Carbohydrate Research, 190 (1989) 29–37
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

D-GLUCOSE ADDUCTS WITH ZINC-GROUP METAL IONS. SYNTHESIS, AND SPECTROSCOPIC AND STRUCTURAL CHARACTERIZATION OF Zn(II), Cd(II), AND Hg(II) COMPLEXES WITH D-GLUCOSE, AND THE EFFECTS OF METAL-ION BINDING ON THE SUGAR ANOMERIC STRUCTURES

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(Received July 1st, 1988; accepted for publication in revised form November 15th, 1988)

ABSTRACT

The interaction of the zinc-group metal halide salts in solution with D-glucose has been investigated. Solid adducts of the type M(D-glucose)$X_2 \cdot nH_2O$, where M = Zn(II), Cd(II), or Hg(II); X = Cl^- or Br^-; and n = 4 or 2, were isolated and characterized by f.t.-i.r. and n.m.r. spectroscopy, and by molar conductivity measurements.

The Zn(II)- and Cd(II)–glucose adducts appear structurally similar, binding to one D-glucose molecule, possibly through the 1-OH and 2-OH groups as well as to four H_2O molecules, forming a six-coordinate metal cation. The Hg(II) ion may be bonded to two sugar molecules (unidentately) and to two H_2O molecules, resulting in a four-coordinate structure around mercury. The binding of Zn(II) and Cd(II) is via the α anomer of D-glucose. The possibility cannot be excluded that the Hg(II) ion binds to both the α and β anomers.

INTRODUCTION

Metal–sugar complexes[1] are of biological importance, and the metal–sugar interaction could have significant effect on the anomeric and conformational behavior of sugars. Simple reducing sugars have two or more tautomeric species at equilibrium in solution[2], and the equilibrium compositions are greatly perturbed by the presence of various metal cations[3,4]. Recently, the effects of alkali, alkaline earth, lanthanum, and several other metal cations on the anomeric composition of D-glucose (equilibrated in H_2O solution) have been studied by Raman spectroscopy[4]. It was shown that the Ca(II) and Sr(II) ions favorably complex with α-D-glucose, whereas the Cd(II), Mg(II), and K^+ ions showed little effect on the anomeric composition[4]. We have recently examined the effects of Ca(II) and Mg(II) on the anomeric structures of D-glucose, in solid complexes, by f.t.-i.r. spectroscopy[5].

The aim of this work is the synthesis and characterization of several Zn(II), Cd(II), and Hg(II) halides adducts with D-glucose, both in solution and the solid

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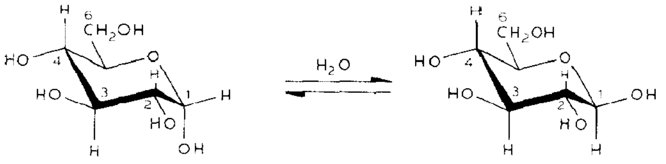
state, using f.t.-i.r., and ^{1}H-n.m.r. spectroscopy, and molar conductivity measurments. A comparison has been made between the spectroscopic properties of these metal–sugar complexes with those of the corresponding alkaline earth metal–glucose adducts, in order to determine characteristic features of each structural type of complex obtained for the zinc-group metal cations. The effects of this metal-ion binding on the anomeric structures of D-glucose (Scheme 1) are also discussed here.



α-D-glucopyranose β-D-glucopyranose

EXPERIMENTAL

Materials and methods. — Anhydrous D-glucose (dextrose) from Aldrich Chemical Company was used as supplied. The individual α- and β-D-glucose anomers were from Kodak and Sigma Chemical Co., and were used without further purification. D_2O (99.8%) and Me_2SO-d_6 (99.8%) were from Cambridge Isotopic Laboratories. Other chemicals were of reagent grade and used as supplied.

Preparation of zinc-group metal–D-glucose adducts. — A solution of D-glucose (1 mmol) in methanol (50 mL) was added to a solution of zinc halide (2 mmol) in methanol (50 mL) or to a solution of cadmium halide (2 mmol) in 1:1 water–methanol (75 mL) or to a solution of mercury halide (2 mmol) in 1:1 water–methanol (50 mL). The solution was heated until the solids were dissolved and was then kept at room temperature under slow evaporation. After one week, a white precipitate formed for the Cd halide– and Hg halide–D-glucose complexes. Acetone (100 mL) was used to precipitate the zinc halide–D-glucose adducts. The white precipitate was filtered off, washed several times with acetone, and dried over $CaCl_2$. Analysis showed the composition M(D-glucose)$X_2 \cdot nH_2O$; where M = Zn(II), Cd(II), or Hg(II); X = Cl^- or Br^-; and n = 4 for the Zn(II) or Cd(II) and 2 for the Hg(II)–D-glucose adducts (the zinc-group metal halide salts used were hydrated). These metal–sugar adducts were very hygroscopic (especially the zinc–D-glucose adducts) and need to be kept in a desiccator over $CaCl_2$; they are soluble in H_2O and methanol.

Physical measurements. — The i.r. spectra were recorded with a Nicolet 5DXB Fourier-Transform i.r. instrument equipped with a DTGS (deuterated triglycine sulfate) detector. The spectra were taken as KBr pellets with a resolution of 2–4 cm^{-1}. The solution spectra (film cast) were prepared by spreading an aqueous solution of D-glucose (10%) on an AgCl plate, followed by evaporation and respreading as needed to ensure uniform thickness. The ^{1}H-n.m.r. spectra were recorded with a Bruker WH-90 MHz instrument for D_2O and Me_2SO-d_6 solutions containing Me_4Si as the reference. Conductance measurements were performed at room temperature, for mM solutions, with a CDM2c type of conductivity meter (Radiometer, Copenhagen).

RESULTS AND DISCUSSION

F.t.-i.r. spectra. — The i.r. spectra of the zinc-group metal–D-glucose adducts, α- and β-D-glucose, and also the anomeric mixtures (in solution) were recorded in the region of 4000–500 cm^{-1} and a comparison was made with spectra of the corresponding alkaline earth metal–D-glucose compounds[5]. The results of these analyses are discussed next.

D-Glucose OH stretching vibrations and binding of zinc-group metal. — It should be noted that the OH stretching modes of the different hydroxyl groups of D-glucose may be coupled, and hence the frequencies appearing in the OH stretching region could not be assigned to individual hydrogen-bonded OH group[3]. However, the tentative assignments of the OH stretching vibrations of α-D-glucose used here and in the previous paper[5] are based on the intermolecular O···O distances of the H-bonding network, and the hydrogen-bonding energies and geometrical parameters reported in the literature[6–10]. There are five distinct intermolecular H-bonding systems in the crystal structure of α-D-glucopyranose[6]. Among them, 3-OH···O-2 and 6-OH···O-5 are strong H-bonds, 4-OH···O-4 and 2-OH···O-6 are less strong, and 1-OH···O-5 is of moderate energy[7]. The energies of these H-bonds are from 14.6 KJ mol^{-1} for 3-OH···O-2 and 9.4 KJ mol^{-1} for the 1-OH···O-5 sysem[7]. Therefore, the five strong and broad absorption bands observed in the i.r. spectrum of crystalline α-D-glucose are assigned to the following OH stretching frequencies (Fig. 1): 3-OH···O-2 (3404 cm^{-1}), 6-OH···O-3 (3342 cm^{-1}), 4-OH···O-4 (3310 cm^{-1}), 2-OH···O-6 (3266 cm^{-1}), and 1-OH···O-5 (3234 cm^{-1}. These assignments are consistent with the results of other workers[10].

The OH stretching vibrations of α-D-glucose showed major changes, with splitting and shifting towards lower frequencies, on interaction with zinc-group metal ions (Fig. 1). The spectral changes observed for the OH stretching vibrations of D-glucose are mainly related to the participation of the sugar hydroxyl groups in metal–ligand bonding. Similar patterns were observed in the spectra of the alkaline earth metal–D-glucose adducts, where metal–sugar bindings were suggested to be *via* the 1-OH and 2-OH groups[5].

Water coordination. — The presence of a strong and broad band at ~3245 cm^{-1} in the spectra of the zinc-group metal–D-glucose adducts, related to the water OH stretching, and a broad band of medium intensity at ~1640 cm^{-1}, due to the H_2O bending mode (absent in the spectrum of the free sugar), are attributed to the bonded H_2O molecule (Figs. 1 and 2).

C–H stretching vibrations of D-glucose. — On the basis of isotopic substitution, assignments of the i.r. and Raman C–H stretching vibrations for α- and β-D-

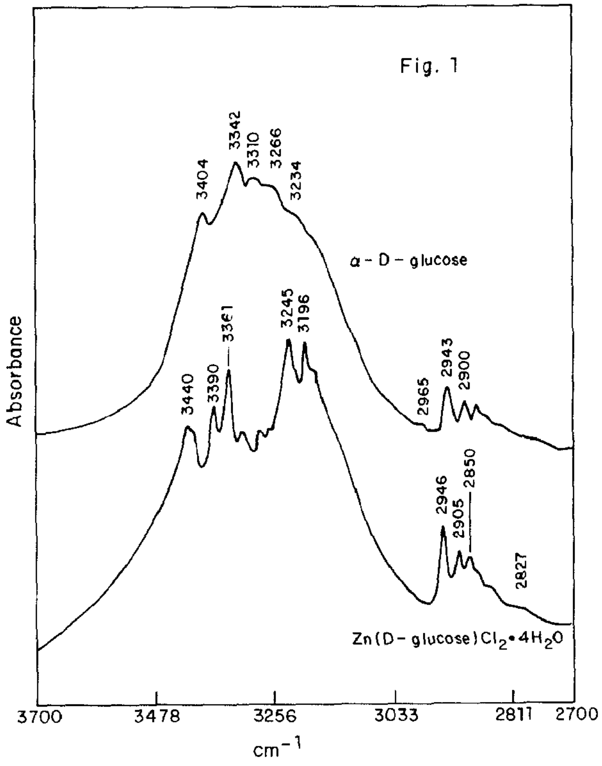


Fig. 1. F.t.-i.r. spectra of free α-D-glucose and its $ZnCl_2$ adduct in the 3700–2700 cm^{-1} region.

glucose have recently been reported[11]. The five i.r. bands observed in the region of 3000–2800 cm^{-1} in the spectrum of free α-D-glucose as studied here are assigned as follows: 2965 (4-C–H), 2943 (6-C–H), 2900 (3-C–H), 2850 (2-C–H), and 2825 cm^{-1} (5-C–H) stretching vibrations (Fig. 1). The C–H stretching vibrations of free α-D-glucose exhibited no major changes, on adduct formation (Fig. 1).

Pyranose ring vibrational frequencies of D*-glucose and metal-ion binding modes.* — The strongly coupled COH, CH_2, and CCH bending modes of α-D-glucose[12–14] appeared as several absorption bands of medium intensity in the region of 1450–1200 cm^{-1}, and exhibited major intensity changes and shifted towards higher frequencies in the spectra of the zinc-group metal–sugar complexes (Fig. 2). The changes observed for OH bending, together with those for the sugar OH stretching vibrations (3500–3200 cm^{-1}), are consistent with the participation of the OH groups of D-glucose in metal–sugar binding. The α-D-glucose C–O stretching vibrations[12–14] were observed as several strong and sharp absorption bands in the region of 1150–950 cm^{-1} and showed marked spectral changes (splitting and shifting towards higher frequencies), on adduct formation (Fig. 2). The observed changes for the ring C–O stretching vibrations evidently result from the metal–sugar binding via sugar OH groups.

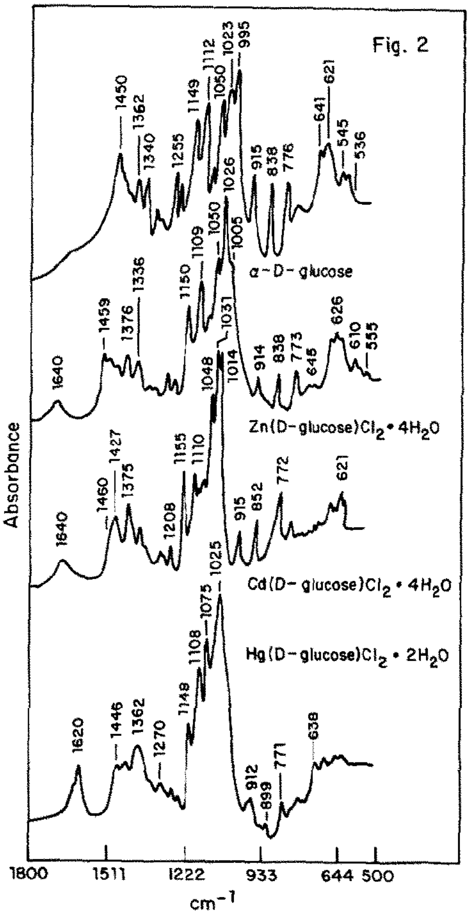


Fig. 2. F.t.-i.r. spectra of free α-D-glucose and its zinc-group metal halide adducts in the 1800–500 cm^{-1} region.

Interestingly, the i.r. spectra of the Hg–D-glucose adducts were substantially different from those of the Zn(II)– and Cd(II)–D-glucose adducts, both in the sugar OH stretching region and in the ring vibrational frequencies (Fig. 2). These marked spectral differences could be related to different binding modes of Hg(II) to the D-glucose molecule.

Anomeric structure of D-*glucose and zinc-group metal ion binding.* — The α- and β-D-glucose anomers and their equilibrium mixtures show different i.r. patterns (Fig. 3), mainly in the anomeric region (950–500 cm^{-1}), where the marker bands for each anomer is shown (Fig. 4). The marker bands for the α anomer are the three sharp bands at 915, 838, 776 cm^{-1} and a broad one at 621 cm^{-1}, which are not present in the spectrum of the β anomer (Fig. 4). The characteristic bands for the β anomer are at 912, 900, 860, 711, and 592 cm^{-1}, and these are absent in the spectrum of the α anomer (Fig. 4). The 2:3 α,β equilibrated mixture in aqueous

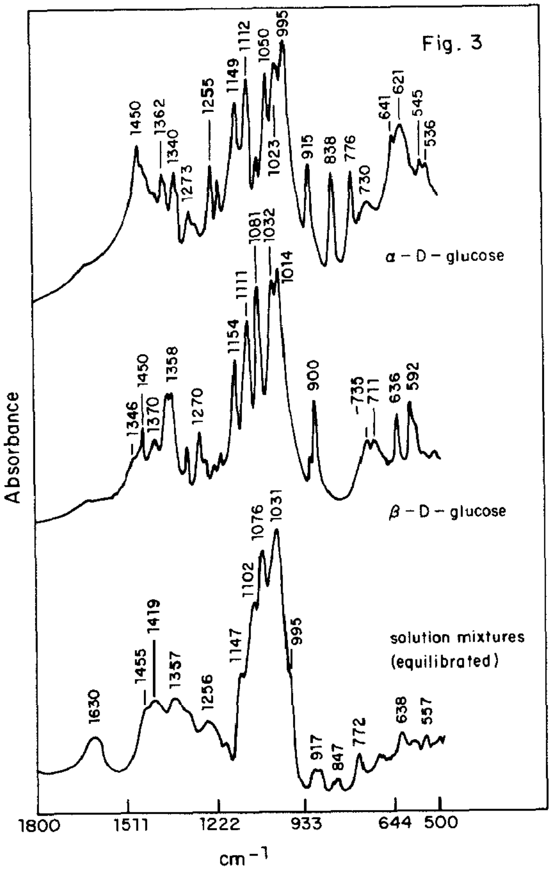


Fig. 3. F.t.-i.r. spectra of α- and β-D-glucose and their solution mixtures in the 1800–500 cm^{-1} region.

solution[15], shows several marker bands related to each anomer (Fig. 4). Comparing the i.r. spectra of the Zn(II)– and Cd(II)–D-glucose adducts with those of α- and β-D-glucose and of the equilibrated solution mixture , shows the presence of several bands (at about 915, 838, 779, and 627 cm^{-1} for zinc and at about 915, 850, and 771 cm^{-1} for cadmium) that are indicative of binding to the α anomer (Figs. 2 and 4). Similar patterns were observed in the spectra of the Mg(II)– and Ca(II)–D-glucose adducts, where bindings were favored to the α anomer[5]. Recent Raman spectroscopic studies in aqueous solution showed only a small effect by Zn(II), Cd(II), and Mg(II) ions on equilibrated D-glucose anomeric mixtures[4]. This may be true in aqueous solutions, where there is little interaction between free D-glucose and these metal cations[5] (see also the following n.m.r. discussion). On the other hand, the presence of several absorption bands (at about 912, 899, 870, 840, 772, 705, 629, and 593 cm^{-1}) in the spectra of the Hg–D-glucose adducts, which are related to both α and β anomers, are indicative of the presence of the β anomer as well as α anomer (Fig. 2). The presence of the β anomer in these mercury–glucose adducts

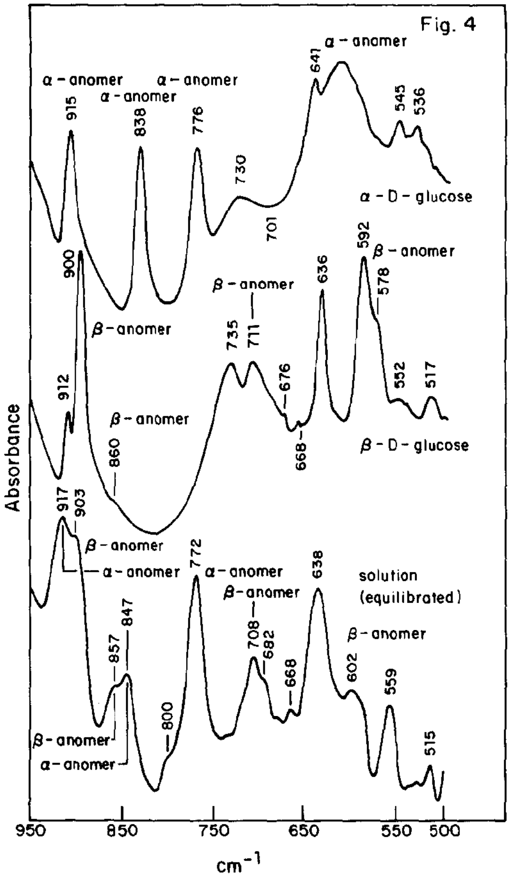


Fig. 4. F.t.-i.r. spectra of α- and β-D-glucose and their solution mixtures in the anomeric region (950–500 cm^{-1}.

might be attributable to impurities (co-precipitation of the β anomer with the α anomer) or binding of the mercury ion to both anomers. It should be noted that the i.r. spectra of the mercury–D-glucose adducts show some similarities to those of the solution mixtures (equilibrated) in the region of 1800–500 cm^{-1} (Figs. 2 and 3), but this similarity is not observed for the OH stretching region (3500–3200 cm^{-1}). Therefore, having markedly different OH stretching patterns for the Hg–D-glucose adducts, with respect to those of the OH stretching regions of the α and β anomers as well as their anomeric mixtures, suggests a direct Hg–sugar binding, but one rather different from that in the corresponding Zn(II)– or Cd(II)–glucose adducts. The different binding mode of the Hg–glucose compounds is evident from the dissimilarity of the spectra of the Hg–sugar compounds from those of the Zn(II)– or Cd(II)–D-glucose adducts (Fig. 2).

^{1}H-N.m.r. spectra. — The chemical shift of H-1 of α-D-glucopyranose is at 5.26 p.p.m. and at 4.68 p.p.m. for β-D-glucopyranose in D_2O solution[16], and is not

significantly changed by the present of salts of zinc-group metal ions. This reflects the absence of strong interaction between these metal cations and D-glucose in aqueous solution. The high molar conductivities observed for these metal–D-glucose adducts in aqueous solution are consistent with the absence of direct metal–sugar interaction in H_2O solution. Raman studies also showed no major effects of these metal cations on the anomeric D-glucoses in aqueous solution[4]. It should be noted that, in Me_2SO-d_6 solution, the β- and α-anomeric 1-OH chemical shifts of free D-glucose, observed at 6.57 and 6.20 p.p.m. respectively[15], show major downfield shifts upon addition of zinc and cadmium ions. The observed downfield shifts of the 1-OH resonance arises from strong metal–sugar interaction, possibly through the 1-OH group. Similar behavior has been observed in Me_2SO-d_6 solution for the ^{1}H-n.m.r. spectra of the alkaline earth metal–D-glucose adducts, where a possible metal–sugar binding *via* 1-OH and 2-OH was suggested[5]. It is worth mentioning that the ^{1}H-n.m.r. spectra of the Hg–glucose adducts are markedly different from those of the Zn(II) and Cd(II) complexes, again consistent with the i.r.-spectral behavior and indicates a different binding-mode for the Hg–D-glucose adducts.

SUMMARY CONCLUSIONS

On the basis of the spectroscopic and structural properties of the zinc-group metal–D-glucose adducts and free D-glucose, as well as its individual anomers, both in the solid state and in solution, the following points can be emphasized: (*1*) Although, there is no major interaction between D-glucose and the zinc-group metal ions in aqueous solution, such interaction is of great importance in the solid state and in non-aqueous solutions; (*2*) A possible mode for binding of D-glucose in the M(D-glucose)$X_2 \cdot 2H_2O$ adducts (M = zinc or cadmium ion and X = Cl^- or Br^-) could be through the sugar 1-OH and 2-OH group; (*3*) The mercury ion may be bonded to two D-glucose molecules (unidentately) through other OH groups of D-glucose than the 1-OH group; (*4*) The Zn(II)- and Cd(II)–D-glucose adducts are possibly isomorphous, but differ from those of the mercury–sugar compounds; (*5*) The binding of the Zn(II) and Cd(II) ion is through the α anomer of D-glucose, whereas the possibility that the Hg(II) ion binds to both α- and β-D-glucose cannot be excluded.

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