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Investigations of different carbohydrate anomers in copper(II) complexes with D-glucose, D-fructose, and D-galactose by Raman and EPR spectroscopy

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Abstract—With the aim of verifying different carbohydrate anomers coordinated to copper(II) ions, some copper(II) complexes with D-glucose (Glc), D-fructose (Fru), and D-galactose (Gal) were prepared and investigated by spectroscopic techniques. Their compositions were verified by elemental, ICP–AES and thermal analyses, in addition to conductivity measurements. The compounds isolated were consistent with the formula $Na_2[Cu_2(carbohydrate)_3]\cdot 8H_2O$ and $Na[Cu_2(carbohydrate)_3]\cdot 6H_2O$ for the aldoses Glc and Gal, respectively, and $Na_2[Cu_3(carbohydrate)_4]\cdot 8H_2O$ in the case of the ketose, Fru. EPR spectra of these solids showed a rhombic environment around the metal center and suggested the presence of different anomers of the carbohydrates in each case. By Raman spectroscopy, it was possible to verify the predominance of the β anomer of D-glucose in the corresponding copper complex, while in the free ligand the α anomer is predominant. In the case of the analogous complex with D-galactose, the spectrum of the complex shows bands of both anomers (α and β) in approximately the same relative intensities as those observed in the isolated free ligand spectrum. On the other hand, for the complex with D-fructose a mixture of both furanose (five-membered ring) and pyranose (six-membered ring) structures was detected with prevalence of the furanose structure. Based on variations in the relative intensities of characteristic Raman bands, the binding site for copper in the fructose ligand was identified as most likely the 1-CH_2OH and the anomeric 1-OH, while in β-D-glucose it is presumably the anomeric 1-OH and the O-5 atom. These results indicated that EPR and Raman spectroscopy are suitable supporting techniques for the characterization of carbohydrate anomers coordinated to paramagnetic ions.

Keywords: Copper(II); Carbohydrates; EPR; Raman spectroscopy

1. Introduction

Transition metal ions are found in living organisms properly coordinated to different biomolecules, participating in many biochemical reactions where they play a crucial role. Although carbohydrates exhibit relatively poor coordinating properties in comparison to other biological ligands, and usually form weak complexes, interactions between metal ions and polyalcohols, nucleosides, nucleotides, and other sugar-type ligands are supposed to be involved in many biochemical processes in living organisms, including recognition processes, immunological events, and pathological conditions.[1] The abundance of electronegative functional groups and a well-defined stereochemistry make saccharides potentially interesting ligands for the binding of metal ions in natural systems, and the understanding of such interactions remains one of the main challenges of carbohydrate chemistry.[1,2] Further, the interest in metal–carbohydrate complexes is by no means restricted to the biological area. Carbohydrates are recognized as enantiomeric compounds that can be

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invaluable synthons for new synthetic methods. They are useful reagents, not only in the separation and analysis of chiral compounds, but also for suitable conversions in stoichiometric or catalytic stereoselective syntheses.[2] Low-molecular-weight carbohydrates, as well as sugar alcohols, diols, triols, and polysaccharides are versatile building blocks for the systematic synthesis of more complex structures, such as fibers, gels, membranes, mono- and multilayers, metal-containing polymers, and supramolecular assemblies where saccharides usually act as polyolato ligands by deprotonation of one or more hydroxyl groups.[3] The binding of metal ions to carbohydrates and related compounds has been mainly studied with the aim of clarifying the coordination mode of the metal center with the hydroxyl groups in the sugar moiety.[4–6] A particular reason for these studies is that the quantitative characterization of metal-ion coordination equilibria of polyalcohols and other sugar-type ligands, containing only oxygen donor atoms, is very difficult, due to the usually low stability of the formed complexes in neutral or acidic aqueous solution.[1] Also, the complex stability constants determined by usual techniques are in fact overall values concerning the association of diverse forms of the ligands.

In solution, simple reducing sugars exist as different anomeric and conformational species in equilibrium (see Fig. 1), and these isomers can interact in different ways with metal centers. Therefore, it is a difficult task to assign the kind of isomer species present in a particular metal complex. Different spectroscopic and structural methods have been used with the purpose of differentiating anomers.[4–11] However, studies of carbohydrate–metal complexes based on Raman spectroscopy are rare. This technique has been successfully performed to elucidate the effect of different cations on the anomeric equilibria of simple sugars such as D-glucose.[12] More recently, low-frequency FT Raman spectra helped with the elucidation and systematization of weak intermolecular interactions in carbohydrates and proteins.[13] Nevertheless, there are still few applications of this technique for discerning the different isomers of coordinated ligands in a transition metal–carbohydrate complex.[10]

Our particular interest in the binding of a copper ion to a sugar moiety is owing to the fact that common pentose and hexose oxidations are implicated in many diseases, such as diabetes mellitus and aging in general, which facilitate protein glycosidation (glycation),[14] where different reactive intermediates can cause severe injury. Particularly, copper(II) ions were verified to markedly increase the rate of those oxidative processes.[15,16] However, the structure of the binding site in the intermediate Cu(II)–carbohydrate in these oxidations is not yet well understood.

The major goal of this work is to use EPR and particularly Raman spectroscopy as the main tools to verify the conformation of this type of ligand around the copper

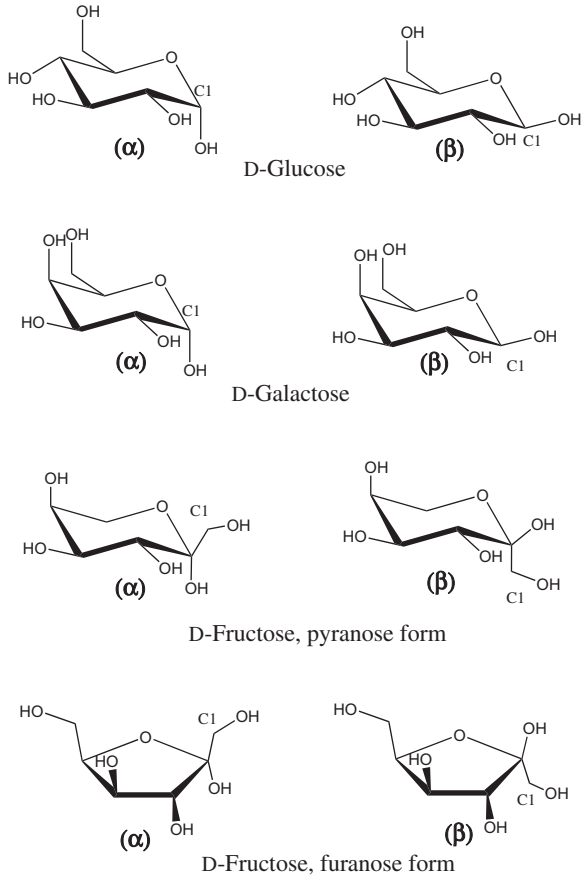

Figure 1. Anomeric forms of the carbohydrates as α and β pyranose (in the $^4C_1$ conformation chair) for D-glucose and D-galactose, and α and β pyranose and furanose, for D-fructose.

ion, elucidating what kind of carbohydrate structure (α or β anomer, as in Fig. 1) is preferentially bound to the copper(II) center, and to look for spectroscopic evidence that the binding site of the carbohydrate moiety to copper(II) ion is the anomeric carbon (C-1). Therefore, some copper(II) complexes were prepared from sodium salts of the most common carbohydrates, D-glucose, D-fructose, and D-galactose, and investigated in the solid state. Additional characterization was provided by elemental, ICP–AES, and thermogravimetric analyses, conductivity measurements, and IR and UV–vis spectroscopy.

2. Experimental

2.1. Materials and methods

D-(+)-Glucose (99%) and D-(−)-fructose (99%) were obtained from E. Merck, and D-(+)-galactose (99%) from Sigma Chemical Co. $Cu(ClO_4)_2{\cdot}6H_2O$ was purchased from Aldrich Chemical Co. Deionized water from a Milli-Q (Millipore, Bedford, MA, USA) or a Barnstead D 4700 apparatus was used in the preparation of all solutions. Elemental analyses were performed

at the Central Analítica of our Institution, using a Perkin–Elmer 2400 CHN Elemental Analyser. Copper analyses were performed on a SPECTRO ICP–AES (Induced Coupled Plasma) instrument. Samples were treated with concentrated nitric acid (PA), followed by addition of 30% H_2O_2 (5 mL each) and heating for 1 h (80–90 °C). A comparative pattern of copper(II) ions (1.000 mg g^{-1}) was used, from TecLab (Indaiatuba, SP), with SRM 3114-NIST (USA). Sodium analyses were performed on a SPECTRO FLAME Modular ICP–AES (Induced Coupled Plasma) instrument. A comparative pattern of sodium was used (1000 ppm) in 0.1% in nitric acid. Infrared spectra of the complexes obtained were recorded on a BOMEM 3.0 instrument using KBr pellets in the range of 4000–400 cm^{-1}. Electronic spectra were determined on a UV-1650PC Shimadzu instrument, with a thermostated cell compartment. Conductivity experiments with the complexes studied (in 1 mmol dm^{-3} aqueous solution) were carried out on a Digimed DM-31 instrument, using a 10.0 mmol dm^{-3} KCl solution as standard (specific conductivity = 1412.0 μS cm^{-1} for aqueous solution or 0.141 μS cm^{-1} for organic solutions, both at 298 K).[17] Thermogravimetric analyses were performed on a TGA-50 Shimadzu instrument with synthetic air in a 50 mL/min flow. EPR spectra were recorded with a Bruker EMX instrument, operating at X-band frequency ($\nu = 9.250$ GHz), using standard Wilmad quartz tubes. DPPH (α,α′-diphenyl-β-picrylhydrazyl) was used as frequency calibrant ($g = 2.0036$) with samples in the solid state, at 77 K. Usual conditions used in these measurements were 2.00×10^4 gain, and 12–15G modulation amplitude. Raman spectra were recorded on a Renishaw spectrometer, model System 3000, with an Olympus BTH-2 microscope, using a 50× objective lens and a Charge Coupled Device (CCD) Detector, with spectral resolution of 2 cm^{-1}. The exciting radiation used was the 632.8 nm line of a Spectra Physics He–Ne laser, model 127, and the laser power was 5 mW.

2.2. Syntheses of the copper(II)–carbohydrate complexes

A general procedure was used to prepare the copper(II) complexes with D-(+)-glucose (Glc), D-(−)-fructose (Fru) and D-(+)-galactose (Gal), similar to that described in the literature, where sodium salts of the sugar ligands were prepared in situ.[7,18]

2.2.1. $Na_2[Cu_2(Glc)_3]\cdot 8H_2O$ (1). To a solution of D-glucose (0.721 g, 4 mmol) in 10 mL of MeOH at 0 °C was added freshly cut sodium (0.184 g, 8 mmol), and the reaction mixture was stirred for 30 min at room temperature. To this in situ generated disodium salt of D-glucose a solution of copper(II) perchlorate, $[Cu\text{-}(H_2O)_6](ClO_4)_2$ (0.740 g, 2 mmol), in 10 mL of MeOH was added dropwise. Immediately, a pale-blue precipitate was formed, and the reaction mixture was stirred at room temperature for 12 h. The final precipitate formed was isolated by filtration and purified by dissolution in hot MeOH, followed by a second precipitation (repeated twice). The final complex obtained was dried under reduced pressure for 9 h to give a blue-green solid, isolated in 40% yield (0.678 g).

Data for **1**: TGA (in air): 16.59% at 137.8 °C. Calcd for the loss of $8H_2O$: 16.86%. $\Lambda_M = 219$ S cm^2 mol^{-1} in water and 59 S cm^2 mol^{-1} in MeOH (both at 298 K). FTIR (cm^{-1}, KBr): 3316 (s, OH); 2920–2878 (s, $C_{sp3}H$); 1030 (m, C–O and C–C). UV–vis (H_2O): 239 nm ($\varepsilon = 3.62 \times 10^3$ M^{-1} cm^{-1}, ILT n→σ or n→σ*), 664 nm ($\varepsilon = 56.3$ M^{-1} cm^{-1}, d→d). Anal. Calcd for $Na_2[Cu_2(Glc)_3]\cdot 8H_2O$: C, 25.30; H, 5.66; Cu, 14.88; Na, 5.38. Found: C, 25.09; H, 5.77; Cu, 15.07; Na, 5.11.

2.2.2. $Na_2[Cu_3(Fru)_4]\cdot 8H_2O$ (2) and $Na[Cu_2(Gal)_3]\cdot 6H_2O$ (3). Complexes **2** and **3** were prepared analogously using the same procedure given for **1**. In the case of complex **2**, a blue solid was isolated in 57% yield (0.665 g), while for **3** a pale-green solid was obtained in 35% yield (0.370 g).

Data for **2**: TGA (air): 13.37% at 138 °C. Calcd for the loss of $8H_2O$: 13.16%. $\Lambda_M = 200.8$ S cm^2 mol^{-1} in water, and 49.8 S cm^2 mol^{-1} in MeOH (both at 298 K). FTIR (cm^{-1}, KBr): 33–64 (s, OH); 2922–2883 (s, $C_{sp3}H$); 1067 (m, C–O and C–C). UV–vis (H_2O): 245 nm ($\varepsilon = 3.64 \times 10^3$ M^{-1} cm^{-1}, ILT n→σ or n→σ*), 672 nm ($\varepsilon = 61.2$ M^{-1} cm^{-1}, d→d). Anal. Calcd for $Na_2[Cu_3(Fru)_4]\cdot 8H_2O$: C, 26.31; H, 5.34; Cu, 17.41; Na, 4.18. Found: C, 26.06; H, 5.53; Cu, 18.07; Na, 3.96.

Data for **3**: TGA (air): 13.41% at 137.8 °C. Calcd for $6H_2O$: 13.59%. $\Lambda_M = 108$ S cm^2 mol^{-1} in water, and 28 S cm^2 mol^{-1} in MeOH (both 298 K). FTIR (cm^{-1}, KBr): 3388 (s, OH); 2938–2878 (s, $C_{sp3}H$); 1065 (m, C–O and C–C). UV–vis: in water solution: 240 nm ($\varepsilon = 3.05 \times 10^3$ M^{-1} cm^{-1}, LT n→σ or n→σ*), 664 nm ($\varepsilon = 78.6$ M^{-1} cm^{-1}, d→d). Data for **3**: TGA (air): 13.41% at 138 °C. Calcd for $6H_2O$: 13.59%. $\Lambda_M =$ 108 S cm^2 mol^{-1} in water, and 28 S cm^2 mol^{-1} in MeOH (both 298 K). FTIR (cm^{-1}, KBr): 3388 (s, OH); 2938–2878 (s, $C_{sp3}H$); 1065 (m, C–O and C–C). UV–vis: in water solution: 240 nm ($\varepsilon = 3.05 \times 10^3$ M^{-1} cm^{-1}, LT n→σ or n→σ*), 664 nm ($\varepsilon = 78.6$ M^{-1} cm^{-1}, d→d). Anal. Calcd for $Na[Cu_2(Gal)_3]\cdot 6H_2O$: C, 27.16; H, 5.68; Cu, 17.05; Na, 2.89. Found: C, 26.90; H, 5.48; Cu, 16.83; Na, 2.97.

3. Results and discussion

3.1. Stoichiometry of the complexes

The results obtained by elemental, ICP–AES and thermal analyses of the complexes are shown in Section 2.

The stoichiometry of these complexes corresponded to three moieties of the carbohydrate ligand coordinated to two copper(II) centers, in the case of the hexoses D-glucose and D-galactose, or four carbohydrate molecules linked to three copper(II) centers for the pentose D-fructose, with several additional coordinated water molecules.

Results from thermogravimetric measurements complement these data, indicating the release of eight water molecules at 138 °C for complexes **1** and **2**, and six water molecules at the same temperature for compound **3**. Copper oxide was verified as final residues on TGA for all the compounds, with total loss of the ligand moiety as CO_2 and water.

Therefore, the minimum formula for these isolated complexes can be defined as $Na_2[Cu_2(Glc)_3]\cdot 8H_2O$ (**1**), $Na_2[Cu_3(Fru)_4]\cdot 8H_2O$ (**2**) and $Na[Cu_2(Gal)_3]\cdot 6H_2O$ (**3**), respectively. They were shown to be highly soluble in water, but insoluble in common organic solvents.

Literature reports of similar species with copper(II) ions include monomeric complexes, mixed with N-donor ligands,[19] dimeric,[20] and polymeric structures,[21] which were always a mixture of different binding modes around the metal center when only carbohydrates were used as ligands. Bandwar et al.[4] have prepared similar complexes, and found that Cu(II)–saccharide complexes, after purification to eliminate some amounts of $Cu(OH)_2$ and sodium salts as byproducts, are mono- ($Na_2[Cu(Mal)Cl_2]$), di- ($Na[Cu_2(Glc)_2Cl_3]$) or trinuclear ($Na[Cu_3(Fru)_2(OH)Cl_4]\cdot CH_3OH$ or $Na[Cu_3(Gal)_2Cl_3]\cdot CH_3OH$) complexes. They also obtained oligomeric species, as $Na[Cu_8(Glc)_4Cl_7Br_2]\cdot 5CH_3OH$, where the proposed formulas were shown, but not the structures. This work suggests that there is an initial formation of higher oligomers in the reaction; however, when $CuCl_2\cdot 2H_2O$ was used, mono-, di-, or trinuclear complexes could be formed. In all these complexes, the carbohydrates are coordinated to Cu(II) usually through deprotonated and free hydroxyl groups, in a polymeric structure, where not only one copper ion binds each carbohydrate ligand moiety.

The conductivity measurements of our studied complexes in deionized water or MeOH at 298 K as indicated in experimental section, were consistent with a 1:2 electrolyte, for both compounds **1** and **2**, and a 1:1 electrolyte for compound **3**,[17] corroborating the previous results by elemental analyses, in relation to the charge or ionized hydroxyl groups in the complexes, prepared as sodium salts of the carbohydrates.

However, the formation of suitable crystals for structural determination was not achieved. Aqueous solutions of these complexes exhibited spectral modifications with time, after a few days. Also, as already demonstrated,[4] this type of complex is not very stable in solution, especially in the pH range below pH 5.0.

3.2. IR and UV–vis spectroscopic data

The IR spectra of the copper complexes $Na_2[Cu_2(Glc)_3]\cdot 8H_2O$ (**1**), $Na_2[Cu_3(Fru)_4]\cdot 8H_2O$ (**2**), and $Na[Cu_2(Gal)_3]\cdot 6H_2O$ (**3**), showed the expected characteristic bands of hydroxylated compounds, as indicated in Section 2. A characteristic broad band in the ν(O–H) range was observed, indicating the presence of water molecules. The bands around 2940–2880 cm^{-1} for all the studied species were attributed to $\nu(C_{sp3}–H)$, while the corresponding bending was verified around 1370 cm^{-1}, indicating a shift from the original range around 1460–1340 cm^{-1} in the free carbohydrates. The band observed around 1640–1610 cm^{-1} can be assigned to bound water molecules, as already described for other compounds.[7a] The C–C and C–O stretching vibrations in the region 1140–990 cm^{-1} were also merged at 1050 cm^{-1} in the complexes.

It was not possible to verify without doubts, the anomeric region in the IR spectra (600–900 cm^{-1}),[4] since the spectra of the sodium salts of the complexes showed extensive rearrangement on their hydrogen-bonding network due to ionization of the monosaccharides, which were characterized by the presence of broad and merged bands in all cases. Therefore, Raman spectroscopy was used to better verify these anomeric effects.

Electronic spectra of **1**, **2**, and **3** were carried out in aqueous solution and showed characteristic bands expected for this type of copper(II) complex.[22] The corresponding maximum wavelengths observed at 239 nm ($\varepsilon = 3.62\times10^3$ mol^{-1} dm^3 cm^{-1}) for **1**, 245 nm ($\varepsilon = 3.64\times10^3$ mol^{-1} dm^3 cm^{-1}) for **2**, and 240 nm ($\varepsilon = 3.05\times10^3$ mol^{-1} dm^3 cm^{-1}) for **3**, can be assigned to the internal ligand transitions (ILT, n→σ or n→σ*), expected to be very similar in all cases. No other bands were detected in these spectra; therefore, LMCT transitions are possibly hidden by the very intense ILT bands. The characteristic d–d band for **1** appears at 664 nm ($\varepsilon = 56$ mol^{-1} dm^3 cm^{-1}), at 672 nm ($\varepsilon = 61$ mol^{-1} dm^3 cm^{-1}) for **2**, and at 664 nm ($\varepsilon = 79$ mol^{-1} dm^3 cm^{-1}) for **3**.

3.3. EPR data

EPR spectra of complexes **1**, **2**, and **3** as solid samples at 77 K showed a characteristic profile of a rhombic environment around the copper(II) centers, with the presence of different parameters, g_{xx}, g_{yy}, and g_{zz}, and the corresponding hyperfine constants, A_{xx}, A_{yy}, and A_{zz}, as expected for a rhombic paramagnet with $S = 1/2$ and $I = 3/2$, at $\nu = 9.250$ GHz[23] (as shown in Table 1 and Fig. 2).[24]

In the case of compound **3**, evidence of the presence of two different copper centers was observed, as indicated by the split of g_{zz} and A_{zz}, provided by the diverse anomers in almost equal proportion. The corresponding

Table 1. EPR parameters, in solid state and at 77 K, for the carbohydrate–copper(II) complexes prepared

Complex	g_{zz}	A_{zz} (G)	g_{xx}	A_{xx} (G)	g_{yy}	A_{yy} (G)
$Na_2[Cu_2(Glc)_3]\cdot 8H_2O$ (**1**)	2.252	190	2.070	26.1	2.022	23.7
$Na_2[Cu_3(Fru)_4]\cdot 8H_2O$ (**2**)	2.261 2.259[a]	189 194[a]	2.062	26.1	2.025	21.7
$Na[Cu_2(Gal)_3]\cdot 6H_2O$ (**3**)	2.252 2.293	189 161	2.065	23.5	2.018	19.6

[a] In lower proportion (see details in Fig. 2).

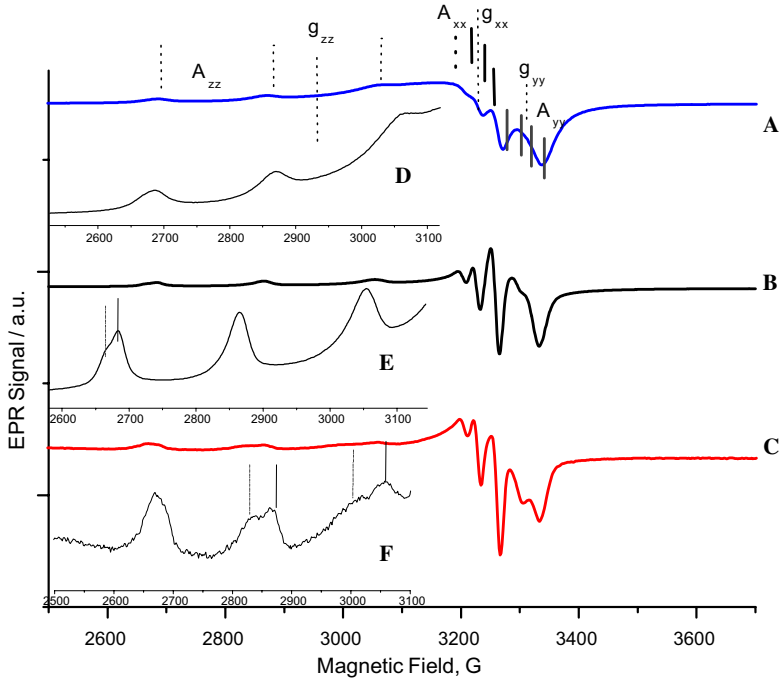

Figure 2. EPR spectra of the copper complexes studied, in the solid state, at 77 K. (A) $Na_2[Cu_2(Glc)_3]\cdot 8H_2O$ (**1**); (B) $Na_2[Cu_3(Fru)_4]\cdot 8H_2O$ (**2**); (C) $Na[Cu_2(Gal)_3]\cdot 6H_2O$ (**3**); with respective inserts (D), (E), and (F).

parameters are significantly different: $g_{zz} = 2.252$ and 2.293, and $A_{zz} = 189$ and 161, respectively. Splitting in the g_{xx} and g_{yy} region was not noticed. On the contrary, in the case of **2**, there is clearly a major species, although the spectroscopic parameters of both species are not very different ($A_{zz} = 189$ and 194, respectively). However, for compound **1**, the spectrum is more consistent with the presence of only one species. The rhombic surroundings around the copper(II) ion is not usual, but consistent in this case. If there are three moieties of carbohydrates around the metal ions enabling this type of environment, the spectra are completely different from that of copper(II) complexes exhibiting an axial environment. The relative positions of the signal is suggestive of a d_{z2} ground state, with short Cu–L bonds in the *xy*-plane and two trans longer ones in the *z*-axis. The small difference observed between g_{xx} and g_{yy} values indicates only a marginal difference observed along the *x*- and *y*-directions. However, for all these complexes, $\Delta M_S = 2$ transitions, which are characteristic of a dimeric intermolecular copper center association in the solid state due to triplet state splitting, were not observed. Analogous results were described in the literature for other carbohydrate–copper compounds, also with a rhombic environment around the metal ion.[4] In this case ternary complexes were obtained, exhibiting also coordinated chloride ions. However, the observed EPR parameters for the species $Na[Cu_2(Glc)_3Cl_3]$, $Na[Cu_3(Fru)_2(OH)Cl_4]$, $Na[Cu_3(Fru)_2Cl_3]$, and $Na[Cu_3(Gal)_2Cl_3]\cdot CH_3OH$ were quite similar to our values, with g_1 in the range 2.26–2.29, g_2 around 2.07 and g_3 between 2.00 and 2.03.[4]

3.4. Raman spectroscopy results

Figure 3 shows the Raman spectra of D-glucose and the corresponding Cu(II)–glucose complex **1**. The presence

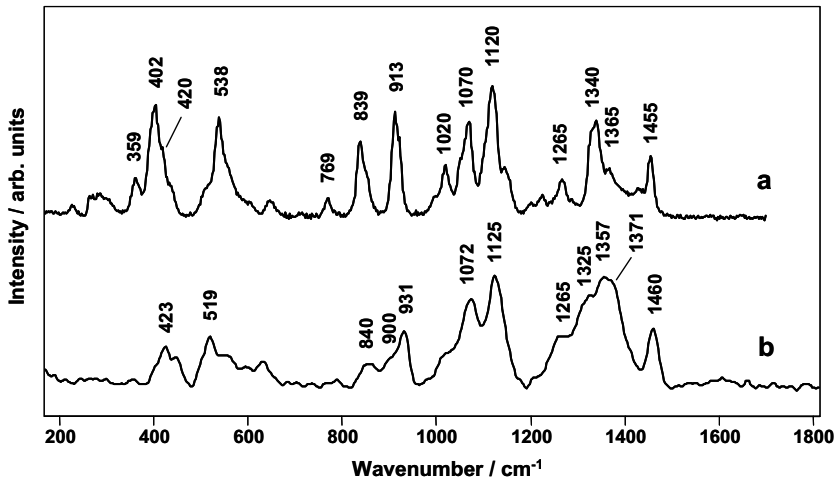

Figure 3. Raman spectra of D-glucose (a) and the corresponding Cu(II)–glucose complex (**1**) (b), both in solid state.

of the characteristic bands of the α anomer 402, 538, 769, 839, 913, 1340, and 1365 cm^{-1} and those of β anomer at 420 (sh), 1070, and 1120 cm^{-1}[1,12,25] indicates that the free ligand, in the solid state, is a mixture of anomers with predominance of the α configuration, as indicated by their relative intensities. However, in the spectrum of complex **1**, the increase in the relative intensities of the β-anomeric bands at 423, 448, 519, 900 (sh), 931, 1072, 1125, 1325, 1357, and 1375 cm^{-1} points to the β anomer as the preferential configuration of the coordinated ligands. This result, allied to the observation of a single type of copper center in the EPR spectrum for compound $Na_2[Cu_2(Glc)_3]\cdot 8H_2O$ (**1**), can indicate that the observed rhombic environment is provided by the same β anomer in diverse coordination modes.

The Raman spectra for D-fructose and the corresponding Cu(II) complex **2** are presented in Figure 4. In the spectrum of free D-fructose, the bands at 464, 871, 922, and 1173 cm^{-1} assigned to the furanose isomer, and the bands at 421, 523, 815, 976, and 1140 cm^{-1} relative to the pyranose,[26] indicate that both isomers are present in the solid ligand. In the Raman spectra of complex **2**, the increase in the relative intensities of the bands at 458, 712, 872, and 931 cm^{-1} due to the furanose isomer, with a concomitant decrease in the relative intensities of bands at 421, 523, 832, and 968 cm^{-1}, which are characteristic bands of pyranose species, suggests that the ligand preferentially shows the furanose structure in the complex. It is important to notice that Etcheverry et al. observed a similar behavior in the fructose oxovanadium(IV) complex.[18] These results are also in agreement with the EPR data, where the presence of one predominant structure around the copper(II) ion was observed, as in the case of compound $Na_2[Cu_3(Fru)_4]\cdot 8H_2O$ (**2**).

The Raman spectra of the D-galactose and the analogous Cu(II)–galactose complex **3** are shown in Figure 5. In this case the two spectra are very similar, with small variations in the relative intensities of the bands, and we can conclude that the proportion of the anomers in the

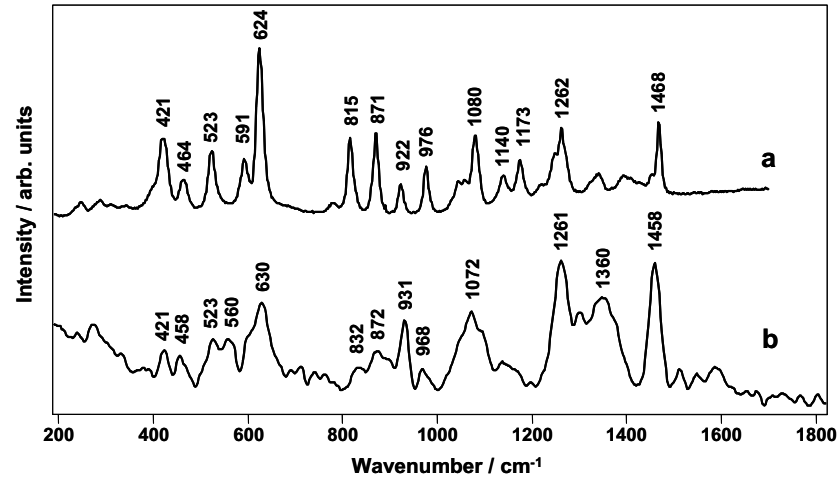

Figure 4. Raman spectra of D-fructose (a) and the corresponding Cu(II)–fructose complex (**2**) (b), both in solid state.

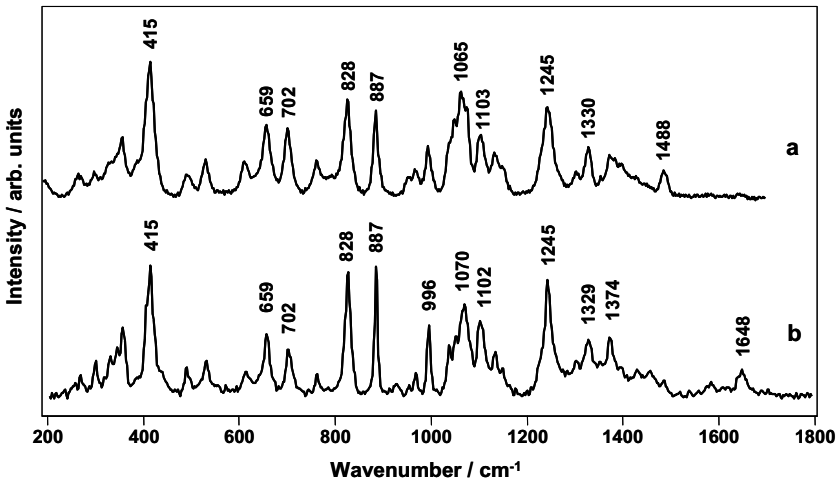

Figure 5. Raman spectra of D-galactose (a) and the corresponding Cu(II)–galactose complex (**3**) (b), both in solid state.

solid free ligand is approximately the same as in the complex, without any preferential coordination of one specific anomer to the copper(II) ions. These results reinforced the EPR data for this complex, indicating a mixture of two types of environment around the copper(II) ion. This could be assigned to different binding sites in the β anomer, or to coordination of copper to both anomers of galactose. Since the proportion of anomers in the free ligand and in complex **3** was verified to be the same, the stability of coordination sites in both anomers seems to be equivalent. Recently, possible ways of D-galacturonic acid (GalA) coordination to copper(II) ions were proposed, based on vibrational data. In this case, α and β anomers are present in the complex with a metal/ligand ratio of 1:2, but both anomers are coordinated only by carboxylate groups.[27]

Some additional information can be inferred from the Raman data. Changes in the relative intensities of the Raman bands corresponding to coordinating sites in the ligand are expected as a result of variations in its electronic density by the metal coordination. Taking this into account, in the Raman spectrum of the D-fructose copper(II) complex the increase in the relative intensities of the bands assigned to the ring-external moiety at 630 and 1072 cm^{-1} (attributed to C–C–O bending and C–O stretching, respectively), and at 1261, 1360, and 1458 cm^{-1} (assigned to the CH_2 torsion, wagging and bending, respectively),[26] suggests that O-1 is one of the preferred coordination sites to copper(II). Using the same argument, in the Raman spectrum of the D-glucose complex the relative high intensities of the bands at 1072, 1125, 1357, and 1375 cm^{-1}, whose normal modes have predominant contributions from the C-1–O-5 and C-1–O-1 bonds,[25] suggest that these ligand sites are the prevalent coordination anchor for the copper(II) ions.

Finally, for all the compounds no characteristic bands were observed in the 1600–1800 cm^{-1} range, indicating that enolized species from tautomeric equilibria are absent, or present in undetectable amounts, in the isolated solid complexes.[28] For the copper–galactose complex the small band at 1648 cm^{-1} can also be attributed to coordinated water molecules.[7a]

4. Conclusions

The complexes studied, $Na_2[Cu_2(Glc)_3]\cdot 8H_2O$ (**1**), $Na_2[Cu_3(Fru)_4]\cdot 8H_2O$ (**2**) and $Na[Cu_2(Gal)_3]\cdot 6H_2O$ (**3**), showed a rhombic environment around the copper(II) ion in the solid state, as indicated by EPR spectroscopy, with a predominant species in the case of complexes **1** and **2**. However, for complex **3** two species in almost equivalent proportion were observed. By Raman spectroscopy it was possible to confirm these EPR data and further verify in what configuration (α or β anomer) and in what kind of isomeric form (furanose or pyranose) the carbohydrate ligands are present in these complexes. It was observed for complex **1** the predominance of the β anomer of D-glucose, suggesting that this is the preferential configuration of this ligand when coordinated to copper. For complex **2**, with D-fructose, despite being a mixture of both furanose and pyranose structures, the furanose form is prevalent. This can be indicative of a higher stability of copper coordination to this configuration. The copper binding sites in the fructose ligand can be suggested as the 1-CH_2OH and the anomeric 2-OH, while the coordination sites for copper in β-D-glucose is most probably the anomeric 1-OH and O-5 atom. For compound **3**, since two species in almost the same proportion were verified by EPR and Raman spectroscopy, both anomers of the D-galactose ligands provide sites of coordination to copper ions. For the β anomer, one of these binding sites is probably the same as in D-glucose, that is, the anomeric 1-OH and O-5 atom, as indicated by the very similar EPR parameters observed (see Table 1). Considering that the only differ-

ence between D-glucose and D-galactose is in the steric position of the hydroxyl group at C-4, the second possible binding site could be the 4-OH and 6-OH. Therefore, through Raman and EPR spectroscopy, it was possible to examine structural details and discriminate among some possibilities of anomer binding in copper–carbohydrate compounds.

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