General Synthesis of Useful Chelating Reagents Having a Sugar Unit, 1,3-Diamino-2-propyl β-D-Glucopyranoside and 1,3-Diamino-2-propyl α-D-Mannopyranoside

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Two 1,3-propanediamine derivatives bearing sugar units, 1,3-diamino-2-propyl β-D-glucopyranoside (2-β-D-Glc-pn) and 1,3-diamino-2-propyl α-D-mannopyranoside (2-α-D-Man-pn), have been prepared and characterized. The structures of two peracetylated diazides, as well as a nickel complex of glucose-type ligand, [Ni(2-β-D-Glc-pn)$_2$SO$_4$] have been determined by X-ray crystallography.

As a significant part of our program to clarify the nature of sugar-transition-metal interactions, we have synthesized and fully characterized metal complexes containing *N*-glycosides formed from polyamines and sugars or amino sugars.[1-3] However, these *N*-glycoside complexes are fairly unstable in water except for amino sugar complexes because cleavage reactions of the *N*-glycosidic bond are easily undergone in water. Therefore the development of new, stable ligands incorporating carbohydrate residues is highly desirable in various fields such as coordination chemistry, bioinorganic chemistry and industry.

In this work, by developing a general reproducible way for sugar residues to be linked to metal ions, we have succeeded in preparing a novel class of chelating ligands as described in Scheme 1. Known dibromides, 1,3-dibromo-2-propyl β-D-glucopyranoside[4,5] or 1,3-dibromo-2-propyl α-D-mannopyranoside[4] were converted to diazides (**1**, **4**) by NaN$_3$ in DMF at 50 °C.[6] After acetyl groups were removed by sodium methoxide, the azido groups were reduced by catalytic hydrogenation to give 1,3-diamino-2-propyl β-D-glucopyranoside (2-β-D-Glc-pn, **3**) and 1,3-diamino-2-propyl α-D-mannopyranoside (2-α-D-Man-pn, **6**). All new compounds gave satisfactory elemental analyses and FABMS Data. The protonation constants determined for **3** are log K_1 9.35(2) and log K_2 7.70(2) and those for **6** are log K_1 9.46(3) and log K_2 7.72(2).

The structures of two diazides (**1**, **4**) have been determined by X-ray crystallography. Perspective drawings of **4** are given in Figure 1 as a representative.[7] The pyranoid rings of the sugar units in **1** and in **4** adopt the β-$^4C_1$ chair conformation and the α-$^4C_1$ chair conformation. These crystal structure studies afforded useful information to predict the final structures of diamines (**3**, **6**) since the following procedures such as deacetylation and hydrogenation can be expected to cause no significant structural change at the sugar. The conformations in pyranoid rings of the sugar units in **3** and in **6** were confirmed by ^{1}H NMR spectroscopy in (CD$_3$)$_2$SO. The proton coupling constants for **3**

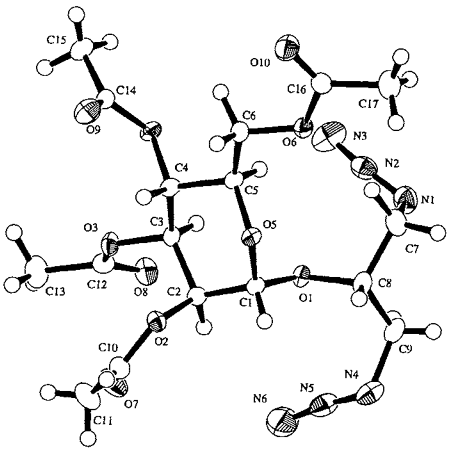
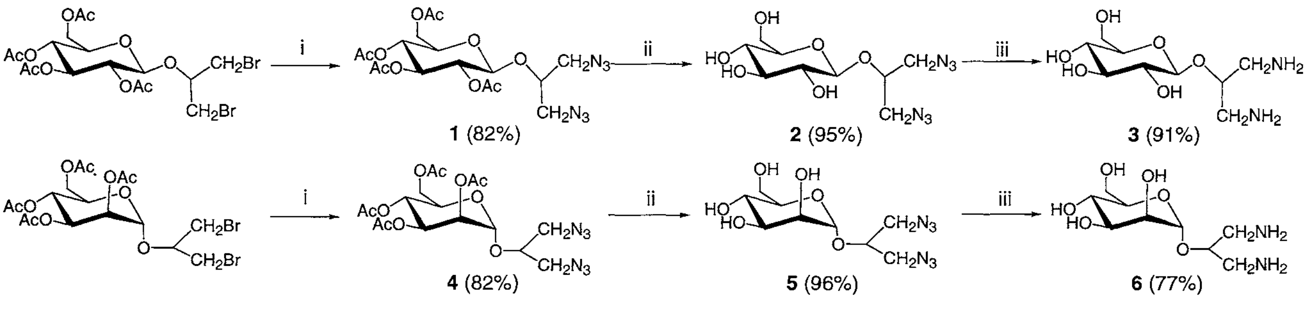


Figure 1. ORTEP diagram of **4**.



Scheme 1. Reagents and conditions: (i) NaN$_3$, DMF, 50 °C, 2 h. (ii) NaOMe, MeOH, rt, 1 h. (iii) PtO$_2$, H$_2$ (1 atm), MeOH, rt, 3 h.

($^3J_{1,2}$ = 7.8, $^3J_{2,3}$ = 8.8, $^3J_{3,4}$ = 8.8, $^3J_{4,5}$ = 9.6 Hz) indicated that the hydrogens at C-1, C-2, C-3, C-4, and C-5 are in the trans axial orientation corresponding to a β-$^4C_1$ conformation. Whereas, those for **6** ($^3J_{1,2}$ = 1.7, $^3J_{2,3}$ = 3.2, $^3J_{3,4}$ = 9.0, $^3J_{4,5}$ = 9.0 Hz) indicated that the hydrogens at C-3, C-4, and C-5 are in the axial orientation and the hydrogens at C-1 and C-2 are in the equatorial orientation corresponding to an α-$^4C_1$ conformation.

The metal-binding ability of the glucose-type ligand **3** was examplified by the synthesis of nickel complex. Addition of **3** into $NiSO_4 \cdot 6H_2O$ in methanol gave skyblue-powder, $[Ni(2\text{-}\beta\text{-D-Glc-pn})_2SO_4]$ (**7**), in which two ligand molecules and one sulfate anion were included per nickel atom.[8] Recrystallization from water-methanol afforded several crystals suitable for X-ray analysis (Figure 2).[9] Surprisingly, in addition to oxygen atom in sulfate part, glycoside oxygen in 2-β-D-Glc-pn also coordinated to octahedrally ligated nickel atom. It should be noted that these happeningly-formed crystals have not been obtained later.

As the results, this method is regarded as a general way to link sugar residues to metal ions. Peracetylated diazides gave suitable crystals for X-ray crystallography. Complexation with the other metal ions is now under investigation.

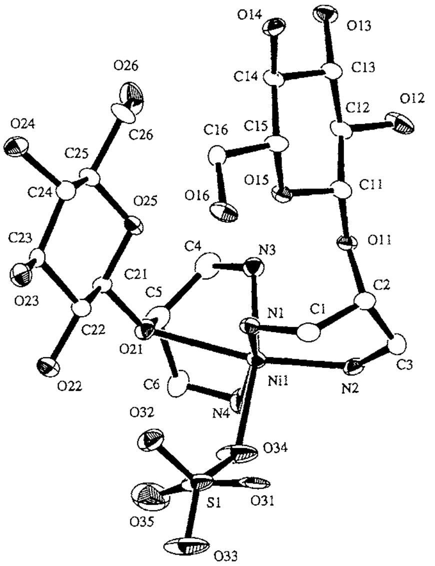


Figure 2. ORTEP diagram of **7**. Sulfate part was disordered and occupancy of 0.5 was adopted to O31 and O35.

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References

1 a) S. Yano, *Coord. Chem. Rev.*, **92**, 113 (1988). b) S. Yano and K. Ohtsuka, "Metal Ions in Biological Systems," ed by H. Sigel and S. Sigel, Marcel Dekker, New York (1996), Vol. 32, p. 27 and references cited therein.

2 T. Tanase, Y. Yasuda, T. Onaka, and S. Yano, *J. Chem. Soc., Dalton. Trans.*, **1998**, 345

3 S. Yano, S. Inoue, R Nouchi, K. Mogami, Y. Shinohara, Y. Yasuda, M. Kato, T. Tanase, T. Kakuchi, Y. Mikata, T. Suzuki, and Y. Yamamoto, *J. Inorg. Biochem.*, **69**, 15 (1998).

4 F. Marquez and A. Gonzalez G., *Tetrahedron Lett.*, **37**, 4395 (1966).

5 M. Horisberger, B. A. Lewis, and F. Smith, *Carbohydr. Res.*, **23**, 175 (1972).

6 This procedure was safety up to ~5 g of sodium azide.

7 Crystal data for **4**: orthorhombic, $P2_12_12_1$ (No. 19), a = 12.898(3) Å, b = 22.212(2) Å, c = 7.601(2) Å, V = 2177.5(7) Å^3, Z = 4, D_{calcd} = 1.441 g cm^{-3}, T = -120.0 °C, R = 0.031, R_w = 0.043 ($w = 1/\sigma^2(F_o)$) for 2347 refs with $I > 3\sigma(I)$. Structures were solved and refined with teXsan program package.

8 Yield: 96 %. Selected data for **7**: calc. for $C_{18}H_{40}N_4O_{16}NiS$: C, 32.79; H, 6.12; N, 8.50; S, 4.86. Found: C, 32.39; H, 6.10; N, 8.32; S, 4.54. ESI-MS: *m/z* 563 ($M\text{-}SO_4$).

9 Crystal data for **7**: monoclinic, $P2_1$ (No. 4), a = 8.120(3) Å, b = 16.633(2) Å, c = 10.306(2) Å, β = 111.83(2), V = 1292.1(5) Å^3, Z = 2, D_{calcd} = 1.694 g cm^{-3}, T = -98 °C, R = 0.034, R_w = 0.053 ($w = 1/\sigma^2(F_o)$) for 2304 refs with $I > 3\sigma(I)$. Structures were solved and refined with teXsan program package.