DOHbzo)py]Br, 109863-84-5; [CNCo(DODOHbzo)Iz]Br, 109863-85-6; $[CH_3Co(DODOHbzo)py]ClO_4$, 109889-31-8; $[CH_3Co(DODOHbzo)Iz]ClO_4$, 109863-87-8; $[CH_3Co(DODOHbzo)PPh_3]ClO_4$, 109863-89-0; $[CH_3Co(DODOHbzo)Me_2BIz]ClO_4$, 109863-91-4; $[C_2H_5Co(DODOHbzo)py]ClO_4$, 109863-93-6; $[C_2H_5Co(DODOHbzo)Iz]ClO_4$, 109863-95-8; [*i*-PrCo(DODOHbzo)py]ClO_4, 109863-97-0; $[C_6H_4CH_2Co(DODOHbzo)py]ClO_4$, 109863-99-2; $[C_6H_{11}Co(DODOHbzo)py]ClO_4$, 109864-01-9; $[Co\{(DO)_2bzoBF_2\}Br_2]$, 109864-02-0; $(DOH)_2bzo$, 75389-07-0; 2,3-butanedione monoxime, 57-71-6; *o*-phenylenediamine, 95-54-5; methyl iodide, 74-88-4; ethyl iodide, 75-03-6; isopropyl bromide, 75-26-3; iodocyclohexane, 626-62-0; benzyl chloride, 100-44-7; vitamin B_{12}, 68-19-9; vitamin B_{12} coenzyme, 13870-90-1.

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Reaction of $[Ni(H_2O)_2(N,N'\text{-}Me_2\text{-}en)_2]^{2+}$ with Carbohydrates. Synthesis and Characterization of a Novel μ-Mannofuranoside Binuclear Nickel(II) Complex Containing *N*-Glycosides

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An unprecedented binuclear nickel(II) complex containing two types of *N*-glycosides formed from *N,N'*-dimethylethylenediamine (*N,N'*-Me_2-en) and D-mannose (D-Man) was synthesized, and its structure was determined by X-ray crystallography. The complex (μ-Man)[$Ni_2(CH_3OH)$(*N*-(D-Man)-*N,N'*-Me_2-en)(*N,N'*-(D-Man)$_2$-*N,N'*-Me_2-en)]$Cl_2\cdot 2CH_3OH\cdot H_2O$ forms orthorhombic crystals with a = 19.647 (35) Å, b = 17.169 (8) Å, c = 13.247 (4) Å, Z = 4, in space group $P2_12_12_1$, where *N*-(D-Man)-*N,N'*-Me_2-en is 1-(*N*-methyl-D-mannosylamino)-2-(methylamino)ethane and *N,N'*-(D-Man)$_2$-*N,N'*-Me_2-en is 1,2-bis(*N*-methyl-D-mannosylamino)ethane. The structure was solved by direct methods followed by least-squares and Fourier techniques. Refinement using 2199 reflections with $|F_o| > 3\sigma(|F_o|)$ gave R = 0.077 and R' = 0.087. The metal center is surprisingly a binuclear nickel complex with a bridging mannose residue. Both nickel atoms have distorted-octahedral geometry, and the Ni···Ni separation is 3.596 (4) Å, indicating that no appreciable metal-metal bonding is present. One of the nickel atoms is coordinated with a methanol and an *N*-glycoside, *N,N'*-(D-Man)$_2$-*N,N'*-Me_2-en. The other nickel is coordinated with a tridentate *N*-glycoside, *N*-(D-Man)-*N,N'*-Me_2-en, and a part of the bridging sugar moiety of *N,N'*-(D-Man)$_2$-*N,N'*-Me_2-en. The bridging sugar ring takes the unusual furanose ring, and the other two sugar rings adopt the usual β-$^4C_1$ chair conformation. When D-glucose was used as a starting sugar instead of D-mannose, a nickel(II) complex containing D-mannose was surprisingly obtained.

Introduction

The interactions of carbohydrates with metals have been of interest in recent years, above all in the field of industry and biochemistry in connection with metal-containing enzymes. In spite of the fact that it has been well-known that sugars can form complexes with various metal ions, those transition-metal complexes containing carbohydrates that were confirmed by their structural details are very few[3] and the field of sugar-metal complexes is still largely unexplored.

In order to elucidate the carbohydrate-transition-metal interaction, we have systematically studied the synthesis and characterization of transition-metal complexes containing *N*-glycosides derived from the reaction of sugars and diamines. During our investigations, the structures of [Ni(en)(D-Fru-en)]$Cl_2\cdot CH_3OH$[4] (**1**), [Ni(en)(L-Sor-en)]$Cl_2\cdot {}^1/_2CH_3OH$[5] (**2**), $[Ni(D\text{-}GlcN\text{-}en)_2]Br_2\cdot 4H_2O$[6] (**3**), and $[Ni(L\text{-}Rha\text{-}tn)_2]Br_2\cdot 2H_2O\cdot CH_3OH$[7] (**4**), and [Ni(*S*-ampr)(L-Sor-*S*-ampr)]$Cl_2\cdot CH_3OH\cdot H_2O$[8] (**5**) [Fru = fructose, Sor = sorbose, Glc = glucose, GlcN = 2-amino-2-deoxyglucose, Rha = 6-deoxymannose, en = ethylenediamine, tn = trimethylenediamine, and ampr = 2-aminomethylpyrrolidine) were determined by X-ray crystallography. The crystal structures of **3** and **4** revealed that an *N*-glycoside from an aldose and a diamine attaches to the nickel atom through the oxygen atom of the hydroxyl group on C-2 of the sugar moiety and through the two nitrogen atoms of the diamine residue, and the two tridentate *N*-glycoside ligands complete a distorted-octahedral coordination around the nickel atom in the meridional mode.[6,7] From these results, it is clear that diamines play an important role in anchoring sugars to metal. It is often observed that the *N*-alkyl groups on the coordinating nitrogen atoms influence the stereochemistry of metal complexes. Prompted by this knowledge, we have chosen *N,N'*-dimethylethylenediamine (*N,N'*-Me_2-N) as a diamine component with the hope of verifying the coordination behavior of *N*-glycoside ligands. Of many aldoses, only in the case using D-mannose, have we obtained the very unprecedented binuclear Ni(II) complex containing *N*-glucosides in moderate yield. To clarify the stereochemistry of this complex, we have undertaken an X-ray crystal structure determination. To elucidate further this specific formation of the binuclear complex, we examined other aldoses and their derivatives as starting sugars. A preliminary account of this work has already appeared.[9]

Experimental Section

Materials. All reagents were of the best commercial grade. [Ni$(H_2O)_2(N,N'\text{-}Me_2\text{-}en)_2]X_2$ (X = Cl, Br) complexes were prepared by the known method.[10] The following abbreviations are used: *N*-(D-Man)-*N,N'*-Me_2-en, 1-(*N*-methyl-D-mannosylamino)-2-(methylamino)ethane; *N,N'*-(D-Man)$_2$-*N,N'*-Me_2-en, 1,2-bis(*N*-methyl-D-mannosylamino)-ethane.

Preparation of the Complexes (μ-Man)[$Ni_2(CH_3OH)$(*N*-(D-Man)-*N,N'*-Me_2-en)(*N,N'*-(D-Man)$_2$-*N,N'*-Me_2-en)]$Cl_2\cdot 2CH_3OH\cdot H_2O$ (6) and (μ-Man)[$Ni_2(CH_3OH)$(*N*-(D-Man)-*N,N'*-Me_2-en)(*N,N'*-(D-Man)$_2$-*N,*-

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N'-Me_2-en)]Br_2·4H_2O (7). To a solution of 2.90 mmol of $[Ni(H_2O)_2(N,N'\text{-}Me_2\text{-}en)_2]Cl_2$ in 50 mL of methanol was added 8.70 mmol of D-mannose. The solution was incubated at 65 °C for 15 min with stirring. The color of solution changed from blue to green; then the green solution was concentrated to about 30 mL by a rotary evaporator at 25 °C, loaded onto a LH-20 gel permeation column, and eluted with methanol. The colored material separated into two major blue-green bands and two minor yellow ones. The blue-green fraction eluted faster is designated Man1(Cl), and the one eluted slower, Man2(Cl). After a few purifications on LH-20 gel, the Man1(Cl) fraction was concentrated to about 10 mL and kept at 5 °C in a refrigerator. The blue-green crystals were obtained from the solution and were recrystallized from a minimum amount of hot methanol. The crystals were collected and washed with ethanol followed by ether and were dried in vacuo (yield 38% based on the starting nickel ions). Anal. Calcd for (μ-Man)[Ni_2-(CH_3OH)(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]-Cl_2·solvent[11] (**6**), $C_{27}H_{56}N_4O_{16}Ni_2Cl_2$·$CH_3OH$·5$H_2O$: C, 33.51; H, 7.03; N, 5.59; Ni, 11.70; Cl, 7.07. Found: C, 33.01; H, 6.68; N, 5.77; Ni, 12.10; Cl, 7.35. The Man2(Cl) compound is too hygroscopic to isolate as a solid and is apt to decompose to the starting materials. When D-mannose was treated with $[Ni(H_2O)_2(N,N'\text{-}Me_2\text{-}en)_2]Br_2$ in the manner described above, the Man1(Br) complex corresponding to Man1(Cl) was obtained as a powder (yield 39%). Anal. Calcd for (μ-Man[Ni_2-(CH_3OH)(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]-Br_2·4H_2O (**7**), $C_{27}H_{56}N_4O_{16}Ni_2Br_2$·4$H_2O$: C, 31.12; H, 6.19; N, 5.38; Ni, 11.26; Br, 15.34. Found: C, 30.51; H, 5.59; N, 5.36; Ni, 11.10; Br, 15.27.

Experiments Using Several Analogues of D-Mannose. Methyl-α-D-mannoside, 2,3,4,6-tetra-*O*-methyl-D-mannose, 2-deoxy-D-mannose, 6-deoxy-L-mannose (L-rhamnose), D-talose, D-xylose, D-lyxose, and D-galactose were examined by experimental methods similar to those described previously. In all cases, any complexes corresponding to Man1-(Cl) have not been obtained. When D-glucose was used as a substrate, a green complex, Glc1(Cl) (**8**), corresponding to Man1(Cl) was obtained as purified solution in a 4% yield, which was determined by atomic absorption spectroscopy.

Measurements. Magnetic susceptibilities were measured at room temperature by the Faraday method using a Shimazu MB-100 Model magnetic balance. Diamagnetic corrections were calculated from tables of Pascal's constants.[12] Visible and near-infrared absorption spectra and reflectance spectra were measured with a Hitachi Model 340 recording spectrophotometer. Circular dichroism spectra were recorded on a Jasco J-500 recording spectropolarimeter. Molar conductivities were determined at room temperature in methanol by using a Model AOC-10 electronic chemical instrument. Nickel concentrations were measured with a Shimazu AA-646 atomic absorption spectrophotometer.

Recovery of Sugars. The complexes Man1(Cl) (**6**) and Glc1(Cl) (**8**) (purified methanolic solution) were dissolved in water. Each solution was kept at pH 6.8 with 1.0 N H_2SO_4 and stirred for 1 h at room temperature. Then the reaction mixture was treated with excess Dowex 50-X8 (H^+) followed by Dowex 1-X2 (HCO_3^-) resin to remove the Ni(II) complexes and chloride anion prior to high-performance liquid chromatography (HPLC). Monosaccharides contained in the solution were confirmed by a TSK HLC-803D chromatographic system using a column of anion-exchange resin. Sugar components were eluted successively with 0.5 M borate buffer adjusted to pH 8.5 and fluorometrically detected by the reaction with 2-cyanoacetamide.[13]

Crystal Data and Intensity Measurements for (μ-Man)[Ni_2-(CH_3OH)(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]-Cl_2·2CH_3OH·H_2O (6). The blue-green block-shaped crystals of the title complex were grown from saturated methanolic solution. In open air the crystals decomposed and lost clearness within a few hours, so a crystal sealed into a glass tube capillary (0.7-mm o.d.) in the presence of a small droplet of the mother liquid[14] was used to collect diffraction data at room temperature on a Rigaku AFC-4 four-circle automated diffractometer; in this case the crystal lattice remained unaltered at least for a few days. Intensities of three standard reflections monitored every 100 reflections exhibited a time-dependent intensity decrease over the course of data collection, and after about 40 h these intensities decreased to 90% of the initial values. At this stage, we exchanged the crystal used with a fresh one, which necessitated the use of four crystals (0.5 × 0.3 × 0.3, 0.3 × 0.1 × 0.1, 0.3 × 0.1 × 0.1, 0.5 × 0.3 × 0.3 mm) to collect adequate diffraction data for the refinement. The unit cell dimensions were determined in a right-hand system ($a > b > c$) by a least-squares method with 20 reflections in the range $20 < 2\theta < 30°$ for each crystal, and the arithmetic mean of four results was used as the accurate unit cell dimensions. Reflections in the one-eighth reciprocal space ($h \geq 0$, $k \geq 0$, $l \geq 0$) were collected for four crystals to cover the sphere of radius $2\theta \leq 44°$. These procedures gave four data sets that overlap one another with about 200 reflections, and for each, data were corrected for the decrease in intensity and scaled by the use of intensities of standard reflections that were common to four crystals. Then four data sets were combined and scaled again with standard reflections to give an averaged reflection data set, which was used in the subsequent structure solution and refinement. Intensities were corrected for lorentz and polarization effects. No absorption correction was made since μ (10.7 cm^{-1}) was low. The crystallographic and experimental data are summarized in Table I.

Table I. Crystal Data for (μ-Man)[Ni_2(CH_3OH)(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]Cl_2·2CH_3OH·H_2O

formula	$Ni_2C_{27}H_{56}N_4O_{16}Cl_2$·2$CH_3OH$·$H_2O$
mol wt	963.14
cryst syst	orthorhombic
space group	$P2_12_12_1$
a, Å	19.647 (35)
b, Å	17.169 (8)
c, Å	13.247 (4)
V, Å^3	4468 (5)
d(obsd), g cm^{-3}	1.47
d(calcd), g cm^{-3}	1.43
Z	4
λ, Å	0.7107 (Mo Kα)
scan method	θ–2θ
μ, cm^{-1}	10.7[a]
scan speed, deg min^{-1}	4
2θ limit, deg	44
stds	3 every 100 rflcns
no. of data	ca. 4000.
no. of obsd. data	2199 ($\|F_o\| > 3\sigma(\|F_o\|)$)
no. of variables	684[b]
R	0.077
R′	0.087

[a] No absorption correction was made since μ was low. Transmission factor ranges for four crystals: 0.73–0.50 (crystal 1); 0.90–0.70 (crystal 2); 0.90–0.70 (crystal 3); 0.73–0.50 (crystal 4). [b] The data:variable ratio is 3.21, and such a low ratio may result in an artificially low *R* value.

Structure Solution and Refinement. The structure was solved by direct methods with the MULTAN 78 program.[15] The two nickel atoms were located in the initial *E* maps, and subsequent Fourier syntheses gave the positions of other non-hydrogen atoms. The structure was refined by block-diagonal least-squares techniques. All hydrogen atoms, other than those of hydroxyl groups and solvent molecules, were located with calculation by assuming a tetrahedral coordination with a C–H bond distance of 1.09 Å and an N–H bond distance of 1.03 Å. The final refinement was carried out in the following manner: non-hydrogen atoms were refined anisotropically and the hydrogen atoms were refined with isotropic temperature factors to give values of $R = \sum||F_o| - |F_c||/\sum|F_o| = 0.077$ and $R' = (\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2)^{1/2} = 0.087$ (unit weight given to all reflections). The atomic scattering factors were taken from ref 16. The known absolute configurations of the asymmetric carbon atoms of D-mannose were used as internal references for asymmetric centers to determine the absolute configuration of the complex. The effects of anomalous dispersion were included in F_c; values of f' f'' for Ni, Cl, O, N, and C were taken from Cromer's tabulation.[17] When the coordinates were inverted at the stage $R = 0.085$ and $R' = 0.110$ in order to test the structure, convergence was reached with $R = 0.088$ and $R' = 0.112$, which are higher than the corresponding values 0.085 and 0.110.

(11) Although the present crystallography indicates two methanols and one water of crystallization, "CH_3OH·5H_2O" as the solvent molecules gives the best fit to the values of elemental analysis. This difference is thought arise from the fact that the hygroscopic crystals are likely to absorb water molecules of atmosphere during the course of purification for elemental analysis and are apt to lose methanol on drying in vacuo.

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Table IIa. Final Positional Parameters[a]

atom	x	y	z	B_{eq}, Å^2
Ni(1)	2291 (1)	3065 (2)	1058 (2)	2.9
Ni(2)	2073 (1)	1981 (2)	-1220 (2)	3.3
O(1)	1331 (6)	2660 (8)	943 (10)	3.3
O(2)	-39 (7)	2164 (9)	1046 (13)	5.2
O(3)	-36 (8)	1369 (11)	2963 (12)	6.1
O(4)	1447 (7)	2658 (8)	3121 (11)	3.8
O(5)	1835 (9)	1165 (11)	3483 (14)	7.0
O(6)	3334 (6)	3364 (8)	1226 (12)	4.1
O(7)	2640 (6)	2590 (7)	-233 (10)	3.1
O(8)	2988 (6)	4106 (8)	-1261 (11)	4.4
O(9)	2223 (7)	2904 (8)	-2210 (9)	3.7
O(10)	2996 (8)	1648 (10)	-1995 (12)	5.7
O(11)	1151 (6)	2440 (8)	-829 (10)	3.3
O(12)	-141 (7)	3115 (10)	-610 (2)	5.1
O(13)	-191 (7)	3922 (10)	-2500 (14)	5.7
O(14)	1019 (8)	2313 (8)	-3004 (11)	4.3
O(15)	1478 (8)	3781 (10)	-3630 (12)	5.6
O(16)	2512 (7)	2025 (9)	1873 (11)	4.6
N(1)	2312 (9)	4169 (8)	263 (13)	3.3
N(2)	1868 (9)	3724 (10)	2261 (12)	3.8
N(3)	2020 (9)	1052 (10)	-214 (14)	4.5
N(4)	1390 (9)	1262 (11)	-2122 (14)	4.5
C(1)	2290 (11)	4739 (11)	1106 (18)	4.1
C(2)	1686 (13)	4516 (14)	1866 (18)	4.9
C(3)	1241 (12)	3322 (14)	2561 (18)	4.7
C(4)	876 (10)	3033 (13)	1591 (16)	3.9
C(5)	290 (11)	2486 (14)	1856 (19)	4.8
C(6)	556 (11)	1818 (13)	2578 (15)	4.0
C(7)	939 (12)	2154 (13)	3449 (16)	4.6
C(8)	1323 (18)	1521 (18)	4088 (18)	7.7
C(9)	2315 (13)	3818 (12)	3195 (20)	5.4
C(10)	1757 (11)	4304 (14)	-456 (18)	4.7
C(11)	3008 (11)	4232 (12)	-211 (17)	3.9
C(12)	3469 (10)	3564 (14)	207 (19)	4.8
C(13)	3273 (9)	2870 (11)	-498 (15)	3.3
C(14)	3263 (9)	3357 (11)	-1530 (18)	4.0
C(15)	2937 (11)	3013 (14)	-2427 (16)	4.5
C(16)	3224 (12)	2227 (16)	-2692 (19)	6.0
C(17)	1439 (17)	658 (18)	-391 (29)	10.5
C(18)	1197 (12)	555 (12)	-1435 (22)	5.3
C(19)	804 (13)	1728 (13)	-2289 (19)	5.5
C(20)	578 (9)	2100 (12)	-1279 (17)	3.8
C(21)	38 (11)	2791 (14)	-1475 (19)	5.1
C(22)	304 (11)	3337 (13)	-2275 (21)	5.2
C(23)	537 (11)	2924 (15)	-3252 (18)	5.1
C(24)	850 (13)	3435 (14)	-4003 (19)	5.5
C(25)	2576 (14)	569 (15)	-136 (22)	6.5
C(26)	1630 (14)	965 (14)	-3097 (19)	5.6
C(27)	3166 (12)	1658 (17)	2067 (23)	7.6
Cl(1)	4165 (3)	4658 (4)	2165 (6)	5.8
Cl(2)1	801 (38)	6272 (44)	-339 (40)	46.2
Cl(2)2	-557 (33)	4688 (32)	-191 (53)	24.5
Cl(2)3	0 (30)	4600 (45)	0 (64)	18.3
Cl(2)4	293 (45)	5796 (58)	-825 (75)	18.3
O(1)′	3526 (8)	186 (8)	-2798 (12)	5.1
O(2)′	-110 (12)	23 (15)	1979 (22)	11.4
O(3)′	4010 (22)	1391 (29)	4669 (33)	24.5
C(1)′	4082 (16)	415 (15)	-2105 (28)	9.3
C(2)′	-221 (18)	35 (19)	841 (21)	8.9

[a] Values are multiplied by 10^4; estimated standard deviations are given in parentheses.

This result agreed with the earlier determination using the known absolute configurations of the D-mannose residues. Final difference Fourier synthesis still showed peaks at heights up to 0.6 e/Å^3 around the solvent atoms. The final positional parameters and the final thermal parameters are listed in Table II.[18] Compilations of observed and calculated structure factors are available as supplementary material. All calculations were performed on a FACOM M-380 computer at the Computer Center of the Institute of Physical and Chemical Research. Programs used were the UNICS III universal computing program[19] and MULTAN 78 (direct method).[15]

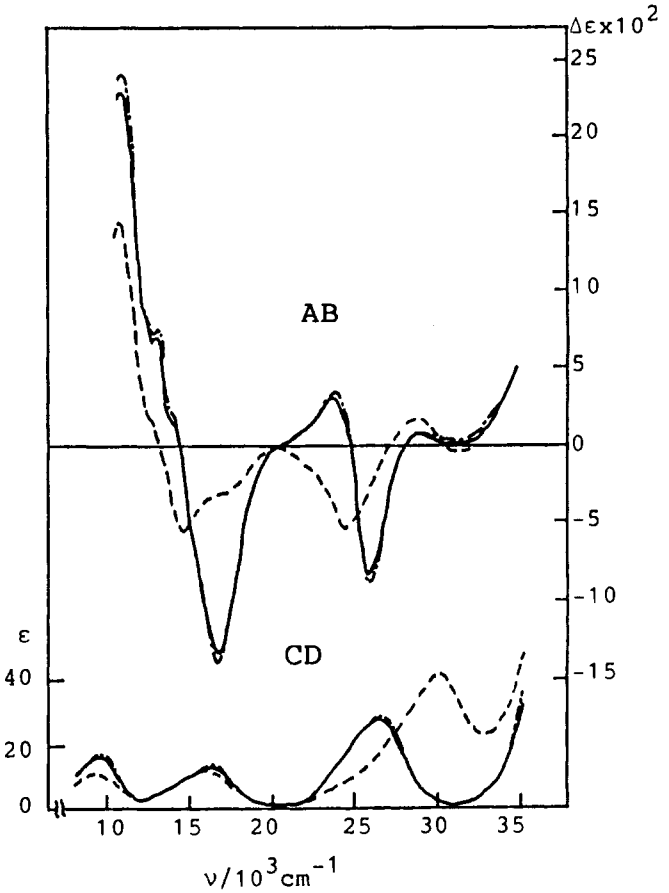

Figure 1. Absorption and circular dichroism spectra: —, Man1(Cl) (**6**); -·-, Man1(Br) (**7**); ---, Glc1(Cl) (**8**).

Results and Discussion

When $[Ni(H_2O)_2(N,N'\text{-}Me_2\text{-}en)_2]X_2$ (X = Cl, Br) complexes are refluxed in methanol for 15–20 min with 3 equiv of aldose (D-mannose, D-glucose, D-galactose, D-talose, D-xylose, or D-lyxose), only in the case using D-mannose as a starting sugar, have we obtained stable blue-green complexes, Man1(Cl) (**6**) and Man1(Br) (**7**), in moderate yields. In addition, D-glucose treated with $[Ni(H_2O)_2(N,N'\text{-}Me_2\text{-}en)_2]Cl_2$ gave a green complex, Glc1(Cl) (**8**), as a purified solution corresponding to the Man1(Cl) complex, although its yield was very low. Other aldoses and their derivatives gave no stable complex. Thus, a selective complexation was observed when the secondary diamine, *N*,*N*′-Me_2-en, was used. This is partly attributable to the fact that the *N*-glycosidic bonds formed from secondary amines and aldoses are more labile than those from primary amines.[20] Further, we characterized complexes **6** and **7** to clarify this selective complexation.

Analytical data indicated that the complexes Man1(Cl) (**6**) and Man1(Br) (**7**) contain three monosaccharide residues and two diamine moieties for two nickel(II) atoms. The magnetic moments of these complexes are 3.38 and 3.25 μ_B, which fall within the range reported for octahedral complexes of nickel(II)[21] and indicate no direct spin–spin interaction between the two nickel atoms. The near-infrared–visible absorption and circular dichroism spectra of **6** and **7** in methanol are illustrated in Figure 1, and representative spectral data and reflectance spectral data are presented in Table III. No significant differences are observed between the spectra of the solid and the methanolic solution except for the typical lower resolution obtained from the reflectance spectra. It shows no gross changes in electronic or geometrical structures that might occur on dissolution. The solution spectra of **6** and **7** in

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Table III. Electronic Absorption, Circular Dichroism, and Reflectance Spectral Data

complex	AB max,[a] 10^3 cm^{-1} (ϵ, M^{-1} cm^{-1})	CD max,[a] 10^3 cm^{-1} ($10^2\Delta\epsilon$, M^{-1} cm^{-1})	ref max, 10^3 cm^{-1}
(μ-Man)[$Ni_2(CH_3OH)$(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]Cl_2·2CH_3OH·H_2O (**6**)	9.5 (16.9) 16.3 (13.3) 26.3 (28.3)	10.3 (+23.0) 16.6 (−13.3) 23.3 (+3.2) 25.6 (−8.4)	9.8 16.3 26.5
(μ-Man)[$Ni_2(CH_3OH)$(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]Br_2·4H_2O (**7**)	9.6 (18.4) 16.4 (14.1) 26.3 (29.0)	10.2 (+24.2) 16.5 (−13.8) 23.4 (+3.4) 25.6 (−8.8)	9.7 16.4 26.3

[a] In methanolic solution.

Table IV. Selected Bond Distances (Å)[a]

Ni(1)---Ni(2)	3.596 (4)	Ni(1)–O(1)	2.02 (1)
Ni(1)–O(6)	2.12 (1)	Ni(1)–O(7)	2.02 (1)
Ni(1)–O(16)	2.15 (2)	Ni(1)–N(1)	2.19 (2)
Ni(1)–N(2)	2.13 (2)	Ni(2)–O(7)	2.02 (1)
Ni(2)–O(9)	2.09 (1)	Ni(2)–O(10)	2.16 (2)
Ni(2)–O(11)	2.04 (1)	Ni(2)–N(3)	2.10 (2)
Ni(2)–N(4)	2.19 (2)	O(1)---O(11)	2.41 (2)
O(2)---O(12)	2.76 (2)		

[a] Estimated standard deviations are given in parentheses.

Table V. Selected Bond Angles (deg)[a]

O(1)–Ni(1)–O(6)	173.6 (6)	O(1)–Ni(1)–O(7)	96.3 (5)
O(1)–Ni(1)–O(16)	86.1 (5)	O(1)–Ni(1)–N(1)	106.7 (6)
O(1)–Ni(1)–N(2)	83.2 (6)	O(6)–Ni(1)–O(7)	82.1 (5)
O(6)–Ni(1)–O(16)	87.7 (5)	O(6)–Ni(1)–N(1)	79.5 (6)
O(6)–Ni(1)–N(2)	99.5 (6)	O(7)–Ni(1)–O(16)	90.7 (5)
O(7)–Ni(1)–N(1)	86.9 (6)	O(7)–Ni(1)–N(2)	170.3 (6)
O(16)–Ni(1)–N(1)	167.2 (6)	O(16)–Ni(1)–N(2)	99.0 (6)
N(1)–Ni(1)–N(2)	84.0 (6)	O(7)–Ni(2)–O(9)	85.7 (5)
O(7)–Ni(2)–O(10)	89.3 (6)	O(7)–Ni(2)–O(11)	96.8 (5)
O(7)–Ni(2)–N(3)	91.2 (6)	O(7)–Ni(2)–N(4)	172.7 (6)
O(9)–Ni(2)–O(10)	77.9 (6)	O(9)–Ni(2)–O(11)	89.1 (5)
O(9)–Ni(2)–N(3)	174.8 (6)	O(9)–Ni(2)–N(4)	100.6 (6)
O(10)–Ni(2)–O(11)	165.2 (6)	O(10)–Ni(2)–N(3)	97.9 (7)
O(10)–Ni(2)–N(4)	95.7 (7)	O(11)–Ni(2)–N(3)	95.5 (6)
O(11)–Ni(2)–N(4)	79.7 (6)	N(3)–Ni(2)–N(4)	82.8 (7)
Ni(1)–O(7)–Ni(2)	125.2 (6)		

[a] Estimated standard deviations are given in parentheses.

the near-infrared and visible regions consist of three principal bands with comparatively low intensities, which are characteristic of octahedral nickel(II) complexes,[22] and the spectra of **6** and **7** are almost identical, indicating that no halide anion coordinates to the metal center. The frequencies of the first and second band maxima shift to lower energy compared with those of complexes **1**, **2**, **4**, and **5**, which shows that complexes **6** and **7** are [$Ni^{II}N_2O_4$] type. The molar conductivity of Man1(Cl) (**6**) in methanolic solution is 162.2 ohm^{-1} cm^2 mol^{-1}, which falls within the range for 2:1 electrolytes in methanol.[22] Monosaccharides contained Man1(Cl) (**6**) are recovered by hydrolysis of *N*-glycosides and confirmed by HPLC. Of the obtained sugar components, more than 99% are D-mannose, indicating that complex **6** contained only D-mannose as a sugar component.

X-ray Crystal Structure of (μ-Man)[$Ni_2(CH_3OH)$(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]Cl_2·2CH_3OH·H_2O (6). A perspective view of the (μ-Man)[Ni_2(CH_3OH)(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]$^{2+}$ cation showing ellipsoids of thermal motion is given in Figure 2, and some selected bond distances and bond angles are listed in Tables IV and V. The metal center of the complex is surprisingly binuclear with a D-mannose residue linking the two nickel atoms. So far as we know, this is the first X-ray crystal structural determination of binuclear nickel(II) complexes containing sugar moieties. The Ni(1) atom is coordinated with a methanol and with *N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en (Figure 3a)

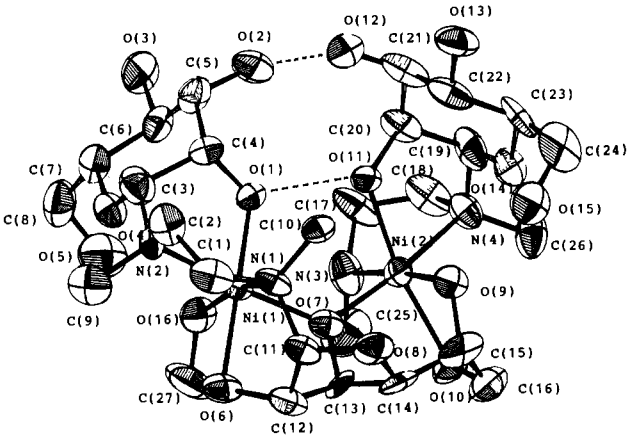

Figure 2. ORTEP view of the (μ-Man)[$Ni_2(CH_3OH)$(*N*-(D-Man)-*N*,*N*′-Me_2-en)(*N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en)]$^{2+}$ ion with the atomic numbering scheme.

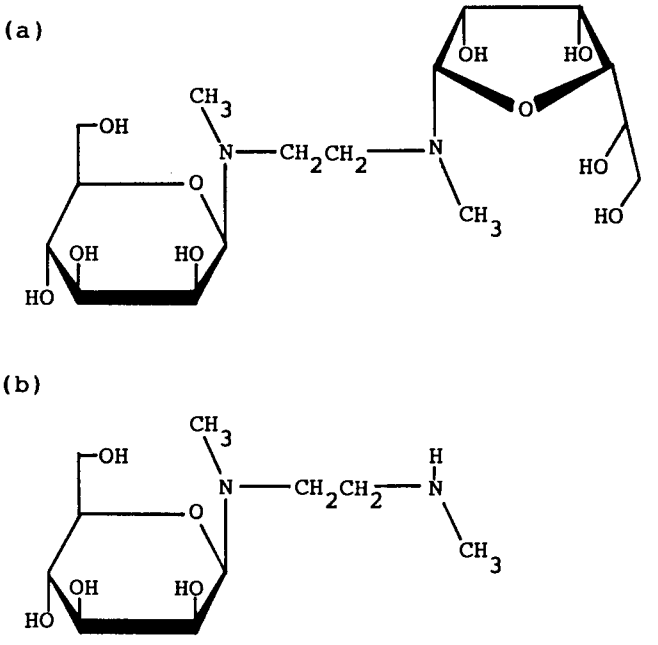

Figure 3. Structures of *N*-glycosides: (a) *N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me_2-en; (b) *N*-(D-Man)-*N*,*N*′-Me_2-en.

through the two nitrogen atoms of the diamine moiety and the C-2 hydroxyl group of the mannose residue taking the pyranose form and through the C-2 and C-3 oxygen atoms of the other mannose moiety taking the furanose form. The Ni(2) atom is coordinated with *N*-(D-Man)-*N*,*N*′-Me_2-en (Figure 3b) through the two nitrogen atoms of the diamine residue and through the C-2 hydroxyl group of the mannopyranose moiety and with a part of the bridging mannofuranose through the oxygen atoms on C-3, C-5, and C-6. Both nickel atoms of the complex cation have distorted octahedral coordination geometry. The distance between Ni(1) and Ni(2) is 3.596 (4) Å, indicating that no appreciable metal–metal bonding is present, and that between O(2) and O(12)

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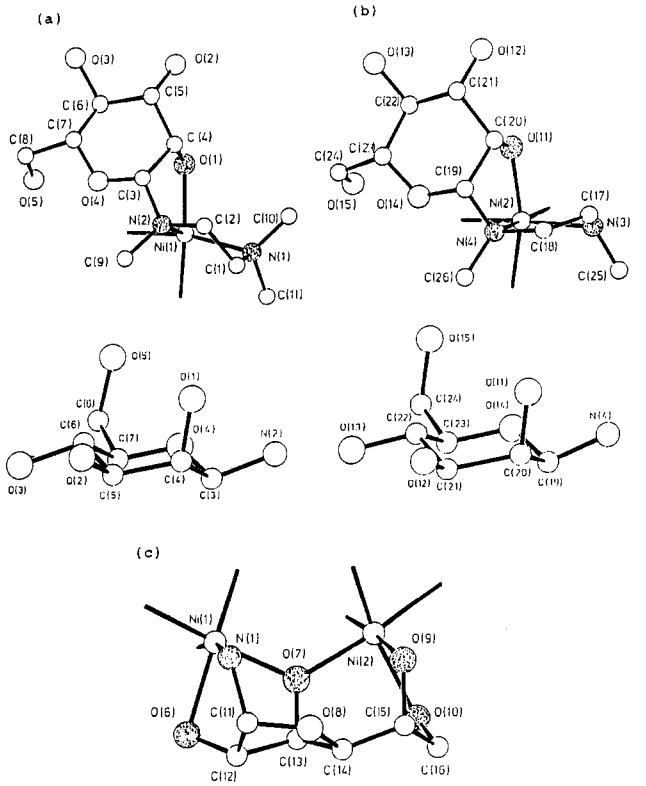

Figure 4. ORTEP views with atomic numbering schemes: (a) mannose-A component; (b) mannose-B component; (c) mannose-C component. The atomic radii are used to give the obvious views.

is 2.76 (2) Å, which is thought forming hydrogen bonding.

The molecules of D-mannose left above, right above, and below the center of the complex cation in Figure 2 are designated mannose-A, mannose-B, and mannose-C, respectively. The mannose-A moiety contained in the *N*-glycoside *N*,*N*′-(D-Man)$_2$-*N*,*N*′-Me$_2$-en takes the β-$^4C_1$ chair conformation and coordinates to Ni(1) at two points through the glycosidic nitrogen atom and hydroxyl oxygen atom on C-2 (Figure 4a). The tridentate ligand, *N*-(mannose-A)-*N*,*N*′-Me$_2$-en, attaches to the metal in the facial mode owing to the steric hindrance of the *N*-methyl group, unlike the case for complexes **3** and **4**. The glycosidic nitrogen configuration is found to be *S* in the notation of Cahn, Ingold, and Prelog.[23] The diamine chelate ring (Ni(1)–N(1)–C(1)–C(2)–N(2)) has the asymmetrical δ-gauche conformation, which is opposite to that of en in complex **3**, and the five-membered chelate ring involving the sugar moiety (Ni(1)–O(1)–C(4)–C(3)–N(2)) adopts the asymmetrical δ-gauche form but is significantly flattened. These chelate conformations indicate that the conformation of a five-membered chelate ring involving a sugar moiety will be determined from the absolute configuration of C-2 of the sugar residue,[4] but that of a diamine chelate ring is apt to undergo modifications so as to releave the strain. The mannose-B moiety forming the *N*-glycoside *N*-(D-Man)-*N*,*N*′-Me$_2$-en also has the stable β-$^4C_1$ chair conformation and coordinates to Ni(2) at three points in the facial mode through the two nitrogen atoms and through the hydroxyl oxygen atom on C-2 in a manner similar to that of the mannose-A component (Figure 4b). The absolute configuration of the glycosidic nitrogen atom is *S*, and that of the other secondary nitrogen atom is *R*. The diamine chelate ring (Ni(2)–N(3)–C(17)–C(18)–N(4)) adopts the envelope form, which deviates from a λ-gauche conformation, and another five-membered chelate ring involving the sugar moiety (Ni(2)–N(4)–C(19)–C(20)–O(11)) has the flattened asymmetrical δ-gauche form. A perspective drawing of mannose-C is given in Figure 4c. This part has the most conspicuous characteristics of the complex cation. Mannose-C takes the unusual

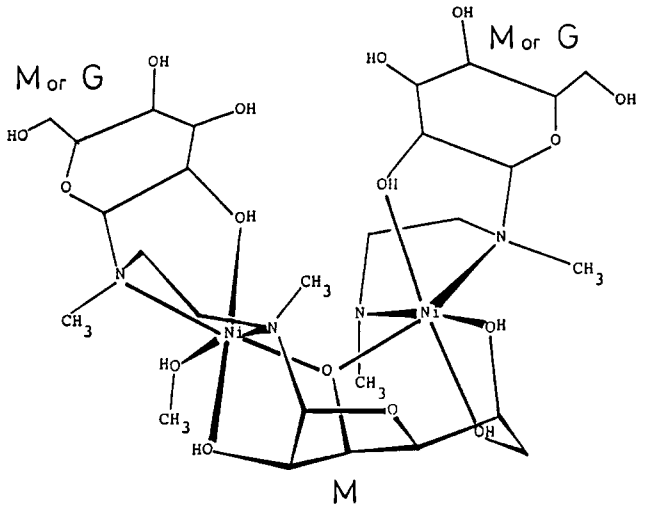

Figure 6. Estimated structure of Glc1(Cl) (**8**). M = D-mannose; G = D-glucose.

β-furanose form, linking two nickel(II) atoms with the oxygen bridge of the C-3 hydroxyl group; furthermore, it attaches to Ni(1) through the glycosidic nitrogen atom and C-2 hydroxyl oxygen atom and to Ni(2) through the C-5 and C-6 hydroxyl oxygen atoms. Thus, all donor atoms of mannose-C are used to complete the binuclear complex. This form of D-mannose is fairly rare as far as we know, but it seems to be the most suitable form to link two nickel atoms, because in the furanose form all donor atoms are pushed out of the ring plane in the same direction. In the case of D-lyxose with Mo(VI), Taylor and Waters showed that D-lyxose takes a furanose form and links two Mo(VI) atoms with a double oxygen bridge.[3c] The present complex is very similar to that case. The furnanose ring conformation of mannose-C is close to the ^3E envelope form, considering torsional angles around the furanose ring and the best-plane calculations (Tables VI and VII[18]).

The bite angles around the nickel atoms for the five-membered chelate ring range from 77.9 (6) to 84.0 (6)° (Table V), which were normal for Ni(II) five-membered chelate rings.[24] The ring angle at the nickel atom for the six-membered chelate ring (O(7)–Ni(2)–O(9)) is 85.7 (5)°, which is smaller than the normal value for a Ni(II) six-membered chelate ring (90°), suggesting that some strains exist in the mannose-C coordination system. This strain presumably comes from the triple chelation of O(7), O(9), and O(10) atoms. The Ni–N distances range from 2.10 (2) to 2.19(2) Å. These values are much larger than those of complexes **1**–**5**. Thus, *N*-methyl nitrogen to Ni bonds are weakened considerably by their steric hindrance. As for the Ni–O bonds, we can separate them into two groups. One of them has longer bond distances (the average of them is 2.13 Å), and the other has much shorter bond distances (2.02 (1) Å = Ni(1)–O(1), 2.02 (1) Å = Ni(1)–O(7), 2.02 (1) Å = Ni(2)–O(7), 2.04 (1) Å = Ni(2)–O(11)). In this structure analysis, the coordinations of hydroxyl hydrogen atoms were not refined. But from these bond distances, the hydroxyl groups containing O(7) and O(1) appear to be deprotonated. The coordination pattern of the O(7) atom is a typical alkoxide oxygen bridge that is common in the polynuclear Mo and W complexes.[25] The distance between O(1) and O(11) is 2.41 (2) Å, and this value falls within the range of O$^-$---H–O hydrogen-bond distances.[26] The crystal packing of the unit cell contents is available (Figure 5).[18]

Structural Prediction for the Complex Glc1(Cl) (8). Since Glc1(Cl) was too hygroscopic to isolate as a powder suitable for elemental analysis, it was obtained as a purified methanolic so-

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lution (yield 4% based on the starting nickel ions). The electronic absorption and circular dichroism spectra of the complex in methanol are given in Figure 1. We have already reported that when a primary diamine, en or tn, is used, the structural features of nickel(II) complexes containing monosaccharides are evident in CD spectra.[4,6,7] That is to say, the CD curves of the D-glucose and D-mannose complexes are nearly mirror images of the corresponding CD curves in the first absorption region. However, in this study, the CD curve of **8** is not a mirror image of but is similar to the CD curve of the complex Man1(Cl) (**6**). HPLC analysis shows that the ratio of monosaccharide to nickel ion in **8** is 2.8:2.0, suggesting a binuclear complex. Further, of the monosaccharides recovered from the complex, 28% are D-glucose and 72% are surprisingly D-mannose, indicating that the starting D-glucose was partially epimerized during the reaction. From these results, it is assumed that **8** is the mixture of the binuclear complexes having the structure of mannofuranoside bridging (Figure 6). This observation is very important in relation to the transformation of sugars by metal complexes and, in fact, gave us a significant clue to develop the C-2 epimerization of aldoses promoted by nickel(II)-diamine complexes.[27]

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Supplementary Material Available: Listings of anisotropic thermal parameters (Table IIb), atomic parameters of hydrogen atoms (Table IIc), torsional angles (Table VI), least-squares-plane data (Table VII), and bond distances and bond angles and a stereoscopic view of the unit cell (Figure 5) (10 pages); a table of structure factor amplitudes (11 pages). Ordering information is given on any current masthead page.

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Equilibrium and Kinetic Analysis of the Interaction of Mercury(II) with Cadmium(II) Metallothionein

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The reaction of Cd-metallothionein (MT) with mercury(II) has been studied. The Cd_7-MT was titrated with from 1 to 14 equiv of $HgCl_2$, following which the cadmium(II) and mercury(II) contents, the partition coefficient on a size-exclusion HPLC column, and the UV spectra were measured. The results showed that mercury(II) quantitatively displaces cadmium(II) from the protein. An analysis of the UV spectral data by the method of singular value decomposition (SVD) was used to determine the number of spectrally distinct components and their fractional abundance throughout the titration. A minimum of three spectrally distinct components were found by this method; they corresponded to tetrahedral Cd-S, tetrahedral Hg-S, and linear Hg-S coordination geometries. Initially the mercury(II) occupies tetrahedral sites; however, above a Hg/MT stoichiometry of 4, there is a shift to linear coordination. The size-exclusion data indicate a shift to a more compact structure upon addition of mercury(II) to the metallothionein. Finally, the analysis of a UV spectrum of a mixture of the all-cadmium(II) and the all-mercury(II) metallothioneins indicates that the two forms undergo facile interprotein metal ion exchanges. The analysis of the kinetics of this reaction is best fit by second-order kinetics, which would be consistent with a mechanism whereby there was a direct interaction between the two MTs.

Introduction

Metallothioneins (MTs) are a unique class of low-molecular-weight proteins that are characterized by a high content of cysteine and a capacity to bind multiple moles of heavy metal ions.[1-3] MTs are nearly ubiquitous in nature, occurring in organisms ranging from fungi (*Neurospora* and *Saccharomyces*) to the mammals. While the physiological functions of MT have not been clearly defined as yet, it has been postulated to function both in providing a protective mechanism against an overload of toxic heavy metal ions such as cadmium and mercury and in maintaining a homeostasis of the essential metal ions, zinc and copper.[4]

Extensive use has been made of both chemical and optical spectroscopic techniques to characterize the nature of the MT metal binding sites and their relative affinities for different metal ions.[5,6] While these studies clearly show all 20 cysteine sulfurs in the mammalian MTs to be involved in metal ligation, the most explicit details about the metal ion-ligand coordination number and geometry were first revealed by ^{113}Cd NMR studies.[7] For the ^{113}Cd derivatives of rabbit liver MT, these studies indicate that the cadmium(II) ions are bound in two clusters consisting of four and three metals each, with the metal tetrahedrally coordinated to 11 and 9 cysteines, respectively. Recently, the structure of this protein has been more completely defined by both X-ray crystallography[8] and two-dimensional ^1H and ^1H-^{113}Cd NMR spectroscopy.[9] While these two studies differ in their assignment of specific cysteine residues to specific metal ions in the structure and hence differ in the predicted folding of the polypeptide chain, they both confirm the essential arrangement of bridging and terminal cysteine-metal ligands elucidated by the earlier ^{113}Cd NMR studies.

In comparison to the progress that has been made in the detailed structural elucidation of the cadmium(II) and cadmium(II)-

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