Carbohydrate Research, 237 (1992) 203–210
Elsevier Science Publishers B.V., Amsterdam

Soluble complexes of early first-row transition-metal ions with D-glucose

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(Received February 19th, 1991; accepted in revised form June 10th, 1992)

ABSTRACT

Glucose complexes of Ti^{4+}, V^{4+}, Cr^{3+}, and Mn^{2+} ions were synthesized by simple, reproducible procedures in nonaqueous media, isolated in the solid state, and characterized using several analytical and spectroscopic techniques. These are soluble both in water and in several polar organic solvents.

INTRODUCTION

Saccharides belong to an interesting class of chemical compounds that play important roles in various forms of living systems by being present as small integral parts of diverse biological molecules, including nucleic acids, polysaccharides, antibiotics, glycoproteins, glycolipids, and aminosugars. Saccharide molecules possess several functional hydroxyl groups that may play key roles in complexing with transition metal ions to produce variety of metal–saccharide complexes differing in their nature and utility.

While the chemistry and structure of saccharide complexes of alkali and alkaline earth metal ions were well studied and have been the subject of several reports in the literature, the corresponding transition metal–saccharide chemistry is largely unexplored[1-3]. However, there are some reports indicating the reactivity between amines of Co^{2+} and Ni^{2+} and saccharide molecules that give rise to *N*-glycosyl complexes[4,5]. Metal–saccharide complexes have been recently reviewed[6]. The lack of knowledge regarding homoleptic saccharide complexes seems to be due to the lack of synthetic methodologies available to make soluble, characterizable, and useful complexes while avoiding the formation of polymeric materials[7,8] and further due to the lack of crystal-clear demonstrations of such interactions in the solid state. In view of these aspects and also due to the involvement and

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importance of early transition elements in biology and catalysis, we have initially synthesized D-glucose complexes of Ti^{4+}, V^{4+}, Cr^{3+}, and Mn^{2+} ions, and thereby demonstrated the feasibility of the formation and isolation of characterizable low molecular weight complexes. Corresponding results are presented in this paper.

EXPERIMENTAL

Materials.—D-Glucose was purchased from Sigma Chemical Co., sodium metal was from E. Merck (Germany), and metal salts were purchased from local commercial sources. All the solvents were dried and distilled using established procedures immediately before use.

Methods.—Absorption spectra were measured on a Shimadzu UV-265 spectrophotometer. FTIR spectra were measured on a Varian Nicolet spectrometer in KBr. EPR spectra were recorded on a Varian ESR-112 spectrometer where tetracyanoethylene was used as a field marker ($g = 2.00277$). ^1H NMR spectra were recorded on a Varian XL-300 spectrometer.

Sodium salts of D-*glucose.*—All the glucose complexes reported in this paper were synthesized using either mono- or di-sodium salts of the ligand. A typical procedure for the preparation is as follows. The disodium salt of D-glucose was prepared by dissolving D-glucose (0.54 g, 3 mmol) and pieces of sodium (0.145 g, 6.3 mmol) in MeOH and stirring for 2 h. Similarly, the monosodium salt of D-glucose was prepared by mixing β-D-glucose (0.9 g, 5 mmol) and sodium (0.138 g, 6 mmol) and stirring for 2 h.

Titanium–D-*glucose complex.* All steps of the reaction were carried out in a glove box under a dry N_2 atmosphere. The disodium salt of β-D-glucose (2.02 g, 9 mmol) was separated as a solid by completely removing MeOH from the mixture in situ under vacuum. The resultant powder was suspended in 50 mL of MeCN. To this solution was added $(Et_4N)_2TiCl_4Br_2$ in 80 mL of MeCN with continuous stirring for 48 h. The latter was prepared by adding MeCN dropwise to $TiCl_4$ (0.3 mL, 3 mmol) to form $TiCl_4 \cdot 2MeCN$[9] and further reacting this with Et_4NBr (1.26 g, 6 mmol) in excess MeCN. The solution was filtered, the filtrate was concentrated, and ether was added in order to precipitate the product upon cooling the mixture in the refrigerator. An orange-red product was collected by filtration, washed several times with ether, and dried under N_2. Removal of all six equivalents of halide was confirmed from a gravimetric estimation of the residue as the silver halide. Several attempts to get an acceptable elemental analysis have been hampered by the presence of the tetraethylammonium salt, which could not be washed out by the usual procedure due to the high solubility of both the compound and the salt. In the case of other compounds the unreacted materials, as well as impurities, were removed through repetative washing as mentioned in the procedure for each compound.

Vanadium–D-*glucose complex.* A solution of $VOSO_4 \cdot 2H_2O$ (1.0 g, 5 mmol) in 50 mL of MeOH was added to 80 mL of a methanolic solution of the monosodium salt of β-D-glucose (11 mmol as generated in situ), with continuous stirring for ~ 1 day and gave rise to a green solution. The mixture was concentrated to give a green solid, filtered through a fritted glass funnel and washed thrice with cold EtOH and finally with ether before drying under vacuum. The final green product gave a yield of 1.02 g (59%) and corresponds to a molecular formula $Na[VO(D\text{-}Glc^{1-})(OMe)_2 \cdot H_2O]$, based on the elemental analysis. *Anal.* Calcd for $C_8H_{17}NaO_9V \cdot H_2O$: C, 27.52; H, 5.48; Na, 6.58; V, 14.59. Found: C, 27.58; H, 5.61; Na, 6.54; V, 14.33.

Chromium–D-glucose complex. The $CrCl_3(Thf)_3$ (0.937 g, 2.5 mmol) (prepared as per the literature procedure[10]) in 50 mL of MeOH was reacted with 8 mmol, of the disodium salt of D-glucose generated in situ in 100 mL of MeOH, and the mixture was refluxed for 48 h. The green solid obtained upon filtration was washed three times with hot MeOH, followed by an ether wash, and finally drying under vacuum. The presence of Cr(III) and absence of halide were confirmed through chemical tests. A yield of 0.57 g (44%) of pure material was obtained, and the molecular formula was shown by elemental analysis to be $Na_2[Cr(D\text{-}Glc^{2-})_2(OH)(H_2O)_3]$. *Anal.* Calcd for $C_{12}H_{21}CrNa_2O_{13} \cdot 3H_2O$: C, 27.44; H, 5.18; Cr, 9.89; Na, 8.75. Found: C, 27.17; H, 5.17; Cr, 9.74; Na, 8.80.

Manganese–D-glucose complex. The $(Et_4N)_2MnCl_2Br_2$ (1.092 g, 2 mmol) was prepared by mixing Et_4NBr (0.84 g, 4 mmol) with $MnCl_2 \cdot 4H_2O$ (0.396 g, 2 mmol) in EtOH to give a pale-green solid that was separated, washed with MeOH, and dried under vacuum. To 20 mL of a methanolic solution of this metal salt was added a solution of the disodium salt of D-glucose (8 mmol), and the mixture was stirred continuously for 2 days. The product was separated by filtration and then washed with hot MeOH several times until the filtrate was found to be halide free. The solid was washed with ether and dried under vacuum. A yield of 0.64 g (62%) of halide-free product was obtained, corresponding to a molecular formula of $Na_2[Mn(D\text{-}Glc^{2-})(OMe)_2]$ as shown by elemental analysis. *Anal.* Calcd for $C_8H_{16}MnNa_2O_8$: C, 28.17; H, 4.73; Mn, 16.11; Na, 13.48. Found: C, 28.21; H, 4.54; Mn, 16.26; Na, 13.45.

RESULTS AND DISCUSSION

All the metal–saccharide complexes were soluble in H_2O. However, the titanium and vanadium complexes were soluble in MeOH and Me_2SO, and the titanium complex was also soluble in MeCN.

FTIR spectra showed characteristic $\nu_{O\text{-}H}$ bands for the solid D-glucose (Fig. 1a) in the range 3240–3400 cm^{-1} corresponding to intermolecular H-bonded species[11]. In the case of the complexes (Figs. 1b–f) the bands in this region become almost symmetric (3380 ± 20 cm^{-1}) with a small shoulder around 3270 ± 20 cm^{-1}, indicating the breakage of intermolecular H-bonds due to the interaction of the metal ions with glucose. Further, the position of the main band itself is indicative of some H-bonding between the free hydroxyl groups of adjacent complex molecules.

The band observed around 1640 cm^{-1} in the case of the titanium complex (Fig. 1b) and that observed around 1625 cm^{-1} in the case of the vanadium and chromium complexes (Figs. 1c and e) can be assigned to the bending vibration of H_2O present in the compound. On the other hand, the well-resolved and relatively strong band observed at 1596 cm^{-1} for the disodium salt of glucose (Fig. 1d) and 1590 cm^{-1} for the manganese complex (Fig. 1f) seem to be characteristic of the bending vibrations arising from C–O–H groups interacting with Na^+. This implies that the metal–saccharide complexes are connected through sodium ions via ion-dipole interactions to give an extended network. It is evident from Fig. 1 that the sharp bands observed in the case of free ligands in the regions 1340–1460 cm^{-1} [δ(OCH, CH_2, CCH)], 990–1140 cm^{-1} [ν(CO, CC)], and 770–840 cm^{-1} [δ(CCH, CH), ν(CC, CO)] are merged and become broad in the complexes. While the free ligand showed several sharp bands in the 400–600 cm^{-1} range, the metal complexes exhibited a broad envelope making the assignment of $\nu_{\text{M-O}}$ rather difficult. Though the spectra of the sodium salt of D-glucose can be differentiated from the transition metal complex spectra, the information obtained in the region 600–900 cm^{-1} is not sufficient to derive any definite conclusions regarding the anomeric nature of the complexes[12]. However, information regarding the anomeric nature is derived from the ^1H NMR spectra. The changes noticed in the IR spectra are indicative of a metal–glucose complex formation through the oxygens of the ligand.

The absorption spectrum of the Ti–saccharide complex (Fig. 2) was characteristic of its orange-red colour as indicated by the LMCT band observed at 350 nm, which is different from the spectra of either of its precursor molecules. The complex is highly soluble in acetonitrile as expected. Further, the FTIR (Fig. 1b) and ^1H NMR spectra showed the presence of the tetraethylammonium cation and glucose moiety and, hence, complex formation. A titanium–ascorbate complex [$Cp_2Ti(ascorbate)_2$] (Cp = cyclopentadienyl) has been reported, wherein the interaction of titanium with ascorbate is via the O^- of the C-3 group[13]. Impetus for the study of titanium–saccharide chemistry is derived from several reports, such as a reported increase in body weight in experimental animals and their offspring when fed the ascorbate complex[14], the reported anticancer activity of Cp_2TiCl_2[15,16], and the involvement of titanium–alkoxide species in asymmetric epoxidation[17,18].

The product obtained in the vanadium–saccharide reaction is bluish-green in solution and exhibited an absorption spectrum different from that of $VOSO_4 \cdot 2H_2O$, indicating a change in the primary coordination sphere of vanadium. The absorption bands are compatible with those of other VO^{2+} complexes of oxygen-containing ligands[19]. Both the $d \rightarrow d$ and the LMCT bands are indicative of complex formation (Fig. 2). The FTIR spectrum showed the presence of a $\nu_{V=O}$ band[20] (990 ± 10 cm^{-1}) and the disappearance of the SO_4^{2-} bands (Fig. 1c), which indicates the presence of VO^{2+}, even in the saccharide complex. An 8-line EPR spectrum was obtained which is characteristic of a V(IV) species having $g = 1.953$. A careful comparison of ^1H NMR spectra measured both for the ligand and the

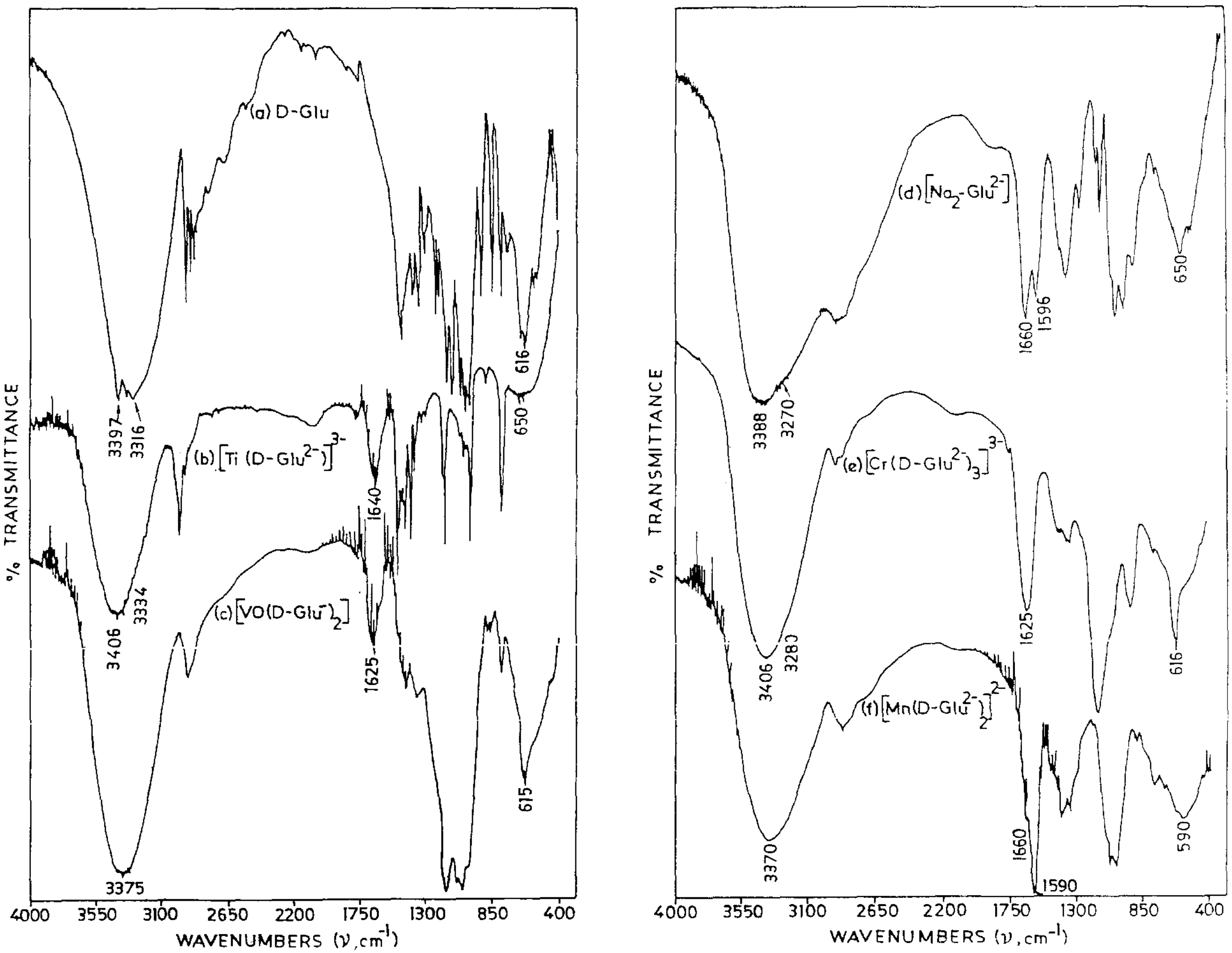

Fig. 1. FTIR spectra (KBr matrix) of (a) D-glucose; (b) D-glucose–Ti^{4+} complex; (c) D-glucose–V^{4+} complex; (d) D-glucose, disodium salt; (e) D-glucose–Cr^{3+} complex; (f) D-glucose–Mn^{2+} complex.

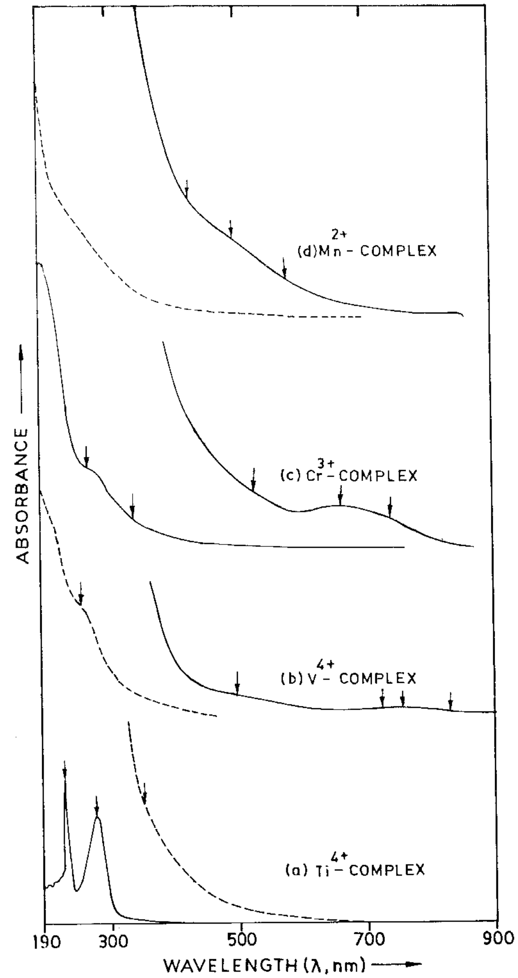

Fig. 2. Absorption spectra of D-glucose complexes (solvent in parentheses) of (a) Ti^{4+} (MeCN); (b) V^{4+} (H_2O); (c) Cr^{3+} (H_2O); and (d) Mn^{2+} (H_2O).

product in D_2O and Me_2SO-d_6 revealed information regarding the shifts in H-1, H-2, and HO-1 protons corresponding to both α and β isomers. Upfield shifts were observed for α-HO-1 and β-HO-1 protons of 0.143 and 0.178 ppm, respectively. Downfield shifts were observed for α-H-1 and α-H-2 protons of 0.144 and 0.06 ppm, respectively. Of course the disappearance of the HO-2 proton resonance is noted in the Me_2SO spectrum. A strong peak corresponding to two methoxy groups was observed at 3.394 ppm. All the data are consistent with the formation of a five-membered chelate via the O^- of O-2 and the OH of the HO-1 groups to give the $Na[VO(D\text{-}Glc^-)(OMe)_2(H_2O)]$ product with both α and β isomers. Such changes are not observed in the ^1H NMR spectra of the sodium salt of D-glucose. Vanadium(V) has been reduced to V(IV) with the interaction of D-galacturonic acid[21]. However, the details about these interactions are not clear. Geraldes et al.[22] reported extensive NMR studies of the interactions of Mo(VI) and W(VI) oxo species with several aldoses. Electrophoresis[23] has been used to study vanadate–polyol interactions, wherein metavanadate was suggested to be the complexing species in the pH range of 5–9.5. Solution ^{51}V NMR studies between vanadate and saccharide ligands indicated the formation of several mono- and bi-nuclear complexes, but no solid complex was isolated[24]. In view of these solution studies, it is interesting to note that our vanadium–saccharide complexes were isolated in the solid state.

The absorption spectrum of the product obtained from the $CrCl_3$–D-glucose reaction is distinctly different from that of the $CrCl_3$ and also the Cr^{3+}-aquo species, indicating that in the complex, Cr^{3+} is in an octahedral oxygen environment (Fig. 2). The asymmetry observed in the 600–800 nm band can be attributed to distorted octahedral species arising from the type of coordinating ligands and also due to the presence of α and β products formed in the reaction. The changes noticed in the ^{1}H NMR spectrum and the broad EPR spectrum ($g = 1.959$) identified for the complex were characteristic of Cr(III) in the octahedral oxygen environment, which provides further evidence for Cr(III)–glucose complex formation. Comparison of ^{1}H NMR spectra of both the ligand and its disodium salt and the product measured in D_2O revealed that, while H-1 resonances shifted upfield by 0.053 and 0.104 ppm, respectively, in the α and β isomers, the H-2 protons are shifted downfield by 0.20 and 0.215 ppm, for the same isomers. Thus the data strongly favour the formation of five-membered chelate rings through deprotonated oxygens of the HO-1 and HO-2 groups of both the α- and β-D-glucose molecules. The collapse of the fine structure observed in the ^{1}H NMR spectra is indicative of the paramagnetic broadening interaction of the metal ions. The studies presented in this paper strongly support the formation of a $Na_2[Cr(\text{D-Glc}^{2-})_2(OH)(H_2O)_3]$ complex. Solution studies reported in the literature have shown the interaction of $CrCl_3(\text{pyridine})_3$ with several monosaccharides by the replacement of only pyridine, but not halide; furthermore, no solid complex was isolated[25]. In an accompanying paper we report binuclear chromium complexes of D-glucose and D-fructose as obtained by chromate reduction[26].

The absorption spectrum of the orange-red Mn^{2+}–saccharide complex is indicative of a d^5 system in the tetrahedral field (Fig. 2). The presence of Mn(II) and the absence of halide in the complex have been confirmed through chemical tests. The absence of the tetraethylammonium cation has been confirmed both by FTIR (Fig. 1f) and ^{1}H NMR. The ^{1}H NMR spectrum taken in D_2O showed relatively broad peaks for saccharide protons and a strong peak for methoxy protons at 3.527 ppm. The Mn–saccharide complex exhibited a six-line EPR spectrum ($g = 2.0015$) that is different from that of its synthetic precursors [$MnCl_2 \cdot 4H_2O$ and $(Et_4N)_2MnCl_2Br_2$]. Thus the data supports the formula $Na_2[Mn(\text{D-Glc}^{2-})(OMe)_2]$. Polyhydroxy ligands have been found to form stable and soluble complexes with Mn(II), Mn(III), and Mn(IV) ions in alkaline media[27–29], which supports the isolation of our Mn^{2+}–D-glucose complex.

CONCLUSIONS

The present work offers simple methods to synthesize soluble and characterizable D-glucose complexes with early transition elements. While we have shown sufficient evidence for metal–D-glucose complex formation through ligand oxygens, a three-dimensional structure determination, which is currently underway, will ultimately be required for structural proof. As the literature indicates that the transition metal–saccharide complexes are of paramount importance in several fields related to medicine, biology, and catalysis, the generalization of synthetic methodologies and structure–activity/reactivity correlations stand as challenges to be tackled.

ACKNOWLEDGMENTS

The authors thank the Department of Science and Technology, New Delhi, and Centre for Scientific and Industrial Research, New Delhi for financial support and RSIC, IIT, Bombay for providing the spectral data. The authors thank both the refrees and the editor for their constructive suggestions made on this article.

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