ELSEVIER

Carbohydrate Research 297 (1997) 341–346

CARBOHYDRATE
RESEARCH

Transition-metal saccharide chemistry: synthesis and characterization of D-glucose, D-fructose, D-galactose, D-xylose, D-ribose, and maltose complexes of Ni(II)

Rajiv P. Bandwar, Chebrolu P. Rao *

Bioinorganic Laboratory, Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai 400 076, India

Received 25 July 1996; accepted 7 October 1996

Abstract

Monosaccharide (D-Glc, D-Fru, D-Gal, D-Xyl, D-Rib) and disaccharide (Mal) complexes of Ni(II) were synthesised using $[NEt_4]_2[NiCl_2Br_2]$ or $NiCl_2 \cdot 6H_2O$ in nonaqueous medium. The compounds synthesised from these two starting materials are different. The isolated complexes were characterized by diffuse reflectance, aqueous solution absorbance, CD, FTIR, magnetic susceptibility, and EXAFS and XANES studies. © 1997 Elsevier Science Ltd. All rights reserved.

Keywords: Transition metal; Ni(II); Complex; Monosaccharide; Maltose

1. Introduction

Ni(II)–saccharide interactions are of biological significance [1]. Aqueous solution studies have clearly demonstrated the binding of Ni(II) to various saccharides or their derivatives [2]. The N-glycosides of Ni(II) are the only complexes that are crystallographically characterized [3]. Continuing our earlier studies on the saccharide complexes of VO^{2+} [4,5], Cr(III) [4,6], Mn(II) [7], Fe(III) [8], Co(II) [9], Cu(II) [10], and Zn(II) [11], we now report the synthesis and characterization of Ni(II) complexes of D-glucose (D-Glc), D-fructose (D-Fru), D-galactose (D-Gal), D-xylose (D-Xyl), D-ribose (D-Rib), and maltose (Mal).

2. Experimental

Saccharide complexes of Ni(II) were synthesised using either $[NEt_4]_2[NiCl_2Br_2]$ or $NiCl_2 \cdot 6H_2O$. Typical procedures for the synthesis of complexes are described below.

Synthesis of Ni(II) – D - Glc complex (**1**) *from* $[NEt_4]_2[NiCl_2Br_2]$.—D-Glc (1.62 g, 8.99 mmol) was suspended in 100 mL of MeOH and continuously stirred. To this, freshly cut metallic sodium (0.43 g, 18.7 mmol) was added in pieces, resulting in the dissolution of D-Glc as its sodium salt. About 30 min later, $[NEt_4]_2[NiCl_2Br_2]$ (1.65 g, 3.00 mmol) in 25

---

[*] Corresponding author.

PII S0008-6215(96)00282-0

mL of MeCN was added slowly to this reaction mixture, resulting in the formation of a pale-green precipitate. The reaction mixture was stirred for one additional day. The crude product of Ni(II)–D-Glc (**1**) was isolated by filtration under suction and was purified by stirring three times in a mixture of 9:1 MeOH–H_2O, followed by absolute MeOH (twice), and drying in vacuo. Complexes of Ni(II)–D-Fru (**2**) and Ni(II)–D-Gal (**3**) were synthesised similarly, whereas the Ni(II)–Mal complex (**9**) was synthesised using 2 mmol of $[NEt_4]_2[NiCl_2Br_2]$ and employing a 1:2 metal-to-ligand ratio.

Synthesis of Ni(II)–saccharide complexes (**4–8**) *from $NiCl_2 \cdot 6H_2O$*.—Synthesis of Ni(II)–D-Glc (**4**), Ni(II)–D-Fru (**5**), Ni(II)–D-Gal (**6**), Ni(II)–D-Xyl (**7**), and Ni(II)–D-Rib (**8**) complexes was carried out using a similar procedure to that described above, except that $NiCl_2 \cdot 6H_2O$ was used in MeOH. The complexes were isolated in an identical manner and purified from a 9:1 MeOH–H_2O mixture.

Yields of these Ni(II)–saccharide complexes were found to be 60–65% based on metal content. The elemental analysis of all the complexes **1–9** is given in Table 1.

3. Results and discussion

Earlier, we reported the synthesis and characterization of Ni(II) complexes of D-Fru and D-Glc [12]. The complexes obtained were of the type Na[Ni(Sacch)(OMe)Cl] (where Sacch = D-Fru or D-Glc) and are different from those reported here. In general, the Ni(II)–saccharide complexes obtained were yellowish-green to green in colour and were soluble only in water. All the aqueous solution spectral analyses were carried out using freshly prepared solutions. The results of various studies are discussed below.

Diffuse reflectance and aqueous solution absorption studies.—All the Ni(II)–saccharide complexes **1–9** exhibited identical diffuse reflectance and identical aqueous solution absorption spectra typical of Ni(II) in an octahedral environment, suggesting the

Table 1
Elemental analysis (%) with proposed molecular formulae and observed magnetic moment per ion for Ni(II)–saccharide complexes **1–9**

Complex			C	H	Ni	Na	μ_{eff} (μ_B)
1	$C_{12}H_{30}Cl_3NaNi_2O_{16}$	Calcd:	21.27	4.43	17.34	3.40	4.05
	$Na[Ni_2(Glc)_2(H_2O)_4Cl_3]$	Found:	21.40	4.21	17.34	3.00	
2	$C_{13}H_{32}Cl_3NaNi_2O_{16} \cdot 3CH_3OH$	Calcd:	24.40	5.59	14.92	2.92	4.01
	$Na[Ni_2(Fru)_2(H_2O)_3(CH_3OH)Cl_3] \cdot 3CH_3OH$	Found:	24.49	4.44	14.63	2.33	
3	$C_{15}H_{35}Cl_4NaNi_2O_{15} \cdot 0.5CH_3OH$	Calcd:	24.69	4.91	15.58	3.05	4.01
	$Na[Ni_2(Gal)_2(CH_3OH)_3Cl_4] \cdot 0.5CH_3OH$	Found:	24.68	4.50	15.38	3.25	
4	$C_{16}H_{36}Cl_3NaNi_3O_{16}$	Calcd:	24.32	4.56	22.30	2.91	3.24
	$Na[Ni_3(Glc)_2(CH_3OH)_4Cl_3]$	Found:	24.47	4.27	21.89	2.72	
5	$C_{18}H_{41}Cl_6NaNi_4O_{22}$	Calcd:	20.00	3.80	21.74	2.13	3.23
	$Na[Ni_4(Fru)_3(H_2O)_4Cl_6]$	Found:	20.24	3.51	21.90	2.56	
6	$C_{16}H_{36}Cl_3NaNi_3O_{16}$	Calcd:	24.32	4.56	22.30	2.91	3.29
	$Na[Ni_3(Gal)_2(CH_3OH)_4Cl_3]$	Found:	24.51	4.24	22.72	2.39	
7	$C_{14}H_{34}Cl_3NaNi_2O_{14}$	Calcd:	24.66	4.87	17.87	3.50	3.51
	$Na[Ni_2(Xyl)_2(CH_3OH)_4Cl_3]$	Found:	24.75	4.63	17.86	3.02	
8	$C_{14}H_{34}Cl_3NaNi_2O_{14}$	Calcd:	24.66	4.87	17.87	3.50	3.39
	$Na[Ni_2(Rib)_2(CH_3OH)_4Cl_3]$	Found:	24.95	3.98	17.65	3.46	
9	$C_{13}H_{25}Cl_2NaNi_2O_{13}$	Calcd:	25.98	4.16	19.55	3.83	3.46
	$Na[Ni_2(Mal)(CH_3OH)(OH)Cl_2]$	Found:	26.15	4.26	19.40	3.95	

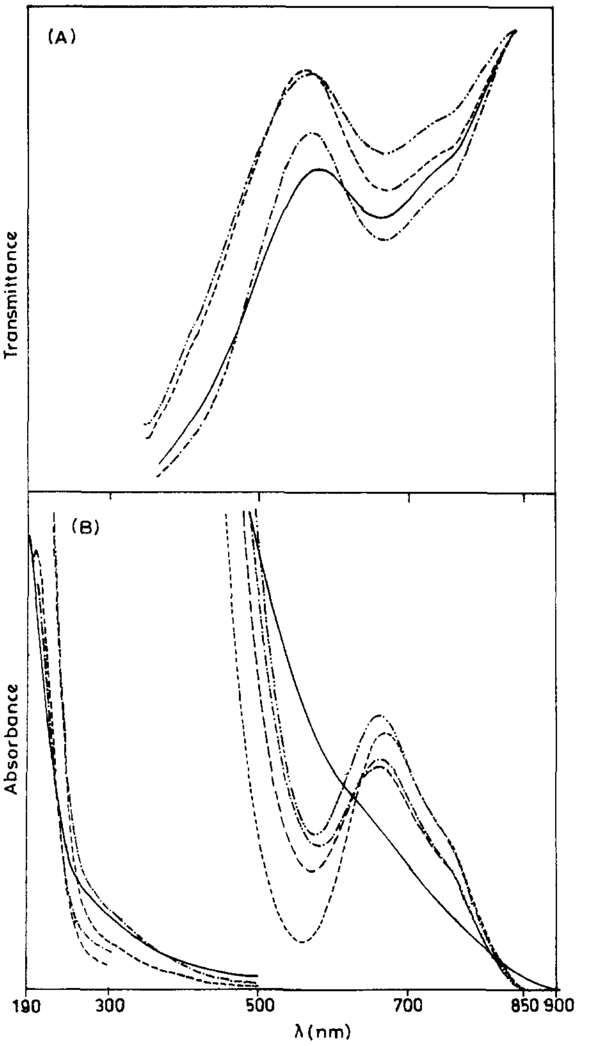

Fig. 1. (A) Diffuse reflectance and (B) aqueous solution absorption spectra of Ni(II)–D-Glc (**4**) (– · –), Ni(II)–D-Fru (**5**) (---), Ni(II)–D-Gal (**6**) (————), Ni(II)–D-Xyl (**7**) (– · · –), and Ni(II)–D-Rib (**8**) (– – –).

involvement of water coordination. Fig. 1 shows the diffuse reflectance and aqueous solution absorption spectra of Ni(II)–D-Glc (**4**), Ni(II)–D-Fru (**5**), Ni(II)–D-Gal (**6**), Ni(II)–D-Xyl (**7**), and Ni(II)–D-Rib (**8**) complexes. The bands observed in the visible region, 655 ± 15 nm (ε, 8–14 M^{-1}cm^{-1}) with a shoulder at ~ 745 nm (ε, 5–9 M^{-1}cm^{-1}), were assignable to the ${}^3A_{2g} \rightarrow {}^3T_{1g}$(F) transition arising from a distorted octahedral d^8 system [13]. However, the ${}^3A_{2g} \rightarrow {}^3T_{1g}$(P) transition was masked by a strong LMCT band at ~ 370 nm (ε, 200–250 M^{-1}cm^{-1}), which was otherwise present in the spectra of the precursors. The similarity of the diffuse reflectance and the aqueous solution absorption spectra of the complexes suggests their structural integrity in the solid state as well as in freshly prepared solutions.

CD studies.—Typical CD spectra in the region 350–700 nm of Ni(II)–D-Glc (**4**), Ni(II)–D-Fru (**5**), and Ni(II)–D-Gal (**6**) complexes are shown in Fig. 2. The presence of a weak cotton effect of the complexes **1**–**9** as compared to that obtained in the case of Co(II)–saccharide [9] and Cu(II)–saccharide [10] complexes indicated only a weak octahedral distortion and a small dissymmetry around the Ni(II) ion in these complexes [13]. The Ni(II)–D-Gal (**3** and **6**) and Ni(II)–D-Xyl complexes (**7**) exhibited curves of the opposite sign to other Ni(II)–saccharide complexes. Thus the pattern for signs of rotation of various Ni(II)–saccharide complexes was found to be identical with their Co(II)–saccharide counterparts [9] and hence exhibited similar coordination geometries.

FTIR studies.—The FTIR spectra of the Ni(II)–saccharide complexes **1**–**9** in KBr exhibited merging and broadening of bands in the O–H and C–H stretching regions as compared to the spectra of free saccharides. These spectral characteristics were similar to those observed with other first-row transition-metal saccharide complexes, and, hence, suggested similar changes in the intermolecular hydrogen-bonding network of the saccharides upon ionization and subsequent complex formation [4–12]. Strong coupling between the bands resulted in merging and broadening in the spectra and complicated the assignment of these to individual vibrational modes. Hence, inconclusive evidence was provided regarding the exact binding nature of the saccharide moieties, although it was clear that the saccharides were involved in coordination through some deprotonated hydroxyl groups as observed from the broad bands in the ν_{O-H} region, 3200–3500 cm^{-1}.

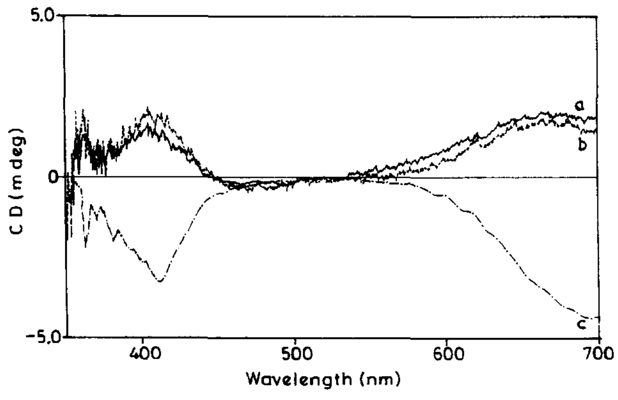

Fig. 2. CD spectra of (a) Ni(II)–D-Glc (**4**), (b) Ni(II)–D-Fru (**5**), and (c) Ni(II)–D-Gal (**6**) complexes in aqueous solution.

Magnetic studies.—Table 1 lists the observed magnetic moments per Ni ion at 298 K for the Ni(II)–saccharide complexes **1**–**9**. The μ_{eff}/Ni were found to be in the range 3.2–4.0μ_B and were within the range of μ_S (2.83μ_B) and μ_{S+L} (4.47μ_B) for the octahedral Ni(II) ion [13]. For the Ni(II) ion (d^8 system) in an octahedral environment, the quenching of orbital angular momentum in the ground state is expected to be complete; however, the deviation from spin-only behaviour suggests some effect of spin–orbit coupling in these complexes due to orbital mixing of the first excited state ($^3T_{2g}$) with the ground state ($^3A_{2g}$). It can be seen that the Ni(II)–D-Glc (**4**) and Ni(II)–D-Gal (**6**) (trinuclear) complexes and Ni(II)–D-Fru (**5**) (tetranuclear) complexes exhibited a lower value of μ_{eff}/ion due to greater quenching of the orbital angular momenta.

X-ray absorption studies.—The FT extended X-ray absorption fine structure (EXAFS) and X-ray absorption near-edge structure (XANES) spectra of the Ni(II)–D-Fru (**2**), Ni(II)–D-Gal (**3**), and Ni(II)–Mal (**9**) complexes in the solid state (Fig. 3) suggest that the Ni environment is predominantly octahedral in these complexes [14]. The peak at 2.04 Å is due to oxygen coordination (first shell), and the apparent coordination number is ~ 4 (with an accuracy of about 20%). It is frequently found that the apparent coordination number is too low due to disorder in the shell. The peak at ca. 3.04 Å is best fitted with a second-shell Ni–Ni interaction with an apparent coordination number of 2; however, interference due to Ni–C scattering at about the same distance cannot be ruled out. The similarity in the spectra of the Ni(II)–D-Fru (**2**), Ni(II)–D-Gal (**3**), and Ni(II)–Mal (**9**) complexes suggests an identical coordination behaviour in these complexes. The presence of several small outer-shell peaks is probably due to Ni(II)–saccharide interactions, which confirms the presence of an ordered interaction between the Ni and the saccharides. Nagy et al. have reported the EXAFS and XANES studies of Ni(II) complexes formed with carbohydrates [15]. These spectral studies supported the distorted octahedral structure of Ni(II) complexes with a mean Ni–O distance of 2.02 Å irrespective of the conformation of the sugar moiety in the molecule. The Ni–C distances in the second and third shells (2.87 and 3.90 Å) were compatible with the values of chelated compounds of Ni(II) [15]. In a similar study on the Fe(III)–fructose complex by the same group [16], the dimerization of the complex was evidenced from the Fe–Fe distance of 3.10 Å. Yano has reported an Ni–Ni distance of 3.28 Å for an Ni(II)–tmen–mannose (where tmen = N,N,N'-trimethylethylenediamine) complex and suggested a polynuclear structure involving N-mannofuranoside bridging [3]. A similar polynuclear structure was also suggested for the D-Rib and D-Lyx complexes involving N-furanoside bridging as observed in the case of the D-Man complex [3]. Thus, in the present case, the peak at 3.04 Å for the Ni(II)–D-Fru (**2**), Ni(II)–D-Gal (**3**), and Ni(II)–Mal (**9**) complexes suggested an unusually strong Ni–Ni interaction in a dimer.

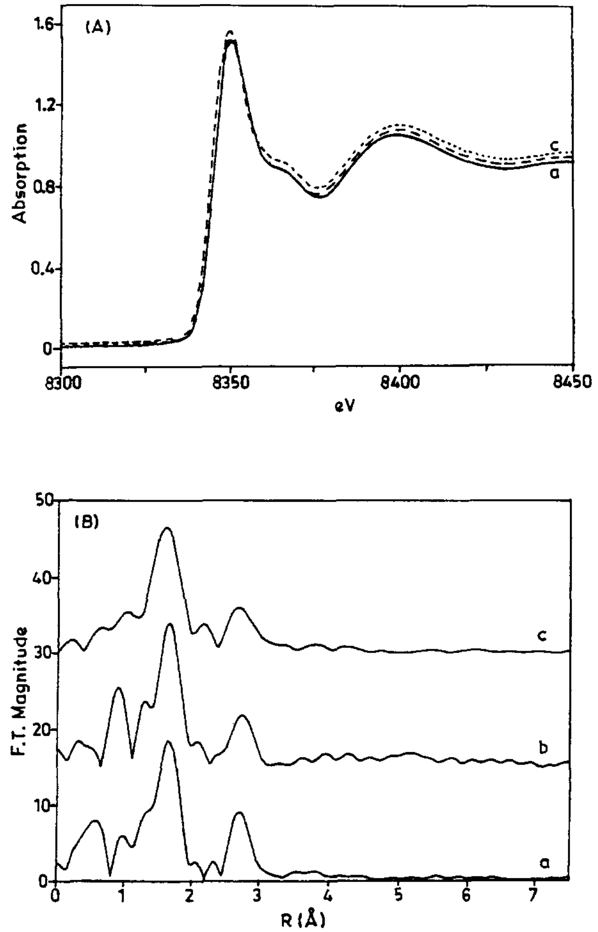

Fig. 3. (A) XANES and (B) FT EXAFS spectra of Ni(II)–saccharide complexes in solid state. (a) Ni(II)–D-Fru (**2**), (b) Ni(II)–Mal (**9**), and (c) Ni(II)–D-Gal (**3**).

Solution stability studies.—The aqueous solution stability of these complexes was studied by observing the rate of hydroxide precipitation from aqueous solutions. The order of hydrolysis among these complexes was found to be as follows: Ni(II)–D-Gal (**3**, **6**) (~ 5 min) ≫ Ni(II)–D-Xyl (**7**) (7–12 h) > Ni(II)–D-Glc (**1**, **4**) (15–20 h) ≥ Ni(II)–Mal (**9**) (18–22 h) > Ni(II)–D-Fru (**2**, **5**) (20–25 h) > Ni(II)–D-Rib

(**8**) (40–45 h), and, therefore, the hydrolytic stability follows a reverse order, i.e., the Ni(II)–D-Rib complex (**8**) is the most stable one. Almost the same order of hydrolysis was observed for Co(II)–saccharide complexes [9]. However, compared to Co(II)–saccharide complexes (where the hydrolysis occurred over a period of 0–15 h), the Ni(II)–saccharide complexes were found to be more stable.

Nature of the products.—The Ni(II)–saccharide complexes **1–9** are hygroscopic in nature and soluble only in water. The complexes were found to be octahedral where Ni(II) is dissymmetrically coordinated to saccharide hydroxyl groups, resulting in differences in their absolute configuration. The proposed molecular formulae of all the complexes are listed in Table 1. While the complexes synthesised from $[NEt_4]_2[NiCl_2Br_2]$ (**1–3** and **9**) were proposed to have dinuclear formulae, those synthesised from $NiCl_2 \cdot 6H_2O$ (**4–8**) exhibited di-, tri-, and tetranuclear formulae, which could be attributed to the differences in the synthetic procedures. However, all of the complexes **1–9** are monoanionic irrespective of the starting material used or the type of saccharide and the nuclearity of the complex. The structures of complexes **2**, **3**, and **9** agree well with the observed EXAFS data. The paramagnetic nature of these complexes (Table 1) was also evidenced from the broadening of proton and ^{13}C NMR signals in the regions 3.5–4.5 ppm and 60–100 ppm, respectively.

4. Conclusions

The synthesis of Ni(II)–saccharide complexes by the procedures reported here has led to the formation of either di-, tri-, or tetra-nuclear complexes, similar to other transition-metal saccharide complexes reported earlier [6–11]. It was proposed that the Ni(II)–D-Gal complexes coordinate through the 3,4-*cis*-diol group and resulted in an inversion of absolute configuration around the distorted octahedral Ni(II) ion as compared to Ni(II)–D-Glc and Ni(II)–D-Fru complexes that utilize 3,4-*trans*-diol groups for coordination. The complexes Ni(II)–D-Fru (**2**), Ni(II)–D-Gal (**3**), and Ni(II)–Mal (**9**) were found to exhibit an unusually strong Ni–Ni interaction, as revealed by EXAFS studies, which to our knowledge is the shortest Ni–Ni distance observed so far in Ni(II) complexes with saccharide type ligands. The formation of Ni(II) complexes with simple saccharides is supported by their existence in mammalian kidneys [1].

Acknowledgements

Financial support from DST and CSIR, New Delhi to C.P.R. is gratefully acknowledged. R.P.B. thanks the CSIR for the award of SRF. We are grateful to Prof. J.E. Penner-Hahn (Michigan, USA) for EXAFS studies. We also thank Prof. S. Mitra and Prof. S. Ramakrishnan (TIFR, Mumbai) for CD spectra and room temperature magnetic measurements, and RSIC (IITB, Mumbai) for ICPAES results.

References

[1] (a) D.M. Templeton and B. Sarkar, *Biochem. J.*, 230 (1985) 35–42; (b) P.F. Predki, D.M. Whitfield, and B. Sarkar, *Biochem. J.*, 281 (1992) 835–841.

[2] (a) S. Deiana, L. Erre, G. Micera, P. Piu, and C. Gessa, *Inorg. Chim. Acta*, 46 (1980) 249–253; (b) G.M. Escandar, L.F. Sala, and M.G. Sierra, *Polyhedron*, 13 (1994) 143–150; (c) J. Lerivrey, B. Dubois, P. Decock, G. Micera, J. Urbanska, and H. Kozlowski, *Inorg. Chim. Acta*, 125 (1986) 187–190; (d) A. Pusino, D. Droma, P. Decock, B. Dubois, and H. Kozlowski, *Inorg. Chim. Acta*, 138 (1987) 5–8; (e) E.B.V. Appelman-Lippens, M.W.G. DeBolster, D.N. Tiemersma, and G. Visser-Luirink, *Inorg. Chim. Acta*, 108 (1985) 209–213; (f) D.M. Whitfield and B. Sarkar, *J. Inorg. Biochem.*, 41 (1991) 157–170.

[3] S. Yano, *Coord. Chem. Rev.*, 92 (1988) 113–156, and references cited therein.

[4] (a) C.P. Rao and S.P. Kaiwar, *Inorg. Chim. Acta*, 186 (1991) 11–12; (b) S.P. Kaiwar and C.P. Rao, *Carbohydr. Res.*, 237 (1992) 203–210.

[5] (a) A. Sreedhara, M.S.S. Raghavan, and C.P. Rao, *Carbohydr. Res.*, 264 (1994) 227–235; (b) A. Sreedhara, C.P. Rao, and B.J. Rao, *Carbohydr. Res.*, 289 (1996) 39–52.

[6] (a) C.P. Rao, S.P. Kaiwar, and M.S.S. Raghavan, *Polyhedron*, 13 (1994) 1895–1906; (b) S.P. Kaiwar, M.S.S. Raghavan, and C.P. Rao, *J. Chem. Soc., Dalton Trans.*, (1995) 1569–1576.

[7] R.P. Bandwar and C.P. Rao, *Carbohydr. Res.*, 287 (1996) 157–168.

[8] (a) C.P. Rao, K. Geetha, and R.P. Bandwar, *Bioorg. Med. Chem. Lett.*, 2 (1992) 997–1002; (b) C.P. Rao, K. Geetha, and M.S.S. Raghavan, *BioMetals*, 7 (1994) 25–29; (c) K. Geetha, S.K. Kulshreshtha, R. Sasikala, and C.P. Rao, *Carbohydr. Res.*, 271 (1995) 163–175.

[9] R.P. Bandwar, M.D. Sastry, R.M. Kadam and C.P. Rao, *Carbohydr. Res.*, (1996), in press.

[10] R.P. Bandwar, C.P. Rao, M. Giralt, J. Hidalgo, and G.U. Kulkarni, *J. Inorg. Biochem.*, (1996), in press.

[11] R.P. Bandwar, M. Giralt, J. Hidalgo, and C.P. Rao, *Carbohydr. Res.*, 284 (1996) 73–84.

[12] (a) S.P. Kaiwar, R.P. Bandwar, M.S.S. Raghavan, and C.P. Rao, *Proc. Indian Acad. Sci. (Chem. Sci.)*, 106 (1994) 743–752; (b) R.P. Bandwar, M.S.S. Raghavan, and C.P. Rao, *BioMetals*, 8 (1995) 19–24.

[13] F.A. Cotton and G. Wilkinson (Eds.), *Advanced Inorganic Chemistry: A Comprehensive Text*, 4th ed., Wiley/Interscience, New York, 1980.

[14] (a) B.K. Teo, *Acc. Chem. Res.*, 13 (1980) 412–419; (b) P.J. Riggs-Gelasco, T.L. Stemmler, and J.E. Penner-Hahn, *Coord. Chem. Rev.*, 144 (1995) 245–286.

[15] L. Nagy, T. Yamaguchi, L. Korecz, and K. Burger, *Metal Ions in Biology and Medicine*, in Ph. Collery, L.A. Poirier, M. Manfait, and J.C. Etienne (Eds.), John Libbey Eurotext, Paris, 1990, pp 558–560.

[16] L. Nagy, H. Ohtaki, T. Yamaguchi, and M. Nomura, *Inorg. Chim. Acta*, 159 (1989) 201–207.