Sugar-Pendant Diamines

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A set of 1,3-propanediamine derivatives connected to carbohydrates (**5**) has been prepared in four steps from peracetylated sugar and 1,3-dibromo-2-propanol in 60−73% yields. D-Glucose, D-mannose, D-galactose, D-xylose, D-ribose, and maltose are utilized as sugar molecules in this work. The diamine moiety was connected to the C1 carbon of the glycopyranose ring via an *O*-glycoside bond. All of the anomeric configurations and sugar puckering conformations, except in the D-maltose derivative, were determined by X-ray crystallography of the diazido or dibromo precursors. While glycosidation of peracetylated galactopyranose with 1,3-dibromo-2-propanol in the presence of boron trifluoride afforded both anomers, the neighboring group participation of the 2-acetoxy group yielded a single anomer for the other substrates. This method has been used to synthesize a library of sugar-pendant diamines including an OH-protected derivative (**6**), and an *N*,*N*′-diisopropyl-substituted derivative (**7**). A similar series of reactions using 2,3-dibromo-1-propanol gave ethylenediamine-type derivatives (**11**), and bis(bromomethyl)bis(hydroxymethyl)methane (**12**) gave bisglucose-pendant derivatives (**16**).

Introduction

Carbohydrates are particularly useful substances because they are inexpensive, highly water-soluble, optically active materials.[1] These properties can be exploited to prepare bioactive materials,[2] molecular recognition devices,[3] and chiral auxiliaries in asymmetric synthesis,[4] as well as for functionalization of hydrophobic materials such as porphyrin derivatives[5] fullerenes,[6] and polymers (dendrimers).[7] The use of carbohydrates in inorganic chemistry, however, has been limited despite their potential importance because of their poor crystallinity.[8] Purification or characterization of carbohydrate com-

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plexes is often unsuccessful because of the complicated coordination behavior of sugar derivatives, which prevents a development of metal-coordination geometry. The investigation of new sugar-pendant ligands with discrete metal binding sites is highly desirable.

Previously we reported practical methods to synthesize sugar molecules derivatized with a polyamine in a one-pot reaction in alcoholic solution via *N*-glycoside bond formation.[9] The metal (Ni, Co, Mn, Zn) coordination spheres were elucidated by ^{1}H and ^{13}C NMR, circular dichroism (CD) spectroscopy, and X-ray crystallography. The Ni complexes with *N*-glycoside ligands provide a new concept for sugar-dependent C−C bond cleavages in the gas phase.[10] Since these *N*-glycoside metal complexes are unstable in water,[11] a new type of ligand is required for further investigation of a sugar−metal complex in aqueous solution.

O-Glycoside bonds are found in many mono-, oligo-, and polysaccharides, glycoproteins, proteoglycans, glycolipids, anitibiotics, and plant hormones.[1,2a,12] Therefore, introduction of a functional group through *O*-glycoside formation bears some similarity to natural structures. Alkyl *O*-glycoside bonds are fairly stable under physiological conditions.[13] Recently, we reported the efficient syntheses of D-glucose and D-mannose linked to a 1,3-propanediamine moiety, and their metal binding properties.[14a,b] We also have reported a synthesis of chiral ethylenediamine derivatives by utilizing the chirality of D-glucose.[14c]

To develop a general methodology to prepare sugar-based metal complexes, we describe the preparation of a novel set of chelating ligands (**5a**−**f**, **6**, (*S*)-**11d**, and **16**) possessing an *O*-glycoside bond that links the diamine moiety to a glycopyranose ring. The ligand library consists of 1,3-propanediamines, chiral 1,2-ethylenediamines, and bisglucose-pendant 1,3-propanediamines (Chart 1). The anomer configurations and sugar puckering conformations of many of these compounds were determined crystallographically from intermediate compounds such as the peracetylated diazide or dibromide.

Chart 1

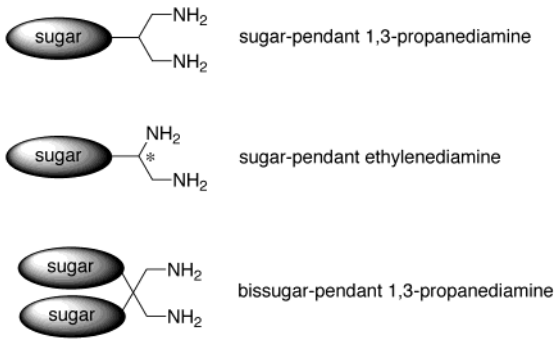
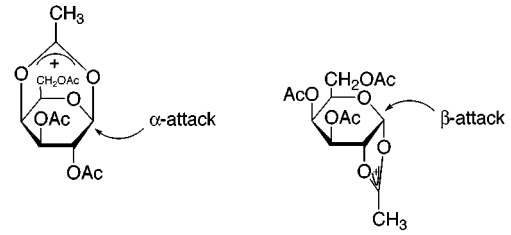


Chart 2



Results and Discussion

Sugar-Pendant 1,3-Propanediamine Derivatives. 1,3-Diamino-2-propyl D-glycopyranosides (**5a**−**f**) were synthesized according to Scheme 1. D-Glucose, D-mannose, D-galactose, D-xylose, D-ribose, and maltose were employed as sugar molecules. Peracetylated glycopyranose (**1**) was glycosylated with 1,3-dibromopropanol in the presence of excess boron trifluoride etherate in dry dichloromethane. The two bromine atoms in compound **2** were converted to azido moieties by treatment with NaN_3 in DMF at 50 °C to afford compound **3**. After the acetyl groups in compound **3** were removed by excess sodium methoxide to give **4**, the two azido groups were hydrogenated (1 atm, 3−4 h) to afford the desired products in 60−73% total yield.

In most cases, a single anomer, whose configuration depends on the configuration of the 2-acetoxy group (β-anomer for D-glucose, D-xylose, D-ribose, and maltose; α-anomer for D-mannose) was obtained by BF_3-catalyzed glycosidation of peracetylated glycopyranose with 1,3-dibromo-2-propanol; however, pentaacetyl-D-galactopyranose afforded mixtures of the two anomers. The mixture was obtained owing to the participation of the 4-acetoxy group in addition to the normal 2-acetoxy neighboring group effect (Chart 2). This anomeric mixture was separated successfully by silica gel column chromatography after conversion to the diazido analogous **3c** (eluent, ethyl acetate/hexane = 3/7; R_f = 0.35 for α-**3c**, 0.24 for β-**3c**).

The other anomers with 1,2-*cis*-configurations, like α-D-glucopyranoside or β-D-mannopyranoside, are generally difficult to prepare.[1,13a,15] In the reaction of pentaacetyl-D-glucose with several alcohols, Lewis acid catalysts such

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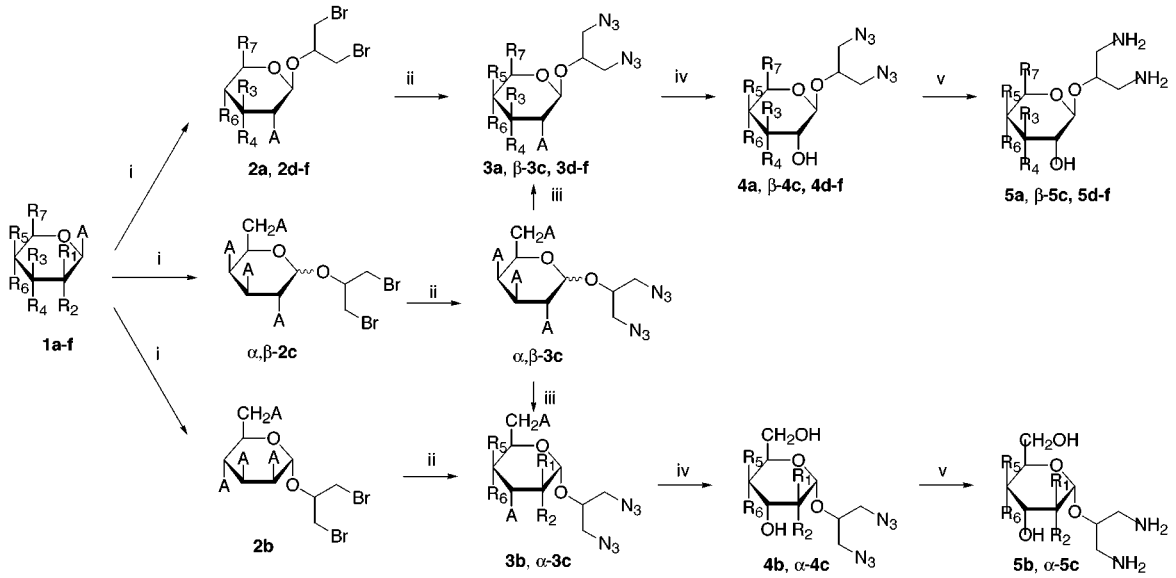
Scheme 1[a]



1-3a: R_1=R_4=R_5=H, R_2=R_3=R_6=OAc, R_7=CH_2OAc
1-3b: R_2=R_4=R_5=H, R_1=R_3=R_6=OAc, R_7=CH_2OAc
1-3c: R_1=R_4=R_6=H, R_2=R_3=R_5=OAc, R_7=CH_2OAc
1-3d: R_1=R_4=R_5=R_7=H, R_2=R_3=R_6=OAc
1-3e: R_1=R_3=R_5=R_7=H, R_2=R_4=R_6=OAc
1-3f: R_1=R_4=R_5=H, R_2=R_3=OAc, R_6=2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl, R_7=CH_2OAc

4,5a: R_4=R_5=H, R_3=R_6=OH, R_7=CH_2OH
4,5b: R_2=R_5=H, R_1=R_6=OH, R_7=CH_2OH
4,5c: R_1=R_4=R_6=H, R_2=R_3=R_5=OH, R_7=CH_2OH
4,5d: R_4=R_5=R_7=H, R_3=R_6=OH
4,5e: R_3=R_5=R_7=H, R_4=R_6=OH
4,5f: R_4=R_5=H, R_3=OH, R_6=α-D-glucosyl, R_7=CH_2OH

[a] A = OAc. Conditions: (i) 1,3-dibromopropanol, BF_3·OEt_2, CH_2Cl_2; (ii) NaN_3, DMF, 80 °C; (iii) silica gel column chromatography; (iv) NaOMe, MeOH; (v) PtO_2/H_2, MeOH.

as $FeCl_3$ in CH_2Cl_2 predominantly afford the α-isomer.[16] Therefore we performed the glycosidation of pentaacetyl-D-glucose with 1,3-dibromopropanol using $FeCl_3$ catalyst in various solvents; however, only the *β*-isomer was obtained under all the conditions examined. 1,3-Dichloro-2-propanol, employed instead of 1,3-dibromopropanol in order to reduce the steric hindrance between the alcohol and the 2-acetyl group of the glucopyranose ring, produced similar results. Likewise, epimerization of the *β*-anomer to the α-glycoside in the presence of the same catalyst[17] failed. In contrast, the glycosidation of pentaacetyl-D-glucose with 2-propanol in the presence of $FeCl_3$ afforded the α-isomer selectively, indicating that the 1,3-dihalogenated 2-propanol affords only the *β*-glucoside in the reaction with pentaacetyl-D-glucose. Other approaches are required to prepare the α-anomers of **5a**, **5d**−**f**, as well as the *β*-anomer of **5b**.

The conformations of the glycopyranoid ring in compounds **5** were investigated by ^1H NMR spectroscopy in $(CD_3)_2SO/D_2O$. The proton−proton coupling constants for **5a** ($^3J_{1,2}$ = 7.8, $^3J_{2,3}$ = 8.8, $^3J_{3,4}$ = 8.8, $^3J_{4,5}$ = 9.6 Hz), *β*-**5c** ($^3J_{1,2}$ = 7.7, $^3J_{2,3}$ = 9.9, $^3J_{3,4}$ = 3.2, $^3J_{4,5}$ = ∼0 Hz), and **5d** ($^3J_{1,2}$ = 7.9, $^3J_{2,3}$ = 9.2, $^3J_{3,4}$ = 9.4, $^3J_{4,5}$ = 5.3, 8.9 Hz) correspond to *β*-$^4C_1$ conformations. Those for **5b** ($^3J_{1,2}$ = 1.7, $^3J_{2,3}$ = 3.2, $^3J_{3,4}$ = 9.0, $^3J_{4,5}$ = 9.0 Hz) and α-**5c** ($^3J_{1,2}$ = 3.7, $^3J_{2,3}$ = 11.3, $^3J_{3,4}$ = 3.0, $^3J_{4,5}$ = ∼0 Hz) correspond to α-$^4C_1$ conformations. For **5e**, the proton−proton coupling constants ($^3J_{1,2}$ = 6.6, $^3J_{2,3}$ = 3.2, $^3J_{3,4}$ = 3.2, $^3J_{4,5}$ = 4.0, 6.8 Hz) indicate that the compound is in equilibrium between the *β*-$^4C_1$ and *β*-$^1C_4$ conformations.[18] These values remain constant throughout the series of precursors **2**−**5**. For example, proton−proton coupling constants for compounds **2**−**5a** are $^3J_{1,2}$ = 7.8−9.0, $^3J_{2,3}$ = 8.8−9.6, $^3J_{3,4}$ = 8.8−9.8, $^3J_{4,5}$ = 9.0−9.9 Hz. This indicates that modification of the side chain and deprotection of hydroxyl group of these compounds does not afford any significant change in sugar ring puckering. The proton−proton coupling constants of precursors **2**−**4f** suggest the *β*-$^4C_1$ conformation for the diaminopropanol-glycosylated ring of these compounds.

Most of the diazides **3** afford X-ray quality crystals after recrystallization. Structures of these precursors, (**3a**, **3b**, α-**3c**, **3d**) as well as the dibromo precursor (**2e**) were determined by X-ray crystallography (Figures S1−S5, Supporting Information). The NMR data of these compounds is in good agreement with these solid-state structures, indicating the similarity in sugar ring puckering in the solid and solution states. For the ribose derivative, although the solution structure is in equilibrium between *β*-$^4C_1$ and *β*-$^1C_4$ conformations (vide supra), compound **2e** crystallizes in the *β*-$^1C_4$ conformation because of a crystal packing interaction. Thus, the crystal structure studies of the diazido or dibromo precursors provide useful information about the structure of the diamine derivatives because the procedures induce significant structural changes in neither the anomeric position nor the stereocenters, as determined by NMR investigations (vide supra).

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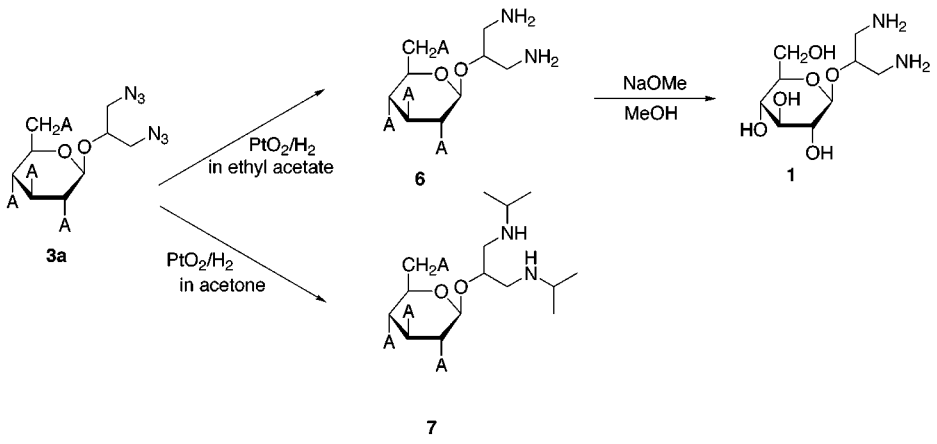
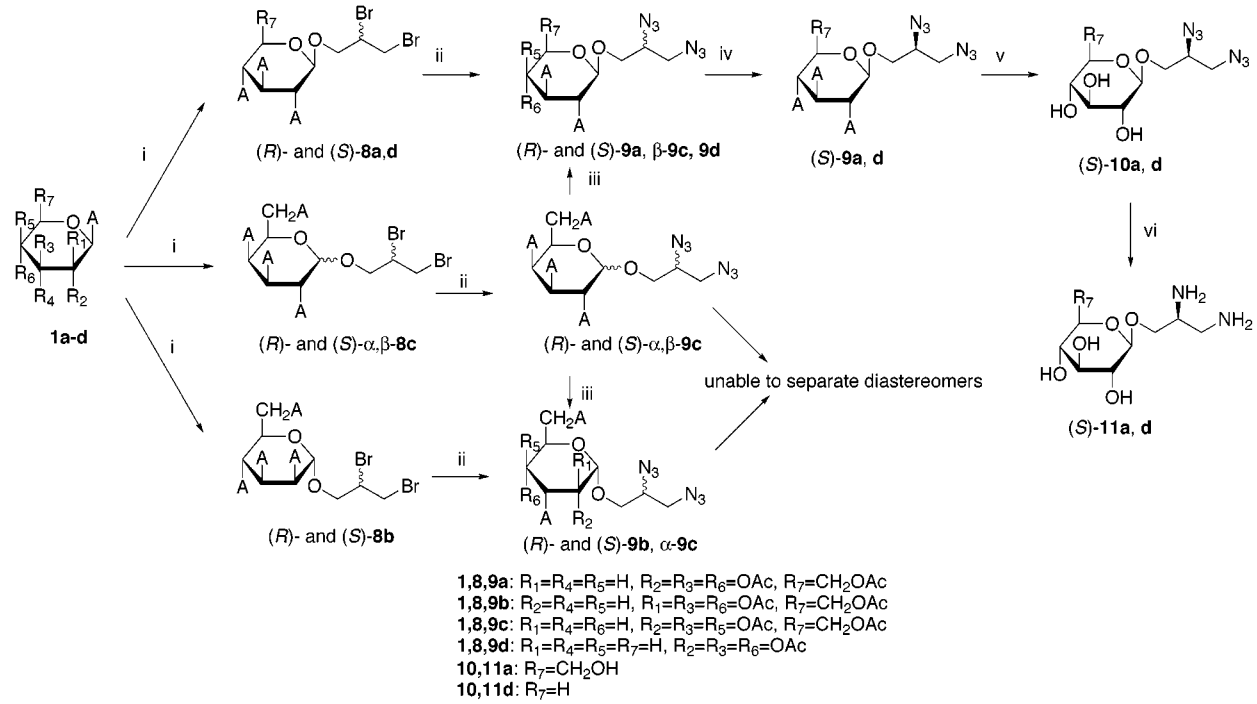
Scheme 2[a]



[a] A = OAc.

Scheme 3[a]



[a] A = OAc. Conditions: (i) 2,3-dibromopropanol, $BF_3{\cdot}OEt_2$, CH_2CL_2; (ii) NaN_3, DMF, 80 °C; (iii) silica gel column chromatography; (iv) repeated recrystallization from EtOH; (v) NaOMe, MeOH; (vi) PtO_2/H_2, MeOH.

When the hydrogenation of compound **3a** was performed in other solvents, modified compounds were obtained. Reaction in ethyl acetate produced the OH-protected diamine **6**, and in acetone produced the OH-protected *N*,*N*′-diisopropyldiamine **7** quantitatively (Scheme 2). It can be expected that **7** was formed via a similar reaction to that observed in the synthesis of 2-isopropylaminoethanol.[19] The compounds **6** and **7** are useful derivatives for the investigation of hydrophilic and steric effects of the amino compounds **5**. These methods are applicable to the other sugar derivatives (data not shown).

Sugar-Pendant Ethylenediamine Derivatives. In contrast to the 1,3-propanediamine compounds, use of an ethylenediamine moiety produces an asymmetric carbon at the point of attachment of the sugar (Chart 1). The control of chiral attachment is an important consideration, along with the control of anomer configuration. Previously, we have reported the separation of diastereomers of the diazido precursor **9a** by recrystallization, in which the D-glucose moiety acts as a chiral auxiliary giving rise to an optically pure sugar-pendant ethylenediamine (*S*)-**11a** (Scheme 3).[14c] This section describes the application and limitation of this methodology to other sugar molecules. D-Mannose, D-galactose, and D-xylose were utilized for this study.

Starting from **1b**−**d** and racemic 2,3-dibromo-1-propanol, a similar treatment as for the preparation of diazides **3** gave diazides **9** as diastereomeric mixtures. The anomeric selectivity in glycosidation was similar to that for 1,3-propanediamine-type compounds. Only one anomer (two diastereomers arising from the carbon center in the ethylenediamine moiety) was obtained as

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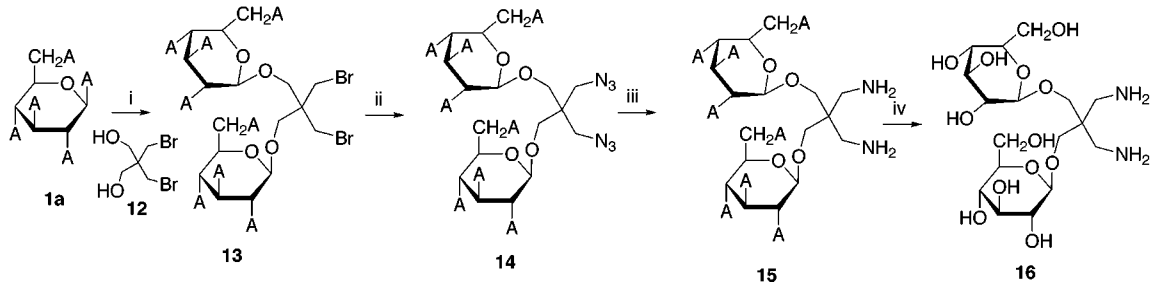
Scheme 4[a]



[a] A = OAc. Conditions: (i) $BF_3{\cdot}OEt_2$, CH_2Cl_2; (ii) NaN_3, DMF, 80 °C; (iii) PtO_2/H_2, ethyl acetate; (iv) NaOMe, MeOH.

judged from the ^{1}H NMR spectrum except for galactose derivative (**9c**), where four possible diastereomers were found. Anomer separation of **9c** was performed successfully by silica gel column chromatography (eluent, ethyl acetate/hexane = 3/7; R_f = 0.35 for α-**9c**, 0.24 for β-**9c**); however, no separation was achieved for diastereomers of the ethylenediamine carbon by chromatography in all derivatives of **9**.

Recrystallization of diastereomeric mixtures of **9b**−**d** was performed in several solvents and in mixed solvents including MeOH, EtOH, *n*-propanol, *i*-propanol, butanol, THF, chloroform. Alcohols were effective for the separation of the diastereomers of the xylose derivative **9d**. As found in glucose derivative **9a**,[14c] X-ray crystallography of crystalline **9d** (Figure S6) revealed that the diastereomer has the *S* configuration at the stereocenter of the ethylenediamine moiety. The deprotection of acetyl groups and the reduction of azides in (*S*)-**9d** were both performed in a manner similar to that described above to give optically pure (*S*)-**11d**. The other sugar derivatives, **9b** and **9c**, did not afford crystals under the conditions used. These sugars are not suitable for the preparation of sugar-pendant chiral ethylenediamines.

Bissugar-Pendant 1,3-Propanediamine. In studies from our group[5b,c] and others,[3a] the effect of numbers of sugars seems to be important for both biological activities and tuning compounds properties. Introduction of additional sugar moieties auguments the solubility of the compounds and alters biological activity.

A procedure similar to that discussed above was adopted in the reaction of **1a** with dibromodiol **12** (Scheme 4). The hydrogenation of diazide **14** in ethyl acetate was performed to give **15**, followed by deprotection of the hydroxyl groups to afford the final diamine **16**. Deprotection of **14** in MeOH was often incomplete as a result of the insolubility of the reduction intermediates. A structural analysis of the dibromo precursor **13** revealed the β-$^4C_1$ conformation for the D-glucose moiety (Figure S7). Other sugar derivatives can be synthesized by this synthetic route (data not shown).

Summary and Conclusions

Compounds **5a**−**f**, **6**, (*S*)-**11d** and **16** were prepared in four steps from peracetyl protected sugar molecules in 21−73% yield. This ligand library includes sugar-pendant 1,3-propanediamine, chiral ethylenediamine with a sugar substituent, and 1,3-propanediamine tethered to two sugar molecules. Although D-galactose afforded both the α- and β-anomers, the other sugars afforded only one anomer, owing to the participation of the 2-acetoxy group during the glycosidation of peracetylglycopyranose with alcohol in the presence of boron trifluoride. All anomer configurations, except in the maltose derivative, were determined by X-ray crystallography of the diazido or dibromo precursors. Since the present method does not require chromatography, except for anomer separation in the case of D-galactose, it is suitable for multigram syntheses of diamine−sugar ligands. Even though other routes are required in order to accomplish the preparation of a complete set of anomers and chiral diastereomers with the ethylenediamine derivatives, this method is useful for preparation of diamine-sugar hybrid molecules. The application of these diamine ligands in metal complexes, including cisplatin-type platinum(II) complexes with pendant sugars is now under investigation in our laboratories.

Experimental Section

1,3-Diazido-2-propyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranoside (3a). 1,3-Dibromo-2-propyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[20] (1.0 g, 1.82 mmol) was reacted with sodium azide (1.42 g, 21.8 mmol)[21] in DMF (30 mL) at 70 °C for 2 h. The product was extracted with ethyl acetate and washed with water five times and brine once. The organic layer was dried and evaporated to give a white microcrystalline product that was recrystallized from ethyl acetate−hexane to give 1,3-diazido-2-propyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside in 82% yield (0.705 g): mp 101−102 °C. FABMS: *m*/*z* = 473.1635 (calcd for $C_{17}H_{25}N_6O_{10}$ $(M + H)^+$ 473.1632). Anal. Calcd for $C_{17}H_{24}N_6O_{10}$: C, 43.22; H, 5.12; N, 17.79. Found: C, 43.08; H, 4.94; N, 17.78.

1,3-Diazido-2-propyl β-D-Glucopyranoside (4a). 1,3-Diazido-2-propyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (2.5 g, 5.3 mmol) was dissolved in 100 mL of MeOH. Sodium methoxide (2.9 g, 54 mmol) was added and the reaction mixture was stirred for an hour at room temperature. The resulting solution was neutralized by Amberlite. After filtration to remove the resin, the solvent was removed by evaporation to give 1,3-diazido-2-propyl β-D-glucopyranoside in 95% yield (1.53 g). FABMS: *m*/*z* = 305.1215 (calcd for $C_9H_{17}N_6O_6$ $(M + H)^+$ 305.1210).

1,3-Diamino-2-propyl β-D-Glucopyranoside (5a). The mixture of 1,3-diazido-2-propyl β-D-glucopyranoside (1.53 g, 5.0 mmol) and PtO_2 (100 mg) in 150 mL of MeOH was hydrogenated under atmospheric pressure of hydrogen at room temperature. After the removal of the catalyst by filtration, the solvent was removed by evaporation to give 1,3-diamino-2-propyl β-D-glucopyranoside in 91% yield (1.15 g): mp 177−178 °C. Anal. Calcd for $C_9H_{21}N_6O_{6.5}$ (**5a**·0.5H_2O): C, 41.37; H, 8.10; N, 10.72. Found: C, 41.43; H, 7.78; N, 10.80.

1,3-Diazido-2-propyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (3b). Compound **3b** was prepared by a method

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(21) This procedure is safe up to 5 g.

similar to preparation of **3a** using **1b**[20] in place of **1a**. Yield: 82% (mp 105−106 °C). FABMS: m/z = 473.1630 (calcd for $C_{17}H_{25}N_6O_{10}$ $(M + H)^+$ 473.1632). Anal. Calcd for $C_{17}H_{24}N_6O_{10}$: C, 43.22; H, 5.12; N, 17.79. Found: C, 43.02; H, 5.03; N, 17.63.

1,3-Diazido-2-propyl α-D-mannopyranoside (4b). Compound **4b** was prepared by a method similar to preparation of **4a** using **3b** in place of **3a**. Yield: 96%. FABMS: m/z = 305.1209 (calcd for $C_9H_{17}N_6O_6$ $(M + H)^+$ 305.1210).

1,3-Diamino-2-propyl α-D-mannopyranoside (5b). Compound **5b** was prepared by a method similar to preparation of **5a** using **4b** in place of **4a**. Yield: 77%. FABMS: m/z = 253.1432 (calcd for $C_9H_{21}N_6O_6$ $(M + H)^+$ 253.1400).

1,3-Diazido-2-propyl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (α-3c) and 1,3-Diazido-2-propyl 2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranoside (*β*-3c). To the dichloromethane solution of 1,2,3,4,6-penta-*O*-acetyl-*β*-D-galactose **1c** (Tokyo Kasei) (10 g, 26 mmol) and 1,3-dibromo-2-propanol (8.71 g, 40 mmol) was added boron trifluoride etherate (23.6 mL, 167 mmol) under argon atmosphere at 0 °C. After stirring at 0 °C the reaction solution was stirred at room temperature overnight. The reaction solution was diluted with ethyl acetate (300 mL) and washed with water several times and brine once. The resulting organic layer was dried and evaporated to give dibromide **2c** as an anomeric mixuture in 83% yield (11.8 g). This substance was used for reaction with sodium azide by a method similar to preparation of **3a** without anomer separation. In this diazide, separation of anomeric isomer was performed by silica gel column chromatography (eluent, ethyl acetate/hexane = 3/7). The α-isomer was further purified by recrystallization from EtOH. **α-3c.** Yield: 5.7%. R_f = 0.35 (ethyl acetate/hexane = 3/7). Mp = 105−106 °C. FABMS: m/z = 473.1606 (calcd for $C_{17}H_{25}N_6O_{10}$ $(M + H)^+$ 473.1632). ***β*-3c.** Yield: 17%. R_f = 0.24 (ethyl acetate/hexane = 3/7). FABMS: m/z = 473.1613 (calcd for $C_{17}H_{25}N_6O_{10}$ $(M + H)^+$ 473.1632).

1,3-Diazido-2-propyl α-D-Galactopyranoside (α-4c). Compound α-**4c** was prepared by a method similar to preparation of **4a** using α-**3c** in place of **3a**. Yield: 98%.

1,3-Diazido-2-propyl *β*-D-Galactopyranoside (*β*-4c). Compound *β*-**4c** was prepared by a method similar to preparation of **4a** using *β*-**3c** in place of **3a**. Yield: 97%.

1,3-Diamino-2-propyl α-D-Galactopyranoside (α-5c). Compound α-**5c** was prepared by a method similar to preparation of **5a** using α-**4c** in place of **4a**. Yield: 67%. FABMS: m/z = 253.1434 (calcd for $C_9H_{21}N_2O_6$ $(M + H)^+$ 253.1400).

1,3-Diamino-2-propyl *β*-D-Galactopyranoside (*β*-5c). Compound *β*-**5c** was prepared by a method similar to preparation of **5a** using *β*-**4c** in place of **4a**. Yield: 91%. FABMS: m/z = 253.1411 (calcd for $C_9H_{21}N_2O_6$ $(M + H)^+$ 253.1400).

1,3-Diazido-2-propyl 2,3,4-Tri-*O*-acetyl-*β*-D-xylopyranoside (3d). Compound **3d** was prepared by a method similar to preparation of **3a** using 1,3-dibromo-2-propyl 2,3,4-tri-*O*-acetyl-*β*-D-xylopyranoside (**2d**)[20b] in place of **2a**. Yield: 81%. Mp = 118−119 °C. Anal. Calcd for $C_{14}H_{20}N_6O_8$: C, 42.00; H, 5.04; N, 20.99. Found: C, 42.00; H, 4.99; N, 20.94.

1,3-Diazido-2-propyl *β*-D-Xylopyranoside (4d). Compound **4d** was prepared by a method similar to preparation of **4a** using **3d** in place of **3a**. Yield: 95%. Mp = 60−61 °C. Anal. Calcd for $C_8H_{14}N_6O_5$: C, 35.00; H, 5.15; N, 30.65. Found: C, 34.73; H, 5.09; N, 30.46.

1,3-Diamino-2-propyl *β*-D-Xylopyranoside (5d). Compound **5d** was prepared by a method similar to preparation of **5a** using **4d** in place of **4a**. Yield: 85%. Mp = 209−211 °C. Anal. Calcd for $C_8H_{18}N_2O_5$: C, 43.24; H, 8.16; N, 12.60. Found: C, 43.05; H, 8.29; N, 12.52.

1,3-Dibromo-2-propyl 2,3,4-Tri-*O*-acetyl-*β*-D-ribopyranoside (2e). Compound **2e** was prepared by a method similar to preparation of **2c** using **1e**[18] in place of **1c**. Yield: 55%. Mp = 86−88 °C. FABMS: m/z = 253.1411 (calcd for $C_9H_{21}N_2O_6$ $(M + H)^+$ 253.1400). Anal. Calcd for $C_{14}H_{20}O_8Br_2$: C, 35.32; H, 4.23; Br, 33.56. Found: C, 35.11; H, 3.99; Br, 33.46.

1,3-Diazido-2-propyl 2,3,4-Tri-*O*-acetyl-*β*-D-ribopyranoside (3e). Compound **3e** was prepared by a method similar to preparation of **3a** using **2e** in place of **2a**. Yield: 79%. FABMS: m/z = 401.1435 (calcd for $C_{14}H_{21}N_6O_8$ $(M + H)^+$ 401.1421).

1,3-Diazido-2-propyl *β*-D-Ribopyranoside (4e). Compound **4e** was prepared by a method similar to preparation of **4a** using **3e** in place of **3a**. Yield: 96% FABMS: m/z = 275.1125 (calcd for $C_8H_{15}N_6O_5$ $(M + H)^+$ 275.1104).

1,3-Diamino-2-propyl *β*-D-Ribopyranoside (5e). Compound **5e** was prepared by a method similar to preparation of **5a** using **4e** in place of **4a**. Yield: 80%. Mp = 90−92 °C. FABMS: m/z = 223.1285 (calcd for $C_8H_{19}N_2O_5$ $(M + H)^+$ 223.1294).

1,3-Dibromo-2-propyl 2,3,6,8,9,10,13-Hepta-*O*-acetyl-*β*-(α-D-glucopyranosyl-(1−4)-D-glucopyranoside) (2f). Compound **2f** was prepared by a method similar to preparation of **2c** using octa-*O*-acetylmaltose[22] in place of **1c**. The crude material was purified by recrystallization from EtOH. Yield: 39%. Mp = 130−131 °C. Anal. Calcd for $C_{29}H_{40}O_{18}Br_2$: C, 41.64; H, 4.82. Found: C, 41.51; H, 4.93.

1,3-Diazido-2-propyl 2,3,6,8,9,10,13-Hepta-*O*-acetyl-*β*-(α-D-glucopyranosyl-(1−4)-D-glucopyranoside) (3f). Compound **3f** was prepared by a method similar to preparation of **3a** using **2f** in place of **2a**. Yield: 77%. Mp = 87−89 °C. FABMS: m/z = 761.2477 (calcd for $C_{29}H_{41}N_6O_{18}$ $(M + H)^+$ 761.2477). Anal. Calcd for $C_{29}H_{40}N_6O_{18}$: C, 45.79; H, 5.30; N, 11.05. Found: C, 45.10; H, 5.29; N, 11.43.

1,3-Diazido-2-propyl *β*-(α-D-Glucopyranosyl-(1−4)-D-glucopyranoside) (4f). Compound **4f** was prepared by a method similar to preparation of **4a** using **3f** in place of **3a**. Yield: 91%. Mp = 78−82 °C. FABMS: m/z = 489.1557 (calcd for $C_{15}H_{26}N_6NaO_{11}$ $(M + Na)^+$ 489.1557).

1,3-Diamino-2-propyl *β*-(α-D-Glucopyranosyl-(1−4)-D-glucopyranoside) (5f). Compound **5f** was prepared by a method similar to preparation of **5a** using **4f** in place of **4a**. Yield: 90%. FABMS: m/z = 415.1928 (calcd for $C_{15}H_{31}N_2O_{11}$ $(M + H)^+$ 415.1928).

1,3-Diamino-2-propyl 2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranoside (6). Compound **6** was prepared by reduction of **3a** in a method similar to preparation of **5a** using ethyl acetate as a reaction solvent. After removal of catalyst, evaporation of the solvent gave pure **6** as an yellow oil in 50% yield.

1,3-Bis(isopropylamino)-2-propyl 2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranoside (7). Compound **7** was prepared by a method similar to preparation of **6** using acetone as a reaction solvent. Yield: 95%. FABMS: m/z = 505.2762 (calcd for $C_{23}H_{41}N_2O_{10}$ $(M + H)^+$ 505.2761).

(*S*)-2,3-Diazido-1-propyl 2,3,4-Tri-*O*-acetyl-*β*-D-xylopyranoside ((*S*)-9d). Diastereomer mixture of compound **10d** was prepared by a method similar to preparation of anomer mixture of **3c** using 1,2,3,4-tetra-*O*-acetyl-*β*-D-xylose **1d**[18] in place of **1c**. Repeated recrystallization from EtOH afforded pure (*S*)-isomer in 6% yield (from **1d**). Mp = 70−72 °C. $[\alpha]_D$ −53.2 ° (*c* 1.1 chloroform). FABMS: m/z = 401.1414 (calcd for $C_{14}H_{21}N_6O_8$ $(M + H)^+$ 401.1421).

(*S*)-2,3-Diazido-1-propyl *β*-D-Xylopyranoside ((*S*)-10d). Compound (*S*)-**10d** was prepared by a method similar to preparation of **4a** using (*S*)-**9d** in place of **3a**. **(*S*)-2,3-Diamino-1-propyl *β*-D-xylopyranoside ((*S*)-11d).** Compound (*S*)-**11d** was prepared by a method similar to preparation of **5a** using (*S*)-**10d** in place of **4a**. FABMS: m/z = 223.1312 (calcd for $C_8H_{19}N_2O_5$ $(M + H)^+$ 223.1294).

Bis(bromomethyl)bis[(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy)methyl]methane (13). Compound **13** was prepared by a method similar to preparation of **2c** using 1,2,3,4,6-penta-*O*-acethyl-*β*-D-glucose (**1a**)[23] and bis(bromomethyl)bis(hydroxymethyl)methane (**12**) (Tokyo Kasei). Yield: 34%. Mp = 173−174 °C. FABMS: m/z = 923.0986 (calcd for

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$C_{33}H_{47}O_{20}{}^{79}Br^{81}Br$ $(M + H)^+$ 923.0986). Anal. Calcd for $C_{33}H_{46}Br_2O_{20}$: C, 42.97; H, 5.03; Br, 17.32. Found: C, 42.92; H, 4.82; Br, 18.00.

Bis(azidomethyl)bis[(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy)methyl]methane (14). Compound **14** was prepared by a method similar to preparation of **3a** using **13** in place of **2a**. Yield: 64%. FABMS: m/z = 847.2848 (calcd for $C_{33}H_{47}O_{20}N_6$ $(M + H)^+$ 847.2845). Anal. Calcd for $C_{33}H_{46}O_{20}N_6$: C, 46.81; H, 5.48; N, 9.92. Found: C, 46.45; H, 5.54; N, 9.78.

Bis(aminomethyl)bis[(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy)methyl]methane (15). Compound **15** was prepared by a method similar to preparation of **6** using **14** inplace of **3a**. Yield: 99%. Mp = 153−154 °C. FABMS: m/z = 795.3069 (calcd for $C_{33}H_{51}O_{20}N_2$ $(M + H)^+$ 795.3035). Anal. Calcd for $C_{33}H_{50}O_{20}N_2$: C, 49.87; H, 6.34; N, 3.52. Found: C, 49.13; H, 5.81; N, 3.47.

Bis(aminomethyl)bis[(*β*-D-glucopyranosyloxy)methyl]methane (16). Compound **16** was prepared by a method similar to preparation of **5a** using **15** in place of **4a**. Yield: 99%. FABMS: m/z = 459.2174 (calcd for $C_{17}H_{35}O_{12}N_2$ $(M + H)^+$ 459.2190). Treatment of **16** by concentrated HCl and MeOH gave dihydrochloric salt (**16**·2HCl). Anal. Calcd for $C_{17}H_{44}O_{16}N_2Cl_2$ (**16**·2HCl·4H_2O): C, 33.84; H, 7.35; N, 4.64; Cl, 11.75. Found: C, 34.06; H, 7.48; N, 3.80; Cl, 11.12.

Crystal Structure Determination. Suitable crystals for X-ray crystallography were obtained by a recrystallization of **3a**, **3b**, **3c**, **3d**, **2e**, (*S*)-**9d**, and **13** from EtOH or ethyl acetate/hexane mixtures. The crystal data and the experimental conditions are listed in Table S1, S6, S11, S16, S21, S26, and S31. Data were collected on a Rigaku AFC7R diffractometer or a Bruker SMART CCD system by using graphite-monochromatized Mo Kα (λ = 0.71069 Å) radiation. Three standard reflections were monitored every 150 reflections, and no systematic decrease in intensity was observed. Reflection data were corrected for Lorentz-polarization and absorption (by ψ-scan method) effects. The structures were solved by direct methods with SIR-88.[24] Hydrogen atoms are included but not refined. The structure was refined with the full-matrix least-squares techniques minimizing $\sum w(|F_o| - |F_c|)^2$. Atomic scattering factors, f', and f'' for O, N, and C were taken from the literature.[25,26] All calculations were carried out on a Silicon Graphics O_2 workstation with the TEXSAN Program.[27] Perspective drawing were drawn by using ORTEP program.[28]

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Supporting Information Available: Tabulations of crystallographic information including ORTEP diagrams (Figures S1−11) for **3a**, **3b**, **3c**, **3d**, **2e**, (*S*)-**9d**, and **13**, and NMR spectra for **3f**, **14**, **15**, and **16**. NMR peak assignments of the newly prepared compounds are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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