations determined in the coordinated carboxylates. It has generally been accepted that these energy differences follow the order $\Delta_{unidentate} > \Delta_{ionic} \sim \Delta_{bridging} > \Delta_{chelating}$ [14- 18]. In the case of acetates, Δ_{ionic} is ca. 160-170 cm^{-1} [14, 15], whereas in the monodentate coordination a redistribution of the electron density takes place and the shift of $\nu_{as}(COO^-)$ to higher energies is observed in comparison with the ionic group, increasing the value of Δ. In the bridging coordination, when one metal cation is bound to one of the oxygens of the COO^- group and another cation to the other oxygen atom, the $\nu_{as}(COO^-)$ band is located at the same position as that of the ionic group. Finally,

in the case of chelating coordination the antisymmetric carboxylate stretching is shifted to lower wavenumbers, lowering the Δ-value.

For acetato complexes Δ-values > 180-200 cm^{-1} have been usually related to unidentate coordination [14, 15, 18]. In Table 2 we have also included Δ-values for all the investigated Cu(II) complexes. As it can be seen these values ranged between 161 and 245 cm^{-1}, in clear agreement with the participation of unidentate bonded carboxylate groups in all the investigated complexes (cf. again Table 1). The small differences between these Δ-values can surely be related to the different strengths of the secondary H-bonds or Cu-O bonds, involving the carboxylate oxygen atom not directly bonded to the metal.

Some years ago, Nara *et al.* performed a molecular orbital calculation of the vibrational frequencies for several carboxylate compounds and derived a quantitative equation establishing a relation between Δ and the coordination structure, expressed as [16]:

$$\Delta = 1818.1\delta r + 16.47(\theta_{OCO} - 120) + 66.8$$

In this equation δr is the difference between the two CO bond lengths (in Å) and θ_{OCO} is the OCO angle (in degrees,°). Using some of the best available structural data, we have applied this equation to some of the investigated Cu(II) complexes. The results, presented in Table 3, show a reasonable agreement between calculated and experimental values. Notwithstanding, these results must be taken with care, because as found in other cases, the proposed equation often leads to erroneous predictions [18, 56]. Besides, it has been shown that the Δ-values are also dependent, to a certain extent, on the chemical characteristics of the bonded metal cations and also on the value of the interaction force constant between the stretching motions of the two CO bonds. As θ_{OCO} becomes smaller, this interaction force constant becomes larger [16]. Another factor which must be considered is the possible mixing of the $\nu_s(COO^-)$ vibration with the OCO bend and the CC stretching mode; this mixing also becomes stronger in species having smaller values of θ_{OCO} [16].

On the other hand, it has been proposed to analyze the COO coordination characteristics through the behavior of other carboxylate modes, in particular by the position of the rocking mode [56]. In the case of the here-discussed Cu(II) complexes, the $\rho(COO^-)$ motion is often not easy to identify because it appears superimposed or coupled with some other vibrations, lying in the same spectral range. In most cases this $\rho(COO^-)$ mode was assigned, tentatively, in the spectral range between 650 and 700 cm^{-1}.

Finally, it is interesting to mention that we have prepared a series of Cu(II) complexes of dipeptides, which have been structurally and spectroscopically characterized [57-59]. They present all closely related structures in which Cu(II) has a pyramidal square-base coordination geometry. The metal cation occupies the centre of the square base, being equatorially coordinated to a dipeptide molecule acting as a tridentate ligand through the N-atom of the terminal NH_2 group, the deprotonated N-atom of the amide group, and one of the oxygen atoms

Table 3. Comparison of Δ-values, calculated with the equation of Nara *et al.* [16], with those experimentally obtained for some Cu(II) complexes of amino acids.

Complex	**Structural parameters**	**Ref.**	$\Delta_{calc.}$	$\Delta_{exper.}$
$Cu(Gly)_2 \cdot H_2O$	δr = 0.050 Å; θ_{OCO} = 123.6°	[19]	217	190
$Cu(Leu)_2$	δr = 0.024 Å; θ_{OCO} = 124.45°	[21]	184	205
$Cu(Ile)_2 \cdot H_2O$	δr = 0.064 Å; θ_{OCO} = 122.0°	[22]	216	198
$Cu(Ser)_2$	δr = 0.039 Å; θ_{OCO} = 124.3°	[24]	209	199
$Cu(Tyr)_2$	δr = 0.018 Å; θ_{OCO} = 123.4°	[27]	155	161
$Cu(Asn)_2$	δr = 0.057 Å; θ_{OCO} = 123.55°	[30]	229	233

Table 4. Behavior of the two carboxylate stretching vibrations (in cm^{-1}) (values obtained fro IR-spectra) of some polymeric Cu(II) dipeptide complexes. (Δ is the energy difference between these two stretching vibrations).

Complex	$\nu_{as}(COO^-)$	$\nu_s(COO^-)$	Δ	Ref.
[Cu(Ala-Val)]	1547	1461	86	[57]
[Cu(Ala-Phe)]	1547	1439	108	[57]
[Cu(Ala-Ile)]	1578	1542	36	[58]
$[Cu(Ala-Thr)]\cdot 0.5H_2O$	1570	1500	70	[58]
$[Cu(Ala-Tyr)]\cdot H_2O$	1581	1511	70	[58]
$[Cu(Gly-Val)]\cdot 0.5H_2O$	1538	1464	74	[59]
[Cu(Val-Gly)]	1551	1461	90	[59]
[Cu(Val-Phe)]	1543	1431	112	[59]
[Cu(Phe-Phe)]	1547	1453	94	[59]

of the carboxylate group. The fourth equatorial ligand is a carboxylate oxygen from a second dipeptide molecule, giving rise to carboxylate bridged polymeric chains. The pyramid apex is occupied by an O-atom of the amide bond belonging to a third dipeptide molecule, which in turn links adjacent chains through amidate bridges [57-59]. The spectroscopic behavior of the carboxylate groups present in these dipeptide complexes is in agreement with the bridging nature of them [14, 15], showing Δ-values lying between 36 and 112 cm^{-1}, as summarized in Table 4.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interests.

REFERENCES

1. Lippard, S. J. and Berg, J. M. 1994, Principles of Bioinorganic Chemistry, University Science Books, Mill Valley, CA.
2. Baran, E. J. 1995, Química Bioinorgánica, McGraw-Hill Interamericana de España S. A., Madrid.
3. Roat-Malone, R. M. 2002, Bioinorganic Chemistry, J. Wiley, Hoboken, NJ.
4. Krebs, B. 2006, Anales Acad. Nac. Cs. Ex. Fís. Nat., 58, 39.
5. DiDonato, M. and Sarkar, B. 1997, Biochim. Biophys. Acta, 1360, 3.
6. Sarkar, B. 1999, Chem. Rev., 99, 2535.
7. Sarkar, B. 2000, J. Inorg. Biochem., 79, 187.
8. Sorenson, J. R. J. 1982, The Anti-Inflammatory Activities of Copper Complexes, H. Sigel (Ed.), Metal Ions in Biological Systems, Vol. 14, Marcel Dekker, New York, 77.
9. Baran, E. J. 1985, Acta Farm. Bonaerense, 4, 125.
10. Farrell, N. 1989, Transition Metal Complexes as Drugs and Chemotherapeutic Agents, Kluwer, Dordrecht.
11. Duncan, C. and White, A. R. 2012, Metallomics, 4, 127.
12. Baran, E. J. 2004, Mini Rev. Med. Chem., 4, 1.
13. Torre, M. H., Viera, I., Facchin, G., Kremer, E., Baran, E. J., Porochin, T., DiDonato, V., Irigoyen, C., Irigoyen, J., Saldanha, S., Bussi, J., Ohanian, M. and Fuentes, J. 2005, Livestock Product. Sci., 95, 49.
14. Nakamoto, K. 2009, Infrared and Raman Spectra of Inorganic and Coordination Compounds, 6th Ed., Wiley, New York.

15. Deacon, G. B. and Philips, R. J. 1980, Coord. Chem. Rev., 33, 227.
16. Nara, M., Tori, H. and Tasumi, M. 1996, J. Phys. Chem., 100, 19812.
17. Robert, V. and Lemercier, G. 2006, J. Am. Chem. Soc., 128, 1183.
18. Zeleňák, V., Vargová, Z. and Györyová, K. 2007, Spectrochim. Acta, 66A, 262.
19. Freeman, H. C., Snow, M. R., Nitta, I. and Tomita, K. 1964, Acta Crystallogr., 17, 1463.
20. Dijkstra, A. 1966, Acta Crystallogr., 20, 589.
21. Fawcett, T. G., Ushay, M., Rose, J. P., Lalancette, R. A., Potenza, J. A. and Schugar, H. J. 1979, Inorg. Chem., 18, 327.
22. Weeks, C. M., Cooper, A. and Norton, D. A. 1969, Acta Crystallogr., B25, 443.
23. van der Helm, D., Lawson, M. B. and Enwall, E. L. 1971, Acta Crystallogr., B27, 2411.
24. van der Helm, D. and Franks, W. A. 1969, Acta Crystallogr., B25, 451.
25. Amirthalingam, V. and Muralidharan, K. V. 1975, Pramana, 4, 83.
26. Rizzi, A. C., Piro, O. E., Castellano, E. E., Nascimento, O. R. and Brondino, C. D. 2000, Inorg. Chim. Acta, 305, 19.
27. van der Helm, D. and Tatsch, C. E. 1972, Acta Crystallogr., B28, 2307.
28. Gramaccioli, C. M. and Marsh, R. E. 1966, Acta Crystallogr., 21, 594.
29. Calvo, R., Steren, S. A., Piro, O. E., Rojo, T., Zuñiga, F. J. and Castellano, E. E. 1993, Inorg. Chem., 32, 6016.
30. Vencato, I., Lariucci, C., Ferreira, K. D., Santana, R. C. and Carvalho, J. F. 2004, Acta Crystallogr., E60, m1428.
31. Schveigkardt, J. M., Rizzi, A. C., Piro, O. E., Castellano, E. E., Santana, R. C., Calvo, R. and Brondino, C. D. 2002, Eur. J. Inorg. Chem., 2913.
32. Ou, C. C., Powers, D. A., Thich, J. H., Felthouse, T. R., Hendrickson, D., Potenza, J. A. and Schugar, H. J. 1978, Inorg. Chem., 17, 34.
33. Baran, E. J. 2005, Z. Naturforsch., 60b, 663.
34. Wagner, C. C. and Baran, E. J. 2004, Acta Farm. Bonaerense, 23, 339.
35. Sartoris, R. P., Ortigoza, L., Casado, N. M. C., Calvo, R., Castellano, E. E. and Piro, O. E. 1999, Inorg. Chem., 38, 3598.
36. Deschamps, P., Kulkarni, P. P. and Sarkar, B. 2004, Inorg. Chem., 43, 3338.
37. Viera, I., Torre, M. H., Piro, O. E., Castellano, E. E. and Baran, E. J. 2005, J. Inorg. Biochem., 99, 1250.
38. Duarte, M. T. L. S., de C. T. Carrondo, M. A. A. F., Simões Goncalves, M. L., Hursthouse, M. B. and Walker, N. P. C. 1985, Inorg. Chim. Acta, 108, 11.
39. Guha, S. and Saha, N. N. 1970, Acta Crystallogr., B26, 2073.
40. Cuevas, A., Viera, I., Torre, M. H., Kremer, E., Etcheverry, S. B. and Baran, E. J. 1998, Acta Farm. Bonaerense, 17, 213.
41. Steren, C. A., Calvo, R., Castellano, E. E., Fabiane, M. S. and Piro, O. E. 1990, Physica B, 164, 323.
42. Bezkorovainy, A. and Rafelson Jr., M. E. 1996, Concise Biochemistry, Marcel Dekker, New York.
43. Parker, F. S. 1971, Applications of Infrared Spectroscopy in Biochemistry, Biology, and Medicine, Adam Hilger, London.
44. Cuevas, A., Viera, I., Torre, M. H., Kremer, E., Etcheverry, S. B. and Baran, E. J. 1999, Afinidad, 56, 263.
45. Baran, E. J., Wagner, C. C., Torre, M. H., Kremer, E. and Kögerler, P. 2000, Acta Farm. Bonaerense, 19, 231.
46. Wagner, C. C. and Baran, E. J. 2002, Acta Farm. Bonaerense, 21, 287.
47. Baran, E. J., Viera, I. and Torre, M. H. 2007, Spectrochim. Acta, 66A, 114.
48. Wagner, C. C., Torre, M. H. and Baran, E. J. 2008, Latin Amer. J. Pharm., 27, 197.
49. Baran, E. J. and Torre, M. H. 2009, Latin Amer. J. Pharm., 28, 789.
50. Baran, E. J., González-Baró, A. C. and Torre, M. H. 2011, Latin Amer. J. Pharm., 30, 1862.
51. Parajón-Costa, B. S. and Baran, E. J. 2012, Spectrochim. Acta, 98A, 252.
52. Wagner, C. C. and Baran, E. J. 2009, Spectrochim. Acta, 72A, 936.

53. Dokken, M. K., Parsons, J. G., McClure, J. and Gardea-Torresdey, J. L. 2009, Inorg. Chim. Acta, 362, 395.
54. Balakrishnan, D. and Ramamurthy, K. 2009, Spectrochim. Acta, 72A, 269.
55. Senthil, S., Pari, S., Joseph, G. P., Sagayaraj, P. and Madhavan, J. 2009, Physica B, 404, 2336.
56. Ishioka, T., Shibata, Y., Takahashi, M., Kanesaka, I., Kitagawa, Y. and Nakamura, K. T. 1998, Spectrochim. Acta, 54A, 1827.
57. Facchin, G., Torre, M. H., Kremer, E., Piro, O. E., Castellano, E. E. and Baran, E. J. 2000, Z. Naturforsch., 55b, 1157.
58. Facchin, G., Torre, M. H., Kremer, E., Piro, O. E., Castellano, E. E. and Baran, E. J. 2002, J. Inorg. Biochem., 89, 174.
59. Facchin, G., Kremer, E., Baran, E. J., Castellano, E. E., Piro, O. E., Ellena, J., Costa-Filho, A. J. and Torre, M. H. 2006, Polyhedron, 25, 2597.