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Transition metal–saccharide interactions: Synthesis and characterization of vanadyl saccharides ☆

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Abstract

Low molecular weight saccharide complexes of vanadium of the type $[VO(sacch)_2]^{2-}$, were synthesized for the first time by simple and reproducible methods in nonaqueous media. These reactions yielded water-soluble products which were characterized by various analytical and spectroscopic techniques and by cyclic voltammetry. The vanadyl D-glucose complex **1** shows a resemblance to a natural vanadium-binding component vanadobin, isolated from the tunicate *Ascidia sydneiensis samea*. All the saccharide complexes are stable in solution for long periods under ambient conditions without being oxidised and showed no hydrolysis in the pH range 2–12. All the saccharide complexes reported in this paper show evidence for the V(IV) species.

1. Introduction

The inorganic and biological chemistry of vanadium in its +3, +4 and +5 oxidation states with various natural and synthetic organic molecules are of current interest, particularly in view of the recent discovery of vanadium as a cofactor in the enzymes like bromoperoxidases [1a,b] and nitrogenases [2] and its various inhibitory interactions with other enzymes [3]. There has been increasing evidence that tunichromes present in the ascidian blood cells have the ability to bind vanadium [4]. A naturally occurring low molecular weight component vanadobin, capable of storing vanadium in the vanadyl form, has been isolated from ascidian blood cells by Michibata et al. [5] and determined to contain a reducing sugar;

☆ Dedicated to Professor C.N.R. Rao, F.R.S. on his 60th birthday.

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however its full characterization has not been reported. There has been a great interest in orally active insulin mimetics, especially soluble vanadyl compounds [6], because insulin replacement is currently the only easy method for controlling chronic diabetes. The interest in the administration of vanadium, especially as vanadyl, has come basically as a result of the fact that aqueous vanadyl sulfate has been shown to lower blood glucose levels and blood lipids in streptozocin-induced (STZ) diabetic rats and it also seems to play a role in preventing secondary complications of diabetes such as cataracts and cardiac dysfunction [7].

Although there exists considerable interest regarding the role of vanadium alkoxides and oxohydroxy species [8], relatively little is known about the interactions of V(V) and V(IV) with saccharides, particularly due to the lack of synthetic methodologies available in the literature to make low molecular weight, soluble, and characterizable saccharide complexes. Our laboratory is currently involved in the synthesis, isolation, and characterization of saccharide complexes of first-row transition metal ions [9]. Very few reports in the literature deal with the interactions between vanadate and vanadyl ions and saccharide moieties in solution [10]. However, there are no reports in the literature regarding the synthesis, isolation, and characterization of saccharide complexes of vanadium.

In this paper, we report the synthesis, isolation, characterization, and possible biological significance of saccharide complexes of oxovanadium(IV) with D-glucose (D-Glc), D-fructose (D-Fru), D-mannose (D-Man), D-galactose (D-Gal), and D-maltose (D-Mal).

2. Experimental

Methods and Materials.—Absorption spectra were measured using a Shimadzu UV-260 spectrophotometer. FTIR spectra were recorded in a KBr matrix on a Varian Nicolet spectrometer. EPR spectra were recorded using a Varian ESR-112 spectrometer with tetracyanoethylene (TCNE) as the field marker ($g = 2.00277$). Cyclic voltammetry was carried out with a BAS100B electrochemical analyser at a hanging mercury dropping electrode (HMDE)–Pt electrode in water, using Me_4NCl as supporting electrolyte and Ag/AgCl as the reference electrode. ^1H NMR spectra were recorded on a Varian XL-300 spectrometer in D_2O. Metal contents were determined using inductively coupled plasma–atomic emission spectroscopy (ICP–AES).

All the saccharides used were procured from Sigma Chemical Co. (USA) or from Aldrich Chemical Co. (USA), and were used without further purification. Sodium metal was from E. Merck (Germany), and other chemicals were from local sources and were purified before using. $VO(acac)_2$ was synthesized according to a literature procedure [11] and recrystallized using chloroform. Solvents were dried and distilled immediately before use by well-established literature procedures.

Synthesis.—All the saccharide complexes were synthesised by the same method and a typical procedure is given below for the VO^{2+}–D-Glc complex.

D-glucose (1.80 g, 10 mmol) was suspended in MeOH (50 mL) and stirred for 0.5

Table 1
Elemental analyses of VO^{2+}–saccharide complexes

Compound	Molecular formula	Analyses (%) [a]				Yield [b] (%)
		C	H	Na	V	
1	$C_{13}H_{24}O_{14}Na_2V$	31.01 (31.16)	4.60 (4.79)	9.29 (9.18)	10.17 (10.17)	60
2	$C_{12}H_{20}O_{13}Na_2V$	30.25 (30.73)	4.76 (4.26)	10.03 (9.80)	11.18 (10.86)	67
3	$C_{13}H_{24}O_{14}Na_2V$	31.21 (31.16)	4.74 (4.79)	9.70 (9.18)	9.83 (10.17)	77
4	$C_{17}H_{39}O_{18}Na_3V$	31.82 (31.36)	6.04 (5.99)	10.31 (10.60)	7.69 (7.82)	70
5	$C_{25}H_{43}O_{24}Na_3V$	35.79 (35.44)	5.21 (5.07)	8.20 (8.15)	5.68 (6.01)	65

[a] Experimental values are given, with calculated (theoretical) values in parentheses.
[b] Yields are based on metal content.

h. To this mixture freshly cut Na (0.46 g, 20 mmol) was added in small amounts with stirring for an additional 2 h. $VO(acac)_2$ (1.325 g, 4.96 mmol) was dissolved in MeOH (50 mL) and was added dropwise to the sodium salt of D-Glc over a period of 30 min. During the reaction the yellow colour changed to green initially and became brown towards the end. The mixture was stirred at room temperature for 24 h. This mixture was then filtered to give a greenish-brown residue. The residue was purified by stirring in dry MeOH, followed by MeCN, and then in hexane for two days, followed by filtration and drying in vacuo to give a green solid product of **1**. Other complexes VO^{2+}–D-Fru (**2**), VO^{2+}–D-Gal (**3**), VO^{2+}–D-Man, (**4**) and VO^{2+}–D-Mal (**5**) were synthesized, isolated, and purified in a similar manner except that the synthesis of **4** took 3 days for completion and yielded a pale green solid complex. The analytical results are provided in Table 1.

3. Results and discussion

Properties.—All the vanadyl–saccharide complexes were found to be moisture sensitive and were highly soluble in water, but less soluble in warm Me_2SO, and insoluble in most common organic solvents.

Absorption spectral studies.—Absorption spectra of **1**–**5** recorded in water show two bands (Fig. 1), one around 680 nm and the other around 530 nm which are assignable to *d*–*d* transitions arising from $B_2 \rightarrow E$ and $B_2 \rightarrow B_1$ as expected for a d^1 system in a square-pyramidal geometry [12]. Corresponding absorption data are provided in Table 2. In the case of complex **2**, both these bands have equal absorbance. On the other hand, in complexes **1**, **3**, and **5**, where an additional MeOH molecule is involved with the complex, the relative intensity of the 680 nm band is lowered as compared to the 550 nm band. In all these complexes the ϵ values are in good agreement with a square-pyramidal geometry [13]. In the case of

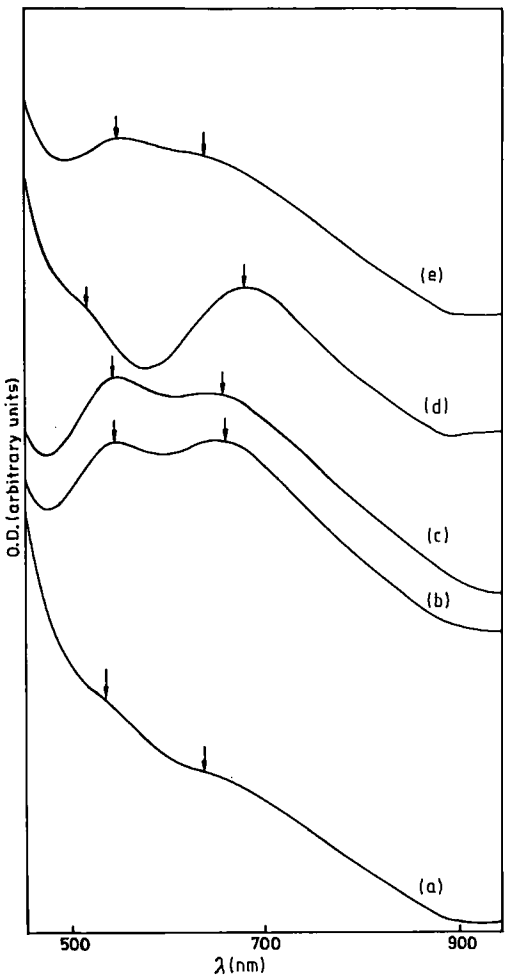

Fig. 1. Absorption spectra recorded in water for complexes: (a) **1** (9.4); (b) **2** (8.2); (c) **3** (7.7); (d) **4** (10.5), and (e) **5** (9.2). Values in parentheses give the pH of the compound in water.

complex **4**, the absorption pattern is different, and a shift in the band position is seen. These two bands are shifted by 20 nm to lower and higher wavelengths, respectively, in case of the 550 and 860 nm bands, and the former is seen as a shoulder. Thus the spectrum of **4** resembles that of a distorted octahedral geometry, a fact further supported by the low ϵ values obtained. However, as observed in various other complexes of vanadyl systems, the $B_2 \rightarrow A$ transition seems to be obscured by the LMCT bands.

Reflectance studies in the solid state in the range of 800–350 nm have also indicated the reflectance peaks at the same positions as in the absorption spectra, and, hence, essentially the structures of the complexes remain unaltered in both the solid and solution states.

Table 2
UV-vis, IR and EPR spectral data for VO^{2+}–saccharide complexes

Complex	UV-vis (λ nm, ϵ, M^{-1} cm^{-1})	IR ($\nu_{V=O}$ cm^{-1})	EPR g_0	A_0 (gauss)
1	640(73), 520(89) 310(650), 270(1417), 210(2696)	945	1.939	106
2	654(68), 552(68) 310(225), 260(400), 198(1928)	945	1.979	94
3	644(41), 553(43) 315(147), 255(524), 195(1455)	960	1.985	72
4	684(32), 510(sh, 29) 285(280), 262(1326), 206(1550)	945	1.989	71
5	650(62), 559(72) 330(110), 255(331)	930	1.961	93

Infrared studies.—IR spectra of the complexes indicate an overall breakage of extensive intermolecular hydrogen bonding upon complex formation. While Tajmir-Riahi [14] had reported sharp bands for the nontransition metal saccharide adducts, the interactions with the transition metals seems to influence the skeletal vibrations, perhaps due to uneven vibronic coupling in the solid state of these complexes. Consequently, the information obtained in the region of 600–900 cm^{-1} was not resolved enough to derive any definite conclusions regarding the anomeric nature of the complexes. As a matter of fact, broad bands are observed in the spectra of almost all complexes of transition metal saccharides [9]. Vanadyl stretching vibrations were seen in the range 945–960 cm^{-1}. The rather low $\nu_{V=O}$ value observed with these complexes is explainable based on the intermolecular hydrogen bonding between free hydroxyls of the complexes and V=O. Differences between the monosaccharide complexes **1–4** and the disaccharide complex **5** can be ascertained by comparing the relative intensities of the skeletal vibrations of the saccharide units in the region of 1100 cm^{-1} to the $\nu_{V=O}$ band.

EPR studies.—EPR spectra recorded in solid state and in aqueous solutions at room temperature showed a characteristic eight-line pattern ($I = 7/2$) for all the vanadyl complexes reported herein. Representative spectra for complexes **1** and **5** are shown in Fig. 2. The hyperfine splitting value A (in gauss) of complex **1** agrees well with that reported for vanadobin, which possesses a reducing sugar. However, the sugar component of vanadobin is not characterized. Corresponding data of g and A are shown in Table 2 and agree well with a $VO(O_4)$ coordination environment [15]. Spectra recorded from samples dissolved in water or Me_2SO and stored for $\sim$ 8 weeks exhibited no changes in their EPR pattern, ruling out any oxidation of vanadium or degradation of the compound and indicating the stable nature of these vanadyl–saccharide complexes. This stability seems to be a special feature of complexes **1–5**, as the oxidation of the vanadyl ion to the vanadate form is quite

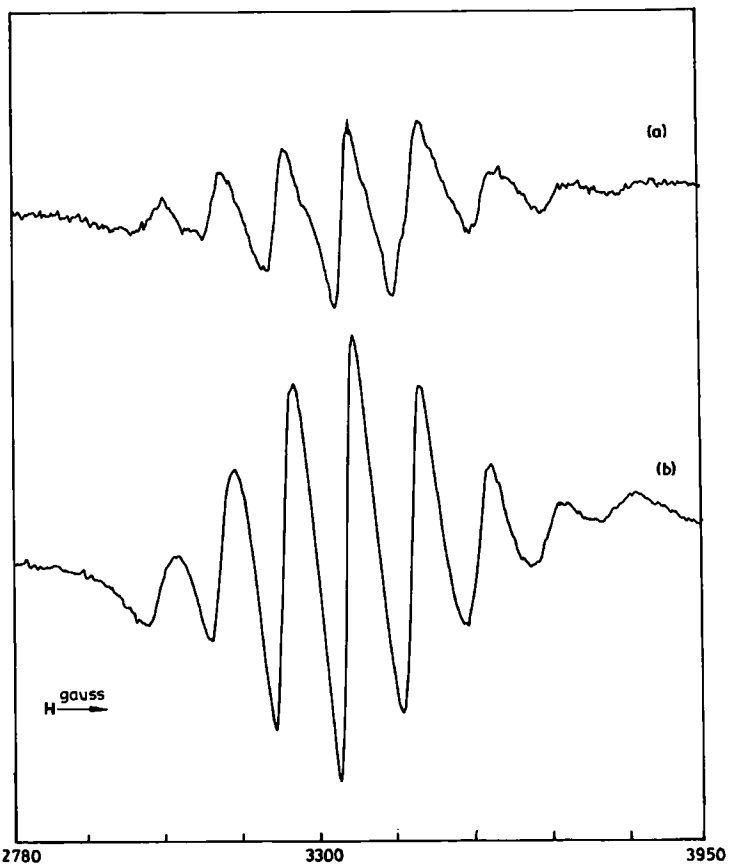

Fig. 2. EPR spectra recorded in water at room temperature for complexes: (a) **1** and (b) **5**.

feasible in solution, especially under ambient conditions. Initial experiments by our group using vanadate as the metal precursor towards reactions with monosaccharides and saccharide derivatives like galacturonic acid and others, have shown that V(V) is reduced to V(IV) and is found to be stable in this state for long periods. Solution studies by others [16] using V(V) in acidic conditions have indicated the same results. Thus the binding of saccharide units to the vanadyl group in complexes **1–5** provides favourable chelation and further stability.

Cyclic voltammetric studies.—All the saccharide complexes **1–5** exhibited a quasi-reversible cathodic reduction peak. Representative voltammograms are shown for complexes **1**, **2**, **4**, and **5** in Fig. 3. Complex **4** shows the most negative potential when compared to the other saccharide complexes. The E_p^c values of these saccharide complexes are found to be in the order: $\mathbf{4} > \mathbf{1} \geq \mathbf{5} > \mathbf{3} \geq \mathbf{2}$. The trend in these potentials can be understood by considering the orientation of hydroxyl groups based on the ligand conformations provided in the literature [10b,17]. It may be noted that the ability to form bis-chelated complexes seems to

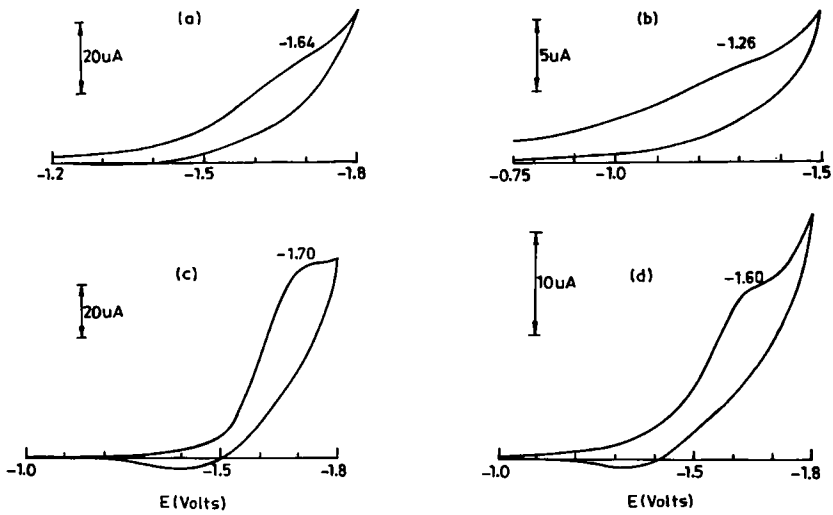

Fig. 3. Cyclic voltammogramms recorded at HMDE in water for the complexes: (a) **1**; (b) **2**; (c) **4**, and (d) **5**. Scan speed: 100 mv/s; supporting electrolyte: Me_4NCl; reference electrode: Ag/AgCl.

be in the order D-Man > D-Glc ≥ D-Mal > D-Gal ≥ D-Fru. The presence of cis hydroxy groups at the C-2 and C-3 positions in D-mannose seems to make this ligand a better candidate for effective binding, and, hence, the observed redox potentials. We have recently reported that the hydroxy group present at the C-2 position is important in the case of chromate reduction with saccharides and their derivatives [18]. Though C-3–C-4 possess *cis* hydroxy groups, the E_p^c values observed in case of complexes **2** and **3** are low as the HO-2 group is not involved in chelate formation. The close agreement noted in the E_p^c of complexes **1** and **5** may be explained based on the presence of two glucose units in case of maltose.

Cyclic voltammograms of all these complexes were recorded at the HMDE at various pH values in the range 2 to 12. It was found that the E_p^c values show linear behaviour with respect to pH. The slopes of these linear trends (mV/pH) are in the order, **5** (63) > **4** (50) > **1** (33) > **3** (25) > **2** (20). The smooth change noted in the slopes (mV/pH) of these complexes seem to reflect their structural rigidity in solution. No precipitation was observed during these studies, indicating the hydrolytic stability of these complexes. Comparison of the slope values (mV/pH) with the cathodic reduction potentials of the corresponding complexes in water revealed that the complexes having low values of slope are easily reducible at the metal center.

Complexes **1–5** were studied for their oxidation behaviour at the Pt electrode. It was found that none of the complexes give any metal ion oxidation peaks under these experimental conditions.

Nature of products.—All the saccharide complexes reported here (**1–5**) possess the vanadyl function, and all of these are anionic with sodium as the counter cation. Based on all these data, together with the elemental analyses, the following

molecular formulas were proposed for the vanadyl–saccharide complexes reported in this paper: $Na_2[VO(D\text{-}Glc)_2] \cdot CH_3OH$ for **1**, $Na_2[VO(D\text{-}Fru)_2]$ for **2**, $Na_2[VO(D\text{-}Gal)_2] \cdot CH_3OH$ for **3**, $Na_3[VO(D\text{-}Man)_2(OCH_3)] \cdot 4CH_3OH$ for **4**, and $Na_3[VO(D\text{-}Mal)_2] \cdot CH_3OH$ for **5**. Although complex formation between oxovanadium and saccharide ligands in solution has been claimed in the literature by Branca et al. [10b], ours is the first case of isolation of these complexes in solid state, followed by characterization by the methods reported in this paper. ^1H NMR spectra showed line broadening in all the complexes due to the binding of the paramagnetic metal ion, and hence could not be used effectively to identify the skeletal protons. However, the methoxy groups in all the cases except **2** were identifiable through the peaks observed at 3.38 ppm.

4. Conclusions

The saccharide complexes of vanadium are unusual and are expected to play influential roles in asymmetric catalysis, in alkoxometal chemistry [19], possibly as insulin mimics, and in metal sequestering and aggregation. The identification of a reducing sugar in vanadobin [5] suggests that the interaction and even complex formation between saccharides and vanadium are biologically important. Complex **1**, in particular, shows the relative importance of these molecules in the context of vanadium sequestering and storage, especially when it has been suggested that tunichromes may not be involved in the bioaccumulation of vanadium in ascidian blood cells [20]. Further, the paper deals with the first-time isolation and characterization of vanadyl–saccharide complexes.

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