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Chiral Inversion around a Seven-Coordinated Cobalt Center Induced by an Interaction between Sugars and Sulfate Anions

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Novel seven-coordinated cage-type cobalt(II) complexes containing *N*-glycosides from mannose-type aldoses and tris(2-aminoethyl)amine (tren), $[Co((aldose)_3tren)]X_2 \cdot nH_2O$ (**1a**$\cdot 5H_2O$, aldose = D-mannose (D-Man), X = Cl^-; **1b**$\cdot 5H_2O$, aldose = 6-deoxy-L-mannose (L-Rha), X = Cl^-; **2a**$\cdot 4H_2O$, aldose = D-Man, X = Br^-; **2b**$\cdot H_2O$, aldose = L-Rha, X = Br^-) and $[Co((aldose)_3tren)]SO_4 \cdot nH_2O$ (**3a**$\cdot 4H_2O$, aldose = D-Man; **3b**$\cdot 3H_2O$, aldose = L-Rha), where $(aldose)_3$tren is tris(2-(aldosylamino)ethyl)amine, were prepared and characterized by elemental analysis, electronic absorption and circular dichroism spectroscopies, and X-ray crystallography. Crystal data are as follows. **2b**$\cdot 2CH_3OH$: $C_{26}H_{56}N_4O_{14}Br_2Co$, monoclinic, space group $P2_1$, $a = 11.045(2)$ Å, $b = 17.283(6)$ Å, $c = 10.996(3)$ Å, $\beta = 117.371(6)°$, $V = 1864(1)$ Å^3, $Z = 2$, $R = 0.072$ for 2787 independent reflections. **3b**$\cdot 3H_2O \cdot CH_3OH$: $C_{25}H_{58}N_4O_{20}SCo$, orthorhombic, space group $P2_12_12_1$, $a = 14.836(2)$ Å, $b = 22.489(2)$ Å, $c = 12.181(3)$ Å, $V = 4064(1)$ Å^3, $Z = 4$, $R = 0.077$ for 2010 independent reflections. The complex cation of **2b** consists of a cobalt atom coordinated by a heptadentate $(L\text{-Rha})_3$tren ligand to produce a mono-face-capped octahedron having pseudo-C_3 symmetry with a Λ (λ_3-*ob* form) configuration around the metal. The complex cation of **3b** has a mono-face-capped octahedron coordinated by a heptadentate $(L\text{-Rha})_3$tren ligand having pseudo-C_3 symmetry with a Δ (λ_3-*lel* form) configuration. The other facial site of the complex cation is capped by the SO_4^{2-} anion through hydrogen bonding with the hydroxy groups of L-rhamnose residues. The C_3 helical-configurational inversion around the cobalt(II) center, $\Delta \leftrightarrow \Lambda$, induced by an interaction between the sugars and the SO_4^{2-} anion, was monitored by circular dichroism spectroscopy, for which the sign of the Cotton effect of **1** and **2**, having halide counteranions, is opposite to that of **3**, having sulfate counteranions, and was found to proceed reversibly upon addition and removal of sulfate anions. The intensities of circular dichroism spectra for $[Co((L\text{-Rha})_3tren)]^{2+}$ and $[Co((D\text{-Man})_3tren)]^{2+}$ were appreciably changed upon addition of sulfate ions. The spectral changes were interpreted in terms of ion-pair formation. On the basis of electrostatic theories of ion association, the closest distance between the sulfate ion and the $[Co((D\text{-Man or }L\text{-Rha})_3tren)]^{2+}$ cation was estimated as ∼5 Å, which is consistent with the Co−S distance of 4.697(6) Å observed in the crystal structure of **3b**. The sulfate ion was suggested to fit into the cavity composed of the sugar hydroxyl groups through hydrogen bonds even in the solution state.

Introduction

Carbohydrates occur widely in nature and are indispensable to living organisms.[1] Naturally rare carbohydrates have also been shown to be involved in many glycoproteins, glycolipids, and antibiotics and play important roles in various biological processes.[2] In some enzymatic reactions of carbohydrates, alkali, alkaline earth, and some transition metal ions were suggested to act in cooperation with sugars.[3] In this regard, it is important to investigate the interactions between sugars and metal ions, including the stereochemical behavior of sugars in transition metal complexes. Detailed coordination behavior of sugar molecules, however, has not been well established due to their complicated stereochemistry and extremely hygroscopic properties. Noncovalent interactions are vital in processes of biological recognition of molecules. Enzyme−substrate, hormone−receptor, and antigen−antibody interactions are among the most important in biological systems and are achieved mainly by the specific side-chain groups of amino acids and sugar chains in proteins. In contrast with the many studies on interactions between side chains of amino acids contained in transition metal complexes,[4] those concerning the structural details of sugar−sugar interactions around a metal center are very few. Synthetic efforts utilizing carbohydrate ligands to construct artificial metal sites for molecular recognition are, therefore, very interesting subjects.

We have reported extensive studies on the synthesis and characterization of nickel(II) and cobalt(III) complexes containing *N*-glycosides derived from the reaction of sugars and diamines,[5−9] results of which suggest that the stereo structure of the sugar complexes can be modified by varying the diamines and metal ions used. During our studies, we discovered new

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sugar transformation reactions resulting from cooperative effects between metal ions and amines.[10−17] We have also developed antitumor[18,19] or antifungal[20] metal complexes containing amino sugars. Recently, a branched polyamine, tris(2-aminoethyl)-amine (tren), having three primary amino groups, was introduced into our research in the hope of assembling three sugar units on a metal center in a symmetrical fashion with effective sugar−sugar interactions. In particular, when mannose-type aldoses having a 2,3-*cis* configuration, D-mannose (D-Man) and L-rhamnose (L-Rha), were used as the sugar components, structures of the nickel(II)−*N*-glycoside complexes, $[\mathrm{Ni((aldose)_2tren)}]^{2+}$ (aldose = D-Man, L-Rha), exhibited novel intramolecular sugar−sugar interactions around the metal center, which facilitated the assembly of the sugars on the metal center.[7] The pyranose ring of the mannose-type sugars, upon coordination to the metal, was oriented nearly perpendicular to the five-membered chelate ring, enabling the sugar ligands to contact each other, whereas the pyranose ring of the glucose-type sugars having a 2,3-*trans* configuration resided in the plane of the five-membered chelate ring, preventing intramoleculer sugar−sugar interactions on the metal center.

We report herein the syntheses and structural determinations of novel seven-coordinated cage-type cobalt(II) complexes containing *N*-glycosides from mannose-type aldoses (D-mannose and L-rhamnose) and tren and an unprecedented chiral inversion around the metal center induced by an interaction between the sugars and sulfate anions in solution. Preliminary results have already been reported.[21]

Experimental Section

Materials. All reagents were of the best commercial grade and were used without further purification. The following abbreviations are used: tren, tris(2-aminoethyl)amine; D-Man, D-mannose; L-Rha, L-rhamnose (6-deoxy-L-mannose); (D-Man)$_3$tren, tris(2-(D-mannosylamino)ethyl)amine; (aldose)$_3$tren, tris(2-(aldosylamino)ethyl)amine; (L-Rha)$_3$tren, tris(2-(L-rhamnosylamino)ethyl)amine.

Preparations of Cobalt(II) Complexes Containing *N*-Glycosides. A methanolic solution (100 mL) containing D-mannose (D-Man) or L-rhamnose (L-Rha) (12.0 mmol, 4 equiv) and tren (3.0 mmol, 1 equiv) was incubated at 60 °C for 1 h. Then, 3.0 mmol of $\mathrm{CoX_2{\cdot}6H_2O}$ ($\mathrm{X = Cl^-}$ or $\mathrm{Br^-}$) (1 equiv) was added to the solution, and the mixture was refluxed for 1 h. Up to this point, all manipulations were carried out under an argon atmosphere. The resultant solution was concentrated by a rotary evaporator to ca. 40 mL, loaded onto a Sephadex LH-20 gel permeation column, and eluted with methanol. The wine-red major band was collected and concentrated to ca. 10 mL. Addition of ethanol to the concentrated solution gave microcrystals of $\mathrm{[Co((aldose)_3tren)]X_2{\cdot}}n\mathrm{H_2O}$ in moderate yields (**1a**·5H$_2$O, aldose = D-Man, X = Cl$^-$, 56%; **1b**·5H$_2$O, aldose = L-Rha, X = Cl$^-$, 34%; **2a**·4H$_2$O, aldose = D-Man, X = Br$^-$, 75%; **2b**·H$_2$O, aldose = L-Rha, X = Br$^-$, 40%). Anal. Calcd for **1a**·5H$_2$O: C, 33.81; H, 6.86; N, 6.57. Found: C, 33.41; H, 6.86; N, 6.50. Calcd for **2a**·4H$_2$O: C, 31.22; H, 6.11; N, 6.07. Found: C, 31.16; H, 6.16; N, 5.57. Calcd for **1b**·5H$_2$O: C, 35.83; H, 7.27; N, 6.96. Found: C, 35.98; H, 7.17; N, 7.07. Calcd for **2b**·H$_2$O: C, 35.09; H, 6.14; N, 6.82. Found: C, 35.13; H, 6.23; N, 6.44. When $\mathrm{CoSO_4{\cdot}7H_2O}$ was used as the metal source, similar pink complexes formulated as $\mathrm{[Co((aldose)_3tren)]SO_4{\cdot}}n\mathrm{H_2O}$ (**3a**·4H$_2$O, aldose = D-Man, 77%; **3b**·3H$_2$O, aldose = L-Rha, 37%) were obtained. Anal. Calcd for **3a**·4H$_2$O: C, 33.53; H, 6.57; N, 6.52. Found: C, 33.15; H, 6.34; N, 6.71. Calcd for **3b**·3H$_2$O: C, 36.32; H, 6.86; N, 7.06. Found: C, 36.33; H, 6.81; N, 7.07. Treatment of **3a** and **3b** with $\mathrm{BaCl_2{\cdot}2H_2O}$ or $\mathrm{BaBr_2{\cdot}2H_2O}$ led to the corresponding halide salts of the complexes, **1a** or **2a** and **1b** or **2b**, respectively.

Measurements. Electronic absorption spectra were obtained on a Shimadzu UV-3100 spectrophotometer, and circular dichroism spectra were recorded on a Jasco J-720 spectropolarimeter. The changes in the CD spectra were measured at 27 °C.

Crystal Data and Intensity Measurements for 2b·2CH$_3$OH and 3b·3H$_2$O·CH$_3$OH. A powdered sample of **2b**·H$_2$O was recrystallized from a minimum amount of hot methanol to yield prismatic pink crystals of **2b**·2CH$_3$OH suitable for X-ray crystallography. Since the crystals were extremely delicate in air, the intensity data were collected quickly within ca. 3 h on a Weissenberg camera type diffractometer equipped with imaging plates as described below. A crystal coated with epoxy cement was used to collect diffraction data at room temperature on a Rigaku R-AXIS II CS instrument with Mo Kα radiation ($\lambda = 0.7107$ Å) within the sphere of $2\theta < 55°$ in about 3 h.

Micro crystals of **3b**·3H$_2$O were recrystallized from a minimum amount of hot methanol to yield prismatic pink crystals of **3b**·3H$_2$O·CH$_3$OH suitable for X-ray crystallography. Since the crystals were extremely delicate in air and lost clarity immediately after removing them from the mother liquor, a crystal sealed into a glass tube capillary (0.7 mm o.d.) with the mother liquor was used to collect diffraction data at room temperature on a Rigaku AFC5S four-circle automated diffractometer. The unit cell dimensions were determined by a least-squares method with 25 reflections in the range $20° < 2\theta < 30°$. Three standard reflections, monitored every 150 reflections, showed no variation in intensity, and no correction was made. The linear absorption coefficient for Mo Kα radiation is 5.42 cm^{-1}. An empirical absorption correction using the ψ-scan method was applied. Reflection data were corrected for Lorentz−polarization effects. Crystallographic and experimental data are summarized in Table 1.

Structure Solution and Refinement. The structure of **2b**·2CH$_3$OH was solved by direct methods (SHELX86) and refined with full-matrix least-squares techniques (SHELXL93). The hydrogen atoms bound to carbon and nitrogen atoms were located at calculated positions and included in the refinement using a riding model. Those of hydroxyl groups were located at hydrogen-bonding positions, and their positional parameters were fixed during refinement. Those bound to solvent molecules were not located. The final refinement, carried out with anisotropic thermal parameters for Br, Co, C, O, and N, converged to $R = \sum||F_o| - |F_c||/\sum|F_o| = 0.072$ and $wR_2 = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2} = 0.184$, where $w = 1/[\sigma^2(F_o^2) + (0.1009P)^2 + 8.71P]$ and $P = (\max(F_o^2,0) + 2F_c^2)/3$. The atomic scattering factors and values of f' and f'' for Br. Co, O, N, and C atoms were taken from refs 22 and 23. The known absolute configurations of the asymmetric

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Table 1. Crystallographic and Experimental Data for $[Co((L\text{-}Rha)_3tren)]Br_2 \cdot 2CH_3OH$ (**2b**·$2CH_3OH$) and $[Co((L\text{-}Rha)_3tren)] \cdot SO_4 \cdot 3H_2O \cdot CH_3OH$ (**3b**·$3H_2O \cdot CH_3OH$)

	2b·$2CH_3OH$	**3b**·$3H_2O \cdot CH_3OH$
empirical formula	$C_{26}H_{56}N_4O_{14}Br_2Co$	$C_{25}H_{58}N_4O_{20}SCo$
fw	867.49	825.74
cryst system	monoclinic	orthorhombic
space group	$P2_1$	$P2_12_12_1$
a, Å	11.045(2)	14.836(2)
b, Å	17.283(6)	22.489(2)
c, Å	10.996(3)	12.181(3)
β, deg	117.371(6)	
V, Å^3	1864(1)	4064(1)
Z	2	4
T, °C	15	23
ρ_{calcd}, g cm^{-3}	1.488	1.349
cryst size, mm	0.50 × 0.40 × 0.20	0.65 × 0.40 × 0.13
scan width	Weissenberg method	$1.42 + 0.3 \tan \theta$
μ(MoKα), cm^{-1}	26.65	5.42
2θ range, deg	55	50
no. of data	2787 ($I > 2\sigma(I)$)	2010 ($I > 3\sigma(I)$)
no. of variables	424	435
R[a]	0.072	0.077
R_w[b] or wR_2[c]	0.184[c]	0. 086[b]

[a] $R = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $R_w = (\sum w||F_o| - |F_c||^2/\sum w|F_o|^2)]^{1/2}$. $w = 1/\sigma^2(F_o)$. [c] $wR_2 = [\sum w(F_o^2 - F_c^2)^2]/\sum w(F_o^2)^2]^{1/2}$. $w = 1/[\sigma^2(F_o^2) + (0.1009P)^2 + 8.71P]$. $P = (\max(F_o^2,0) + 2F_c^2)/3$.

carbon atoms of L-rhamnose were used as internal references for asymmetric centers to determine the absolute configuration of the complex. The final difference Fourier synthesis still showed peaks at heights up to 0.78 and 1.06 e Å^{-3} around the cobalt and bromine atoms, respectively. All calculations were performed on a Sun SPARC Staion 10/41 computer with the SHELX93 program.

The structure of **3b**·$3H_2O \cdot CH_3OH$ was solved by direct methods (MITHRIL). The structure was refined by full-matrix least-squares techniques. The hydrogen atoms bound to carbon atoms were included but not refined. The final refinement, carried out with anisotropic thermal parameters for Co, S, C, O, and N, and converged to $R = 0.077$ and $R_w = (\sum w||F_o| - |F_c||^2/\sum w F_o^2)^{1/2} = 0.086$ ($w = 1/\sigma^2(F_o)$). The solvent molecules were refined isotropically. The atomic scattering factors and values of f' and f'' for Co, S, O, N, and C atoms were taken from refs 22 and 23. The known absolute configurations of the asymmetric carbon atoms of L-rhamnose were used as internal references for asymmetric centers to determine the absolute configuration of the complex. The final difference Fourier synthesis still showed peaks at heights up to 0.95 e Å^{-3} around the cobalt atom. All calculations were performed on a Digital Vax station 3100 M38 computer with the TEXSAN-TEXRAY Structure Analysis Package (Molecular Structure Corp.).[24] The perspective views were drawn by using the program ORTEP.[25] Final atomic positional and thermal parameters for all atoms of **2b**·$2CH_3OH$ and **3b**·$3H_2O \cdot CH_3OH$ are supplied as Supporting Information.

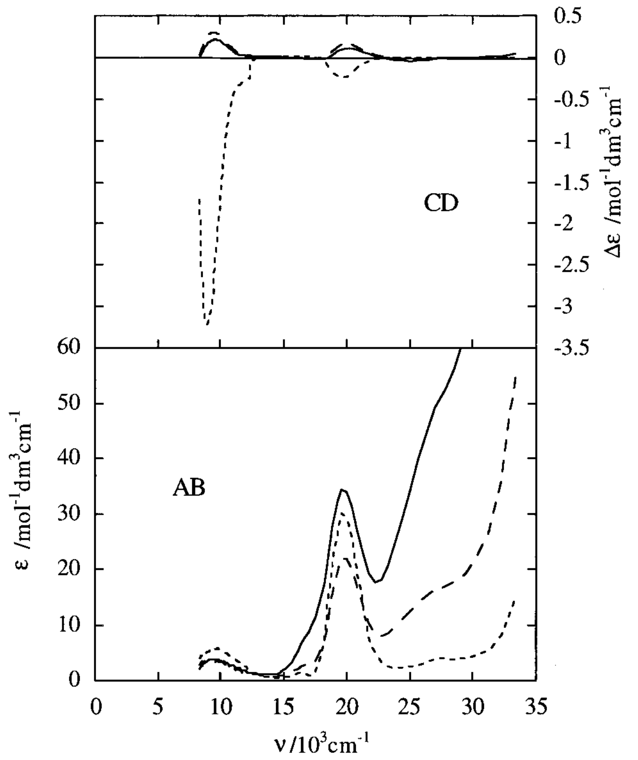

Figure 1. Electronic absorption (AB) and circular dichroism (CD) spectra of (a) $[Co((L\text{-}Rha)_3tren)]Cl_2 \cdot 5H_2O$ (**1b**·$5H_2O$) in methanol (—), (b) $[Co((L\text{-}Rha)_3tren)]Br_2 \cdot 5H_2O$ (**2b**·H_2O) in methanol (– –), and (c) $[Co((L\text{-}Rha)_3tren)]SO_4 \cdot 3H_2O$ (**3b**·H_2O) in methanol/ethylene glycol (- - -).

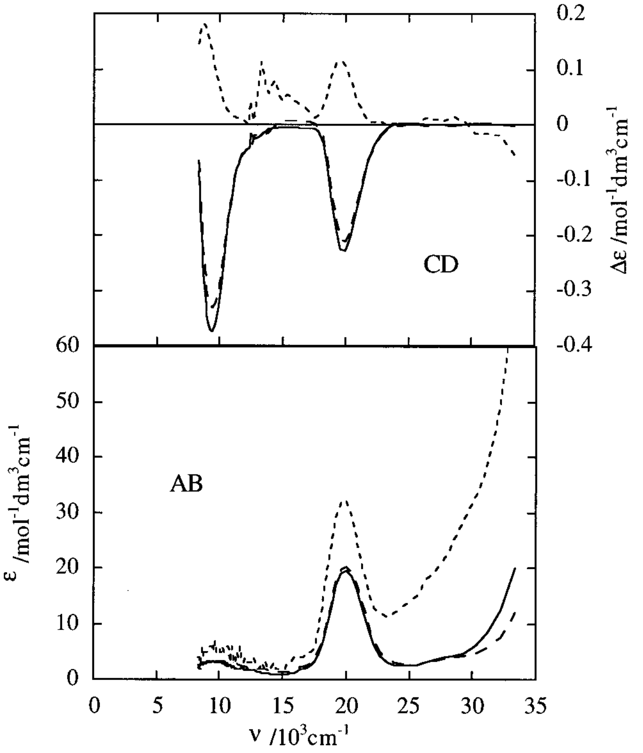

Figure 2. Electronic absorption (AB) and circular dichroism (CD) spectra of (a) $[Co((Man)_3tren)]Cl_2 \cdot 5H_2O$ (**1a**·$5H_2O$) in methanol (—), (b) $[Co((D\text{-}Man)_3tren)]Br_2 \cdot 4H_2O$ (**2a**·H_2O) in methanol/ethylene glycol (– –), and (c) $[Co((D\text{-}Man)_3tren)]SO_4 \cdot 4H_2O$ (**3a**·H_2O) in methanol/ethylene glycol (- - -).

Results and Discussion

A series of cobalt(II)−sugar complexes were prepared by the reactions of cobalt(II) salts, $CoX_2 \cdot 6H_2O$ (X = Cl, Br) and $CoSO_4 \cdot 7H_2O$, with heptadentate *N*-glycoside ligands, (aldose)$_3$-tren, which were derived from tren and D-mannose and from tren and L-rhamnose (6-deoxy-L-mannose). The analytical data indicated that an *N*-glycoside ligand, (aldose)$_3$tren, attached to one cobalt(II) ion. The β-anomeric form of the *N*-glycosidic linkage was presumed on the basis of nickel(II) complexes of 1-(aldosylamino)-2-aminoethane or -propane.[4a] Electronic absorption (AB) and circular dichroism (CD) spectra of these complexes are presented in Figures 1 and 2, and the spectral data are summarized in Table 2. The electronic absorption spectra of **1**−**3** in solution showed a characteristic band around 2.0×10^4 cm^{-1}, corresponding to d−d transitions of Co(II) ions. The positions of the absorption maxima recorded in methanol

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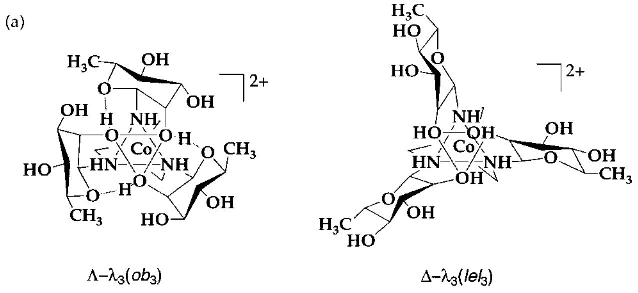
(25) Johnson, C. K. *ORTEP-II*; Oak Ridge National Laboratory: Oak Ridge, TN, 1976.

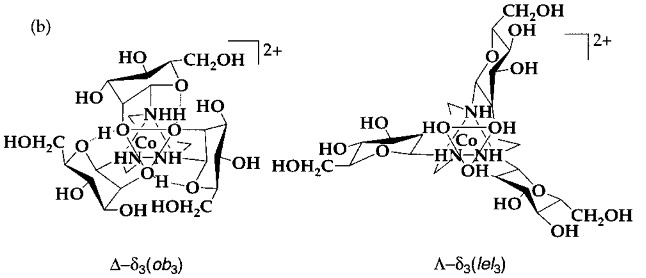
Table 2. Electronic Absorption (AB), Circular Dichroism (CD), and Transmittance (TR) Spectral Data

complexes	AB[a] ν_{max}, 10^3 cm^{-1} (ϵ)	CD[a] ν_{max}, 10^3 cm^{-1} ($\Delta\epsilon$)	TR ν_{max}, 10^3 cm^{-1}
[Co((D-Man)$_3$tren)]Cl$_2$·5H$_2$O	9.72 (3.3)	9.39 (−0.374)	9.90
(**1a**·5H$_2$O)	20.00 (19.5)	19.84 (−0.231)	20.04
[Co((D-Man)$_3$tren)]Br$_2$·4H$_2$O	9.80 (3.5)	9.43 (−0.331)	10.00
(**2a**·4H$_2$O)	20.00 (20.2)	19.90 (−0.213)	20.08
[Co((D-Man)$_3$tren)]SO$_4$·4H$_2$O	9.62 (7.0)	8.75 (+0.182)	9.73
(**3a**·4H$_2$O)	19.88 (32.0)	19.57 (+0.118)	19.72
[Co((L-Rha)$_3$tren)]Cl$_2$·5H$_2$O	9.62 (3.8)	9.59 (+0.213)	9.84
(**1b**·5H$_2$O)	19.72 (34.5)	20.10 (+0.112)	19.69
[Co((L-Rha)$_3$tren)]Br$_2$·H$_2$O	9.78 (3.5)	9.48 (+0.299)	9.89
(**2b**·H$_2$O)	19.84 (22.3)	19.92 (+0.168)	19.67
[Co((L-Rha)$_3$tren)]SO$_4$·3H$_2$O	9.85 (5.8)	8.96 (−0.322)	9.80
(**3b**·3H$_2$O)	19.72 (30.2)	19.67 (−0.250)	19.72

[a] In methanol.



aldose = L-Rha



aldose = D-Man

Figure 3. Possible structures of (a) [Co((L-Rha)$_3$tren)]$^{2+}$ and (b) [Co((D-Man)$_3$tren)]$^{2+}$.

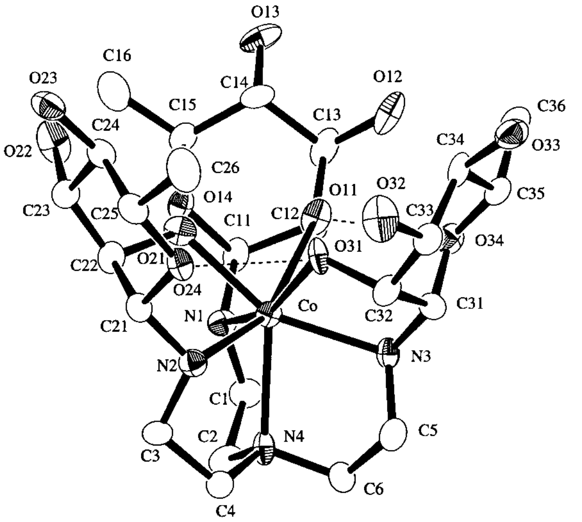


Figure 4. ORTEP drawing (50% probability ellipsoids) of [Co((L-Rha)$_3$tren)]Br$_2$ (**2b**).

Table 3. Selected Bond Lengths and Angles for **2b**·2CH$_3$OH[a]

Bond Lengths, Å			
Co−O(11)	2.21(1)	Co−O(21)	2.20(1)
Co−O(31)	2.236(9)	Co−N(1)	2.23(1)
Co−N(2)	2.24(1)	Co−N(3)	2.23(1)
Co−N(4)	2.41(1)		
Bond Angles, deg			
O(11)−Co−O(21)	78.6(4)	O(11)−Co−O(31)	82.9(4)
O(11)−Co−N(1)	74.9(4)	O(11)−Co−N(2)	150.9(5)
O(11)−Co−N(3)	84.9(4)	O(11)−Co−N(4)	133.5(5)
O(21)−Co−O(31)	82.5(4)	O(21)−Co−N(1)	83.9(4)
O(21)−Co−N(2)	74.8(4)	O(21)−Co−N(3)	153.0(4)
O(21)−Co−N(4)	131.9(5)	O(31)−Co−N(1)	155.9(4)
O(31)−Co−N(2)	82.0(4)	O(31)−Co−N(3)	74.3(4)
O(31)−Co−N(4)	128.2(3)	N(1)−Co−N(2)	113.3(5)
N(1)−Co−N(3)	112.3(5)	N(1)−Co−N(4)	75.2(4)
N(2)−Co−N(3)	114.5(4)	N(2)−Co−N(4)	74.7(5)
N(3)−Co−N(4)	74.6(5)		

[a] Estimated standard deviations are given in parentheses. See Figure 4 for atom labels.

are almost identical to each other, indicating that these complexes have essentially the same structure around the metal center. The transmittance spectra (Nujol mull) were also similar to their solution spectra (Table 2). In the circular dichroism spectra, large Cotton effects were observed at about 2.0 × 10^4 cm^{-1}, suggesting the coordination of sugar moieties to the cobalt ion. Further, it should be noted that the sign of the Cotton effect of **1** and **2**, containing halide counteranions, is opposite to that of **3**, containing the SO_4^{2-} counteranion. The opposite nature of the signs for **1** and **2** vs **3** was tentatively attributed to an inversion of the absolute configuration around the metal. By analogy to [Ni((py)$_3$tren)]$^{2+}$ ((py)$_3$tren = tris(1-(2-pyridyl)-2-azabuten-4-yl)amine,[26] two possible C_3 helical configurations of the potentially heptadentate *N*-glycoside ligand (aldose)$_3$tren around the metal are depicted in Figure 3. In the Δ configuration of [Co((D-Man)$_3$tren)]$^{2+}$, the five-membered chelate rings [CoNC$_2$O] of the sugar moiety, adopting a *δ-gauche* conformation, were assumed to be almost perpendicular to the C_3 axis (*ob* form) and the hydrogen-bonding network between the hydroxy group on the C-2 position of D-Man and the cyclic oxygen atom on the C-5 position was inferred from the crystal structure of [Ni((D-Man)$_2$-tren)]Cl$_2$·CH$_3$OH (**4**).[7] In contrast, in the Λ configuration, the five-membered chelate rings of the sugar moieties were assumed to be nearly parallel to the C_3 axis (*lel* form) and hydrogen bonding could not be expected. The structures of [Co((L-Rha)$_3$tren]$^{2+}$ in the Δ and Λ configurations were assumed to be mirror images of the corresponding structures of [Co((D-Man)$_3$tren)]$^{2+}$ because D-Man and L-Rha (6-deoxy-L-mannose) are almost enantiomeric to each other. In order to clarify the detailed structures, X-ray crystallographic studies were undertaken.

Structural Descriptions. The structures of **2b**·2CH$_3$OH and **3b**·3H$_2$O·CH$_3$OH were elucidated by X-ray analyses. A perspective drawing of the complex cation of **2b**·2CH$_3$OH is given in Figure 4, and some selected bond distances and angles are listed in Table 3. The complex cation consists of a cobalt atom coordinated by a heptadentate tris(2-(L-rhamnosylamino)-ethyl)amine, (L-Rha)$_3$tren, ligand to produce a mono-face-capped octahedron having pseudo-C_3 symmetry. The three nitrogen and three oxygen atoms are disposed approximately at the apices of the octahedron with metal−nitrogen distances of 2.23−2.24 Å and metal−oxygen distances of 2.20−2.24 Å. One of the facial sites is closely capped by the tertiary amino nitrogen of tren, N(4), with Co(1)−N(4) = 2.41(1) Å, which barely falls within the bonding range. The three L-rhamnosyl moieties form *β-N*-glycosidic linkages with the three primary amino groups

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(26) (a) Wilson, L. J.; Rose, N. J. *J. Am. Chem. Soc.* **1968**, *90*, 6041. (b) Kirchner, R. M.; Mealli, C.; Bailey, M.; Howe, N.; Torre, L. P.; Wilson, L. J.; Andrews, L. C.; Rose, N. J.; Lingafelter, E. C. *Coord. Chem. Rev.* **1987**, *77*, 89.

Table 4. Selected Intramolecular Hydrogen Bonds (Å)[a]

2b·2CH_3OH		**3b**·3H_2O·CH_3OH	
O(11)···O(34)	2.80(1)	O(11)···O(41)	2.70(2)
O(14)···O(21)	2.83(1)	O(12)···O(42)	2.80(2)
O(24)···O(31)	2.76(2)	O(21)···O(43)	2.69(2)
		O(31)···O(43)	2.67(2)

[a] Estimated standard deviations are given in parentheses.

Table 5. Selected Bond Lengths and Angles for **3b**·CH_3OH[a]

Bond Lengths, Å			
Co(1)−O(11)	2.26(1)	Co(1)−O(21)	2.38(1)
Co(1)−O(31)	2.39(1)	Co(1)−N(1)	2.13(1)
Co(1)−N(2)	2.15(1)	Co(1)−N(3)	2.13(1)
Co(1)−N(4)	2.31(2)		
Bond Angles, deg			
O(11)−Co(1)−O(21)	80.3(4)	O(11)−Co(1)−O(31)	78.6(4)
O(11)−Co(1)−N(1)	75.7(5)	O(11)−Co(1)−N(2)	80.4(5)
O(11)−Co(1)−N(3)	149.9(5)	O(11)−Co(1)−N(4)	131.1(5)
O(21)−Co(1)−O(31)	75.6(4)	O(21)−Co(1)−N(1)	150.0(5)
O(21)−Co(1)−N(2)	73.3(5)	O(21)−Co(1)−N(3)	79.5(5)
O(21)−Co(1)−N(4)	131.0(5)	O(31)−Co(1)−N(1)	82.2(5)
O(31)−Co(1)−N(2)	145.0(5)	O(31)−Co(1)−N(3)	75.0(5)
O(31)−Co(1)−N(4)	137.7(5)	N(1)−Co(1)−N(2)	119.1(5)
N(1)−Co(1)−N(3)	114.1(6)	N(1)−Co(1)−N(4)	78.8(6)
N(2)−Co(1)−N(3)	114.3(6)	N(2)−Co(1)−N(4)	76.6(6)
N(3)−Co(1)−N(4)	78.9(6)		

[a] Estimated standard deviations are given in parentheses. See Figure 5 for atom labels.

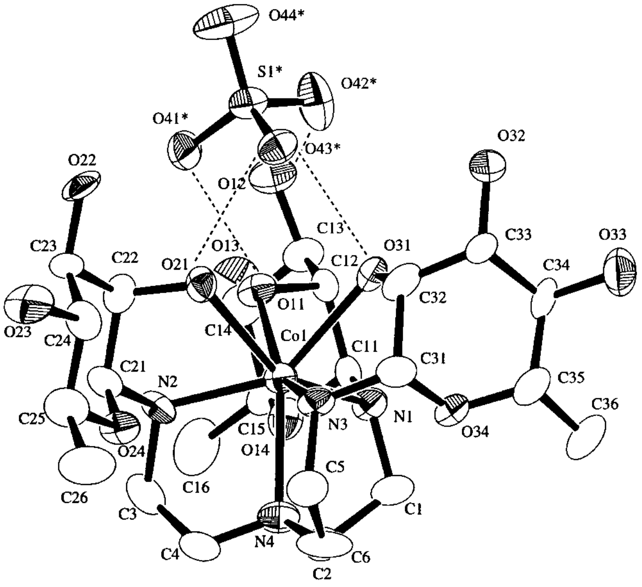

Figure 5. ORTEP drawing (50% probability ellipsoids) of [Co((L-Rha)$_3$tren)]SO_4 (**3b**).

of tren and attach to the metal at two points through the nitrogen atoms on the C-1 position and the hydroxy oxygen atoms on the C-2 position. The five-membered chelate rings of the sugar components adopt a λ-*gauche* conformation. The absolute configuration around the metal with respect to the helical axis is Λ, and the CC vectors in the [$CoNC_2O$] rings are nearly perpendicular to the C_3 axis (λ_3-*ob* form). The most important feature is the intramolecular hydrogen-bonding network between the ring sugar oxygen atoms (O(14), O(24), O(34)) and the C-2 hydroxyl groups ((O21), O(31), O(11)) (Figure 6a and Table 4).

An ORTEP drawing of [Co((L-Rha)$_3$tren)]SO_4 (**3b**) is given in Figure 5, and some selected bond distances and angles are listed in Table 5. A heptadentate (L-Rha)$_3$tren ligand completes a mono-face-capped octahedral coordination around the cobalt atom; the complex cation has pseudo-C_3 symmetry in a Δ configuration, where the five-membered chelate rings of the sugar components adopt a λ-*gauche* conformation and the CC vectors in the [$CoNC_2O$] rings are nearly parallel to the C_3 axis (λ_3-*lel* form). The three nitrogen and three oxygen atoms are disposed approximately at the apices of the octahedron with metal−nitrogen distances of 2.13−2.15 Å and metal−oxygen distances of 2.26−2.39 Å. Each pyranose ring of the sugar moieties has a β-$^4C_1$ conformation. Recently, Gou et al. reported the crystal structures of the tripodal manganese(II) and cobalt(II) complexes with the condensation product of tren and 2-pyridinecarboxyaldehyde *N*-oxide as the ligand.[27] The distance between the cobalt atom and the tertiary amino N atom of tren is 2.44(1) Å. On the basis of this value, they concluded that the strong Co−N coordination bond led to the actual heptacoordinate configuration, although the distance is significantly longer than that between the cobalt atom and the other N atoms (2.149(6) Å). In the present complex, one of the facial sites is closely capped by the unique nitrogen of tren, N(4), with Co(1)−N(4) = 2.31(2) Å, which falls within the bonding range. This is therefore a typical example of actual seven-coordinated mononuclear cobalt complexes. The three L-rhamnosyl moieties form β-*N*-glycosidic linkages with the three primary amino groups of tren and attach to the metal through the nitrogen atoms on the C-1 position and the hydroxy oxygen atoms on the C-2 position. The most remarkable feature is the interaction between the complex cation and the SO_4^{2-} anion. The other facial site of the complex cation is capped by SO_4^{2-} along the C_3 axis (Figure 6b), which is presumably supported by hydrogen bonding between the hydroxy groups on the C-2 and C-3 positions of L-Rha and the three oxygen atoms of SO_4^{2-} as shown in Table 4.

In light of the X-ray structures of **2b** and **3b**, the opposite nature of the signs in the CD spectra for the halide and sulfate anions was interpreted as a configurational inversion around the cobalt center by the sulfate ion.

As stated earlier, the structures of [Co((D-Man)$_3$tren]$^{2+}$ in the Δ and Λ configurations were assumed to be the mirror images of the corresponding structures of [Co((L-Rha)$_3$tren)]$^{2+}$ (Figure 3b) because D-Man and L-Rha (6-deoxy-L-mannose) are almost enantiomeric to each other. It can be expected that [Co((D-Man)$_3$tren)]X_2 (X = Cl^-, Br^-) has a Δ (δ_3-*ob*) helical configuration, which may be stabilized by an inter-ligand hydrogen bonding network as observed in the structure description of **2b**. The observations of the nearly mirror images in the CD spectra between the D-mannose complexes and L-rhamnose complexes (Figures 1 and 2) supported this structural assumption. In contrast, [Co((D-Man)$_3$tren)]SO_4 adopts a Λ (δ_3-*lel*) configuration, where the SO_4^{2-} anion is probably fitted to the large-size shallow cavity at the facial site as observed in the L-rhamnose complex **3b**.

Ion Pairing of *lel*$_3$-[Co((aldose)$_3$tren)]$^{2+}$ with the Sulfate Anion in Solution (aldose = D-Man, L-Rha). The X-ray crystal structure of **3b**·3H_2O·CH_3OH and the CD spectra suggest ion-pair formation between the complex cation and the sulfate anion in solution. In order to confirm the presence of the ion-pair in solution, we tried to estimate the closest distance of approach of ions on the basis of the electrostatic theory for ion association. Figure 7 shows the changes in the CD spectrum of the chloride salt of the L-rhamnose complex upon addition of sulfate ions. The addition of sulfate ions appreciably enhances the CD spectral changes tentatively by ion association and finally gives a spectral pattern similar to that of the sulfate

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[27] Gou, S.; You, X.; Yu, K.; Lu, J. *Inorg. Chem.* **1993**, *32*, 1883.

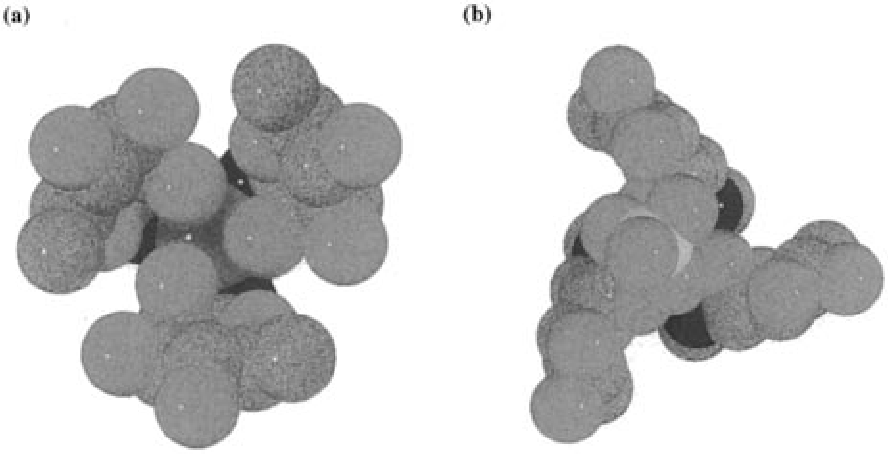

Figure 6. Perspective drawings of (a) the complex cation of **2b** and (b) complex **3b** with van der Waals radii, viewed down the C_3 axis: carbon, gray; nitrogen, dark blue; oxygen, red; sulfur, yellow; cobalt, light blue.

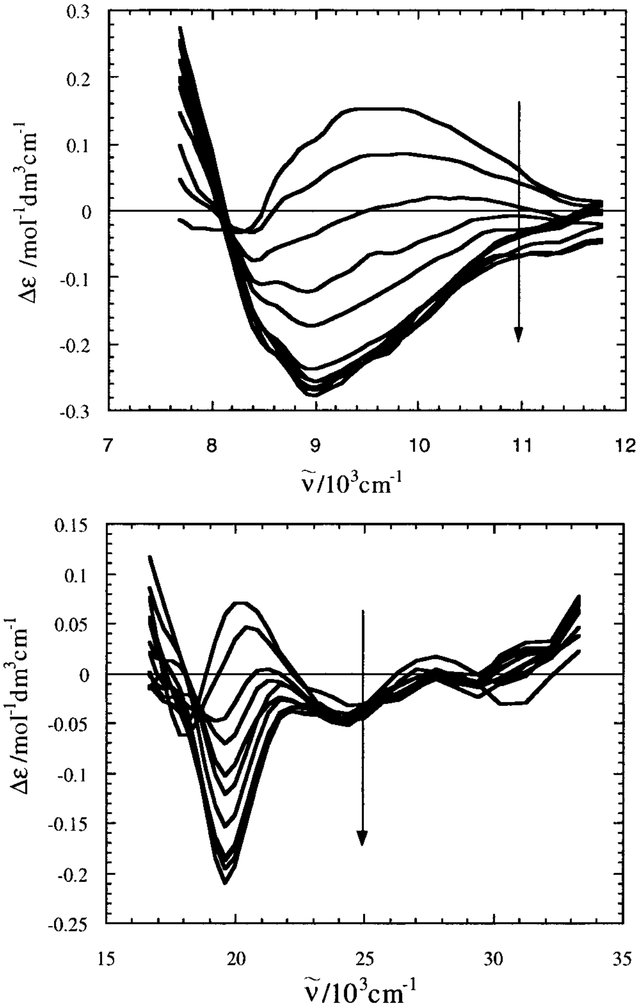

Figure 7. CD spectral changes of $[Co((L\text{-}Rha)_3tren)]Cl_2\cdot 5H_2O$ (**1b**$\cdot$5H_2O) in methanol/ethylene glycol upon addition of sulfate ions observed in the regions of 2.0×10^4 cm^{-1} (upper) and at 9.0×10^3 cm^{-1} (lower).

complex **3b**.[28] Similar CD spectral changes were also observed for the D-mannose complex (Supporting Information, Figure 1S). These changes in sign correspond to the inversions of the absolute configurations of the cobalt(II) complexes by ion pairing between the complex cations and sulfate anions, as confirmed by X-ray analysis of **3b**$\cdot 3H_2O\cdot CH_3OH$. In the present study, the CD spectral changes were measured without controlling the ionic strength and the changes in the ionic strength by the addition of sodium sulfate were estimated using the Debye−Hückel equation.[29]

The changes in the intensities due to the addition of sodium sulfate measured at 9.0×10^3 or 2.0×10^4 cm^{-1} were used to determine the association constants, where the extent of the change was relatively large (Figure 7).[30] Because the change in CD intensity ($\Delta\epsilon$) can be attributed to the formation of the ion pairs, the $\Delta\epsilon$ value can be expressed as a function of the total concentration (c_M) of the cobalt(II) complex cations and the concentration (x) of the ion pair, i.e.

$$\Delta\epsilon = \Delta\epsilon_0\left(1 - \frac{x}{c_M}\right) + \Delta\epsilon_{IP}\frac{x}{c_M} \tag{1}$$

where $\Delta\epsilon_0$ is the CD intensity for the free complex cation and $\Delta\epsilon_{IP}$ is that for the ion pair. In eq 1, $\Delta\epsilon_0$ corresponds to the $\Delta\epsilon$ value in the absence of added salts since the interaction between the chloride counterion and the cobalt(II) cations has little effect on the $\Delta\epsilon$ value at such a low concentration. The $\Delta\epsilon_{IP}$ value in eq 1 can be taken as the saturated $\Delta\epsilon$ value at the highest concentration. The ion-pair formation constant (K_{IP}) can be expressed as

$$K_{IP} = \frac{x}{(c_M - x)(c_A - x)} \tag{2}$$

where c_A is the total concentration of the added anions. The dependencies of the $\Delta\epsilon$ values on the sulfate ion (c_A) can in principle give the K_{IP} and x values from eqs 1 and 2. However, as stated above, the K_{IP} value changes with a change in the sulfate concentration under the present conditions. In order to estimate this change, we can use the following relationship:[31]

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(28) Sakaguchi, U.; Tsuge, A.; Yoneda, H. *Inorg. Chem.* **1983**, *22*, 3745

(29) In quantitative analysis of the spectral changes, it must be considered that the extent is significantly influenced by the ionic strength change. Alternatively, in order to avoid this effect, the spectral changes should be measured under conditions with a constant ionic strength maintained by adding 1:1 electrolytes such as tetramethylammonium chloride and sodium perchlorate. However, when we first used the constant ionic strength (0.01 or 0.05) method, the spectral changes in intensity ($\Delta\epsilon$) due to the sulfate ion were appreciably smaller than those in Figure 7 and Figure 1S.[30] This result indicates that excess perchlorate and chloride ions significantly block the sulfate ion from contacting the cobalt(II) complex ion; that is, both anions also have some specific interactions with the cobalt(II) complex ions in the methanol/ethylene glycol mixed solvent while they have little effect on the CD intensities.

(30) See Supporting Information.

(31) Robinson, R. A.; Stokes, R. H. *Electrolyte Solutions*; Butterworths: London, 1958; p 229.

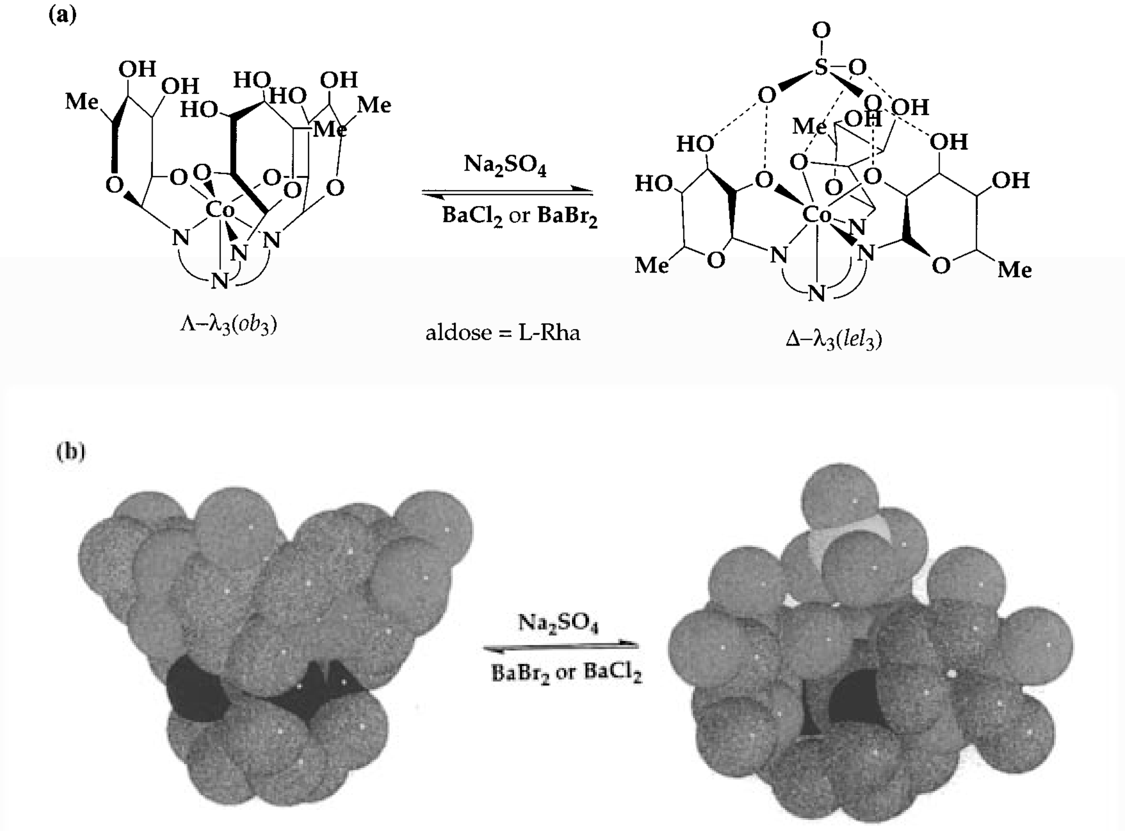

Figure 8. Configurational inversion around the metal center in $[Co((L\text{-}Rha)_3tren)]^{2+}$ induced by an interaction between sugars and SO_4^{2-}: (a) schematic view; (b) van der Waals view, showing carbon (gray), nitrogen (dark blue), oxygen (red), sulfur (yellow), and cobalt atoms (light blue).

$$\log K_{IP}(\mu) = \log K_{IP}(\mu{=}0) - \frac{2A|z_M z_A|\mu^{1/2}}{1 + Ba\mu^{1/2}} \qquad (3)$$

where μ is the ionic strength, z_M and z_A are the valencies of the cation and the anion, respectively, a is the closest distance of approach of the ions, and A and B are the Debye−Hückel parameters. In the present system (27 °C), $|z_M z_A|$ is 4, $\mu = 3c_M + 3c_A$, $A = 350/\epsilon_r^{3/2}$, and $B = 2.90/\epsilon_r^{1/2}$, where ϵ_r is the relative dielectric constant and a is in angstroms. According to the electrostatic ion association theories, $\log K_{IP}(\mu{=}0)$ is a function of the a value. We here use the EYY (Ebeling−Yokoyama−Yamatera),[32] theory which is the most modern among the electrostatic ion association theories. From this theory, $K_{IP}(\mu{=}0)$ in eq 3 can be written as

$$K_{IP}(\mu{=}0) = \frac{8\pi N_A a^3}{1000} \sum_{n=1}^{\infty} \frac{b^{2n+2}}{(2n+2)!(2n-1)} \qquad (4)$$

where N_A is Avogadro's number and b $(=|z_M z_A|e^2/4\pi\epsilon_r\epsilon_0 kTa)$ is the Bjerrum parameter. For the b parameter, we estimated the relative dielectric constant ϵ_r (ϵ_0 is the dielectric constant of a vacuum) of the present methanol ($\epsilon_r = 31.5$)/ethylene glycol ($\epsilon_r = 37.7$) 2:1 mixed solvent as $\epsilon_r = (31.5 \times 2 + 37.7)/3 = 33.6$. In this study, it seemed more informative to determine the best a value than to obtain the association constant, and therefore we tried to directly determine this value to fit the experimental values.[33]

Equations 1−4 can give the most appropriate a value for the measured $\Delta\epsilon$ values. In fact, because the ion-pair formation between M and A is significant, μ should be rewritten as $3(c_M + c_A) - 4x$, where x is the concentration of the ion pair. We performed successive approximations to obtain the exact x values from eqs 2−4 by assuming appropriate a values, where at first μ is taken as $3(c_M + c_A)$. The values calculated by varying the a value are compared with the experimental data at 9.0×10^3 or 2.0×10^4 cm^{-1}, resulting in the most appropriate value of 5 Å for a in both the rhamnose and mannose complexes with $b = 13.3$ and $\log K_{IP}^0 = 4.82$ (Figures 2S and 3S).[30] This value is consistent with the Co−S distance of 4.697(6) Å determined by X-ray crystallography of **3b**·$3H_2O$·CH_3OH.

Configurational Interconversion. Complex **3b** was readily transformed into **2a**,**b** by the addition of BaX_2 (X = Cl, Br), and complexes **2a**,**b** were converted to **3b** by the addition of Na_2SO_4 as mentioned above. The configurational inversion around the metal thus proceeded reversibly, just as flowers open and close (Figure 8). Here, we wish to consider why the novel chiral inversion between the halide and the sulfate complexes occurred. The complexes $[Co((L\text{-}Rha)_3tren)]X_2$ (**1b**, X = Cl^-; **2b**, X = Br^-) have Λ (λ_3-*ob*) helical configuration (**1a** and **2a**: Δ (δ_3-*ob*)). The facial site is blocked by the carbohydrate residues, resulting in a narrow, deep cavity. On the other hand, $[Co((L\text{-}Rha)_3tren)]SO_4$ (**3b**) adopts a Δ (λ_3-*lel*) helical configuration (**3a**: Λ (δ_3-*lel*)), where the SO_4^{2-} anion is fitted to the wide, shallow cavity at the facial site. Generally, the *lel* form is more favorable than the *ob* form on the basis of CPK model. However, in our sugar complexes, the *ob* form may be stabilized

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(32) Ebeling, W. *Z. Phys. Chem. (Leipzig)* **1968**, *238*, 400. Yokoyama, H.; Yamatera, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1770, 3002.

(33) When we used the Fuoss theory,[34] the a value obtained was around 4.5 Å, while a value of ~6.0 Å was obtained by using the Bjerrum theory.[35] These values do not significantly affect the present discussion. However, the EYY theory seems to be most appropriate to estimate the a value, since this theory does not have ambiguous parameters as seen in the Bjerrum theory and is more adequate for complementing the Debye−Hückel than the Fuoss theory.

(34) Fuoss, R. M. *J. Am. Chem. Soc.* **1955**, *77*, 2615.

(35) Bjerrum, N. *K. Dan. Vidensk. Selsk.* **1926**, *7*, No. 9.

by an interligand hydrogen-bonding network of the sugar units as is found in the crystal structure of **2b**·$2CH_3OH$ (Table 4). The approach of the sulfate anion to the sugar complex cation due to the electrostatic attraction between the −2 charged sulfate ions and +2 charged complex cations cleaves the interligand hydrogen bonds and brings about a chiral inversion induced by the sulfate anion in the *lel* form fitting into the large, shallow cavity. The Λ-*lel* form will convert to the Δ-*ob* form again upon a removal of sulfate anions and an addition of Ba(II) halide salts.

In summary, the interaction of cobalt(II) salts with tris(2-(aldosylamino)ethyl)amine from the branched polyamine tren and aldoses afforded the C_3 symmetrical sugar complexes $[Co((aldose)_3tren)]^{2+}$ (aldose = D-mannose and L-rhamnose). We confirmed that the unprecedented configurational inversion proceeded reversibly upon an addition and a removal of sulfate in solution. The values for the closest distance of approach between the sugar complex cations and the sulfate anions estimated with the EYY theory were consistent with the Co−S distance determined by X-ray crystallography. The sugar pocket of these complexes interestingly recognized a sulfate anion through the inversion of configuration around the cobalt center.

Acknowledgment. We thank Prof. Ohya and Dr. Fukui for helpful discussions. This work was partially supported by a Grant-in-Aid for Scientific Research and a Grant-in-Aid for Scientific Research in Priority Areas from the Ministry of Education of Japan and by the San-Ei Gen Foundation for Food Chemical Research.

Supporting Information Available: Listings of crystallographic data, positional and thermal parameters, and bond lengths and angles for **2b**·$2CH_3OH$ and **3b**·$3H_2O$·CH_3OH and figures showing CD spectral changes of **1a**·$5H_2O$ upon addition of sulfate ions and plots of calculated and observed Δϵ values for the L-rhamnose and D-mannose complexes (15 pages). Ordering information is given on any current masthead page.

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