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The Synthesis of α-D-Galactopyranosyl and α-D-Mannopyranosyl 2-Amino-2-deoxy-α-D-glucopyranosides and the Conformation of Their Glycoside Linkage[1]

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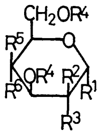
A new analog of trehalosamine, α-D-galactopyranosyl 2-amino-2-deoxy-α-D-glucopyranoside, was synthesized by the glycosylation of 2,3,4,6-tetra-*O*-(*p*-chlorobenzyl)-α-D-galactopyranose with 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranosyl bromide, using silver perchlorate and tribenzylamine in benzene, followed by chromatographic separation and the subsequent removal of the protecting groups. Similarly, α-D-mannopyranosyl 2-amino-2-deoxy-α-D-glucopyranoside was synthesized. The conformation of the glycoside linkage of these α,α-disaccharides is discussed in relation to the ^{13}C chemical shifts of their anomeric carbons.

Trehalosamine (**25**)[2] and its analogs[3] are unique antimicrobial aminoglycosides which are 1,1′-linked disaccharides. However, since the synthesis of **25**,[4] only a few non-symmetrical α-glycosyl α-glycosides with an amino group have thus far been synthesized,[5] although the chemical modification of α,α-trehalose has often been performed recently.[6,7] Interestingly, some antibiotics possess the structure of 1,1′-linked glycosyl glycoside.[8] Such circumstances prompted us to synthesize the *galacto* analog (**17**) as well as the *manno* one (**21**) of trehalosamine. After our work had been completed, a synthesis of **21** *via* a different route was described.[9]



Compound	R^1	R^2	R^3	R^4	R^5	R^6
1	Br	H	NHDp	Ac	H	OAc
2	OH	H	OCb	Cb	OCb	H
3	OH	OCb	H	Cb	H	OCb
4	OH	H	OCb	Cb	H	OCb
5	OH	H	NHDp	Ac	H	OAc

Ac = acetyl, Cb = *p*-chlorobenyl, Dp = 2,4-dinitrophenyl.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranosyl bromide (**1**),[10] occasionally used for synthesizing various 2-amino-2-deoxy-α-D-glucopyranosides,[11] was chosen to perform the glycosylation of 2,3,4,6-tetra-*O*-(*p*-chlorobenzyl)-α-D-galactopyranose (**2**).[12] The condensation using silver perchlorate[13] and tribenzylamine[14] in benzene at room temperature gave the α,α-form of the 1,1′-linked disaccharide derivative (**6**) as the main product. The chromatography of the reaction mixture gave **6** and three other configurational isomers (**7**, **8**, and **8a**) in yields of 35, 15, 9, and 3% respectively.

The protecting groups of **6** were removed in the order of deacetylation with a dil solution of sodium methoxide in methanol, dedinitrophenylation with a basic resin in aq acetone, and dechlorobenzylation by catalytic hydrogenolysis over palladium black in aq acetic acid, followed by deionization with a basic resin to afford **17** in a 16% yield from **2**. When the other three isomers **7**, **8**, and **8a**, were subjected to the above set of deprotection processes, they were converted into **18**, **19**, and **20** respectively.

The glycosylation of the mannose derivative (**3**) with **1** was next performed similarly to furnish the α,α-linked disaccharide derivative (**9**) in a 31% yield. Again, three isomers (**10**, **11**, and **12**) were separated from the glycosylation mixture. The deprotection of **9** gave the *manno* analog of trehalosamine, **21**, in a 16% yield from **3**.

TABLE 1. MOLECULAR ROTATIONS OF α-D-HEXOSYL α-D-GLUCOSAMINIDES AND α-D-HEXOSYL α-D-GLUCOSIDES AND THEIR PER-ACETATES

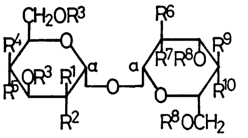
Compound	Unprotected	Acetate
α-D-Gal*p* α-D-GlcN*p*	+702	+1225
α-D-Gal*p* α-D-Glc*p*	+711[a]	+1329[a]
α-D-Man*p* α-D-GlcN*p*	+500	+718
α-D-Man*p* α-D-Glc*p*	+569[b]	+786[b]
α-D-Glc*p* α-D-GlcN*p*	+649	+1022
α-D-Glc*p* α-D-Glc*p*	+680[c]	+1100[d]

a) Ref. 5b. b) Ref. 5a. c) G. Birch, *J. Chem. Soc.*, **1965**, 3489. d) C. S. Hudson and J. M. Johnson, *J. Am. Chem. Soc.*, **37**, 2748 (1915).

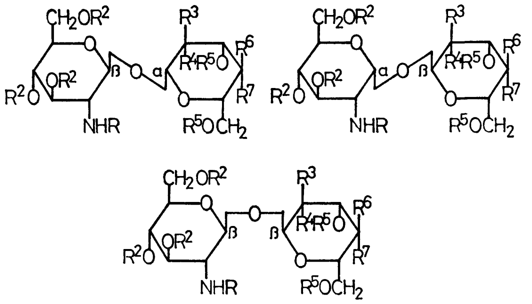
TABLE 2. ^1H CHEMICAL SHIFTS OF ANOMERIC PROTONS OF D-HEXOSYL D-GLUCOSAMINIDES[a]

Compound	Temp[b]	H-1		H-1′	
	°C	δ	$J_{1,2}$[c]	δ	$J_{1,2}$
17	22	5.56	3.7	5.62	3.3
18	22	5.09	8.0	5.74	3.0
19	90	5.75	3.2	5.12	8.0
20	80	5.30	8.0	5.26	7.0
21	22	5.53	3.8	5.51	1.5
22	22	4.97	8.3	5.55	1.6
23	22	5.59	3.7	5.27	0.6
24	50	5.21	8.3	5.48	1.0
25	22	5.60	3.8	5.63	3.3
26	90	5.11	8.0	5.72	3.8
27	80	5.80	4.0	5.22	7.0
28	70	5.27	8.0	5.31	7.0

a) Spectra were measured at 100 MHz in D_2O with ext. TMS. b) Measurement temperature. c) Decoupled by saturating the signal of H-2 at δ 3.1—3.2.



Compound	R¹	R²	R³	R⁴	R⁵	R⁶	R⁷	R⁸	R⁹	R¹⁰
6	H	NHDp	Ac	H	OAc	OCb	H	Cb	H	OCb
9	H	NHDp	Ac	H	OAc	H	OCb	Cb	OCb	H
13	H	NHDp	Ac	H	OAc	OCb	H	Cb	OCb	H
15	H	NHDp	H	H	OH	H	OCb	Cb	OCb	H
16	H	NHDp	H	H	OH	OCb	H	Cb	OCb	H
17	H	NH_2	H	H	OH	OH	H	H	H	OH
21	H	NH_2	H	H	OH	H	OH	H	OH	H
25	H	NH_2	H	H	OH	OH	H	H	OH	H
29	H	NHAc	Ac	H	OAc	OAc	H	Ac	H	OAc
30	H	NHAc	Ac	H	OAc	H	OAc	Ac	OAc	H
31	H	NH_3Cl	H	H	OH	H	OH	H	OH	H
32	H	OCb	Cb	OCb	H	OCb	H	Cb	H	OCb
33	OCb	H	Cb	H	OCb	H	OCb	Cb	OCb	H



Compound	Anomeric configuration	R¹	R²	R³	R⁴	R⁵	R⁶	R⁷
7	β α	Dp	Ac	H	OCb	Cb	H	OCb
8	α β	Dp	Ac	H	OCb	Cb	H	OCb
8a	β β	Dp	Ac	H	OCb	Cb	H	OCb
10	β α	Dp	Ac	OCb	H	Cb	OCb	H
11	α β	Dp	Ac	OCb	H	Cb	OCb	H
12	β β	Dp	Ac	OCb	H	Cb	OCb	H
14	β α	Dp	Ac	OCb	H	Cb	OCb	H
13a	α β	Dp	Ac	OCb	H	Cb	OCb	H
14a	β β	Dp	Ac	OCb	H	Cb	OCb	H
18	β α	H	H	H	OH	H	H	OH
19	α β	H	H	H	OH	H	H	OH
20	β β	H	H	H	OH	H	H	OH
22	β α	H	H	OH	H	H	OH	H
23	α β	H	H	OH	H	H	OH	H
24	β β	H	H	OH	H	H	OH	H
26	β α	H	H	OH	H	H	OH	H
27	α β	H	H	OH	H	H	OH	H
28	β β	H	H	OH	H	H	OH	H

Trehalosamine, **25**, was itself similarly synthesized from **1** and the α-glucopyranose derivative (**4**) *via* the afore-mentioned glycosylation.

Synthetically speaking, two facts are worthy of notice: first, even in the case of a configurationally pure α-D-hexopyranose derivative (**2**, **3**, or **4**),[12] all four configurational isomers of the 1,1′-linked heterodisaccharides were always formed in such glycosylation; secondly, small amounts of the self-condensation products of such hexopyranose derivatives were always formed during the reaction.

Based on the magnitude of the specific rotation of hexosyl glucosaminides (**17**—**28**), the structure of the most *dextro*-rotatory α,α-isomers and the most *levo*-rotatory β,β-isomers were readily assigned. The molecular rotations of **17** and **21** and their acetates (**29** and **30**) reasonably coincide with those of the structurally related 1,1′-linked disaccharides and their acetates (Table 1). The anomeric configurations of twelve 1,1′-linked hexosyl glucosaminides were then checked by measuring the ^1H chemical shifts of the anomeric hydrogens (Table 2). The pH-dependent

TABLE 3. ^{13}C NMR OF D-GALACTOSYL D-GLUCOSAMINIDES

Compound	17			18			19			20		
C pD:	8.7	2.3	Δ	8.5	2.2	Δ	8.8	1.9	Δ	8.7	2.3	Δ
1	94.8	91.9	−2.9	104.8	100.7	−4.1	102.1	97.7	−4.4	101.1	97.1	−2.3
2	55.9	54.8		57.9	56.9		56.4	55.1		57.1	56.5	
3	75.1	70.7	−4.4	76.6	73.2	−3.4	75.0	70.6	−4.4	76.5	73.1	−3.4
4	71.2	70.5		70.8	70.6		70.9	70.9		70.8	70.7	
5	73.6	73.7		77.5	77.6		73.6	73.7		77.4	77.6	
6	61.8	61.4		61.9	61.5		61.8	61.4		61.8	61.4	
1′	94.1	94.7		101.6	102.0		104.6	103.9		101.1	101.1	
2′	70.3	69.9		70.3	70.3		72.0	71.9		71.4	71.3	
3′	71.0	70.3		70.3	70.3		74.1	74.2		73.9	73.6	
4′	69.0	68.6		69.5	69.3		69.6	69.6		69.7	69.7	
5′	72.6	73.1		72.9	73.0		76.5	76.7		76.5	76.6	
6′	62.4	62.5		62.3	62.3		62.2	62.1		62.2	62.3	

TABLE 4. ^{13}C NMR OF D-MANNOSYL D-GLUCOSAMINIDES

Compound	21			22			23			24		
C pD:	8.8	2.7	Δ	8.8	2.3	Δ	9.0	2.0	Δ	8.5	2.0	Δ
1	96.0	92.3	−3.7	104.2	100.0	−4.2	101.6	97.4	−4.2	100.8	97.0	−3.8
2	55.9	54.6		57.6	56.8		56.1	55.0		57.1	56.5	
3	75.3	70.8	−4.5	76.5	73.0	−3.5	74.9	70.9	−4.0	76.4	73.0	−3.4
4	71.0	70.5		70.8	70.7		70.8	70.5		70.7	70.6	
5	74.1	74.2		77.5	77.5		73.8	73.7		77.6	77.6	
6	61.9	61.4		61.9	61.5		61.7	61.4		61.7	61.4	
1′	95.5	96.5		102.6	102.8		101.2	101.2		97.9	97.9	
2′	71.3	71.1		70.8	70.7		71.6	71.8		71.7	71.4	
3′	71.7	71.3		71.3	71.3		74.0	74.1		73.9	73.7	
4′	68.0	67.7		67.7	67.7		67.8	67.6		67.9	67.8	
5′	74.6	75.1		74.7	75.0		77.6	77.6		77.6	77.6	
6′	62.2	62.2		61.9	62.0		62.2	62.1		62.2	62.1	

TABLE 5. ^{13}C NMR OF D-GLUCOSYL D-GLUCOSAMINIDES

Compound	25			26			27			28		
C pD:	9.0	2.7	Δ	8.5	2.0	Δ	8.8	1.8	Δ	8.8	1.7	Δ
1	94.8	91.8	−3.0	105.0	101.9	−3.1	102.1	97.8	−4.3	101.4	97.1	−4.3
2	55.9	54.7		57.8	56.7		56.3	55.1		57.1	56.5	
3	74.9	70.7	−4.2	76.7	73.1	−3.6	74.8	70.9	−3.9	76.8	73.1	−3.7
4	70.8	70.7		70.6	70.5		70.6	70.4		70.8	70.5	
5	73.6	73.7		77.5	77.6		74.2	74.2		77.3	77.2	
6	61.7	61.3		61.8	61.5		61.7	61.4		61.9	61.5	
1′	94.0	94.5		101.4	101.1		104.0	103.4		100.5	100.4	
2′	72.0	71.7		72.5	72.4		74.2	74.2		73.8	73.6	
3′	73.4	73.3		73.8	73.8		77.3	77.4		77.4	77.6	
4′	70.8	70.7		70.6	70.5		70.8	70.5		70.8	70.7	
5′	73.6	73.9		73.8	74.3		76.6	76.7		76.9	76.7	
6′	61.7	61.8		61.5	61.5		61.8	61.7		61.9	61.7	

^{13}C NMR signals[8b,15] (Tables 3, 4, and 5) were quite useful in assigning the signal of C-1[16] of the two anomeric carbons in 1,1′-linked disaccharides, since, at a lower pH, the signal of the C-1 neighboring the carbon bearing amino group moved upfield, while that of C-1′ did not. The differences (Δ) in the value of the pH-dependent ^{13}C chemical shift of C-1 (Tables 3, 4, and 5) are almost constant, regardless of the configurations of C-1 and C-1′ (−3.7±0.2 ppm). The data in Tables 3—5 show that the signal of C-2 was of use in diagnosing the anomeric configuration of glucosaminides (56.1±0.1 ppm for the α-anomers and 57.4±0.1 ppm for the β-anomers), whereas that of C-4′, which is insensitive to the anomeric

TABLE 6. ^{13}C CHEMICAL SHIFTS OF ANOMERIC CARBONS OF SOME D-GLYCOSYL D-GLYCOSIDES

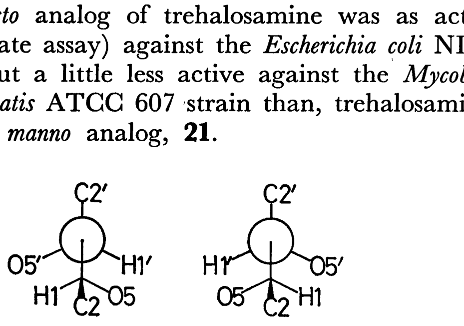
Compound	Unprotected		Per-*O*-benzyl		Per-*O*-(*p*-chlorobenzyl)
α-D-Glc*p* α-D-Glc*p*	94.4	94.8[a]	94.4	94.26[b]	
α-D-Glc*p* β-D-Glc*p*	101.3 104.0	101.3[a] 104.0[a]	99.4 104.1	99.54[b] 104.27[b]	
β-D-Glc*p* β-D-Glc*p*	100.3	100.7[a]	99.3		
α-D-Gal*p* α-D-Gal*p*	94.4	94.32[b]	93.5	93.54[b]	93.6
α-D-Man*p* α-D-Man*p*	96.4		93.3	93.25[b]	93.4
α-D-Gal*p* α-D-Glc*p*		94.3[c] 94.5[c]			
α-D-Man*p* α-D-Glc*p*		94.6[d] 96.1[d]			

a) Ref. 18. b) Ref. 20. c) Ref. 6b. d) Ref. 6a.

configuration, was good as a probe of the galactopyranosyl (69.5±0.2 ppm) and mannopyranosyl (67.9 ±0.1 ppm) moieties.

One of our aims in the present study was to observe the ^{13}C chemical shifts of the anomeric carbons of 1,1′-linked disaccharides, in which the conformation of the glycoside linkage would be influenced by the *exo*-anomeric effect[17] exterted by both glycoside bonds, C-1–O and C-1′–O. The data in Tables 3—5 show that the ^{13}C chemical shifts of the anomeric carbons of the α,α- and β,β-isomers of 1,1′-linked disaccharides always appear at field above those of the α,β- and β,α-isomers; those up-field shifts are the same in nature with those observed in the cases of α,α- and β,β-trehaloses.[18] Because fully benzylated α,α- and β,β-trehaloses also exhibit such properties[19,20] (Table 6), inter-unit hydrogen-bondings[18] seem hardly responsible for them. Instead, the α,α- and β,β-isomers of trehalose are considered to adopt the conformation in which the dihedral angles of O-5–C-1–O–C-1′ and O-5′–C-1′–O–C-1 are ≈+60° (α,α-isomer) or ≈−60° (β,β-isomer), as is shown in Fig. 1. The fact that such an upfield shielding of the ^{13}C chemical shifts of the anomeric carbons of α,α- and β,β-isomers is observed regardless of the configuration at C-2′ (Tables 3—5) is consistent with the conformation in Fig. 1, where the substituents at C-2 and C-2′ are completely separated from each other. It is, then, conceivable that the *gauche* effect[21] would work on such a conformation so that the ^{13}C chemical shifts of both anomeric carbons, C-1 and C-1′, can be expected to appear at an upper field, as has been observed.

The *galacto* analog of trehalosamine was as active (cylinder plate assay) against the *Escherichia coli* NIHJ strain as, but a little less active against the *Mycobacterium smegmatis* ATCC 607 strain than, trehalosamine, **25**, and its *manno* analog, **21**.



α-D-, α-D- β-D-, β-D-

Fig. 1. Projection formula of anomeric carbons of α-D-hexosyl α-D-glucosaminide and β-D-hexosyl β-D-glucosaminide.

Experimental

General. The melting points were determined by means of a MP-1 melting point apparatus (Yanagimoto). The specific rotations were measured in a jacketed 1-dm cell by means of a DIP-180 automatic polarimeter (Japan Spectroscopic) at 20 °C. The IR spectra were determined by means of a JASCO IRA-1 infrared spectrometer. The ^{1}H NMR spectra were recorded by a Varian S-60T spectrometer and a JEOL-PS-100 spectrometer. The ^{13}C NMR spectra were recorded by means of JEOL-PS-100 spectrometer equipped with a JEOL-EC-100 computer using a 8-mm*φ* tube at 37 °C (noise decoupled; pulse width, 13 μs (45°); repetition, 2 s; frequency range, 5000 Hz; 8 K data points). A PT-3D digital pH/mV meter with a PCE-101S electrode (Toyo Kagaku) was used for the determination of the pD value, deutrium chloride (*ca.* 20% in deuterium oxide) was used as a titrant. Chromatography on silica gel (Kanto Kagaku) was done using a mixture of benzene and butanone (Solvent-BB) or of benzene and ethanol (Solvent-BE). TLC was carried out using silica gel (Merck 7731). Ascending paper chromatography was practiced by the use of Toyo filter paper (No. 50), developed by a solvent system of 1-butanol–pyridine–water–acetic acid (6:4:3:1) and then heated after having been sprayed with ninhydrin in ethanol (0.3%) containing pyridine. Compounds **1**, **2**, **3**, and **4**, as well as silver perchlorate (Alpha) and tribenzylamine (Tokyo Kasei), were kept *in vacuo* over phosphorus pentaoxide before use. All the reactions were conducted at room temperature (20—25 °C), while evaporation was done at 35—40 °C under reduced pressure, unless otherwise stated.

*α-D-Galactopyranosyl 2-Amino-2-deoxy-α-D-glucopyranoside (**17**) and Its Isomers (**18**, **19**, and **20**).* A mixture of **1** (854 mg, 1.6 mmol), **2** (1085 mg, 1.6 mmol), silver perchlorate (331 mg, 1.6 mmol), and tribenzylamine (459 mg, 1.6 mmol) in benzene (8 ml) was vigorously stirred in the dark for 24 h. The resulting mixture was poured onto a column of silica gel (30 g), which was then developed with Solvent-BB (100:1→5:1, gradient, 10-ml fraction). Fraction A (Nos. 12 and 13) gave **32** (43.4 mg, 4.1%), identified with the sample prepared alternatively as below. Fraction B (Nos. 19—30) was a mixture (852.2 mg) of **6** and unchanged **2**. Fraction C (Nos. 31—38) consisted of impure **8** (408.9 mg). Fraction D (Nos. 40—42) was a mixture (414.0 mg) of **7** and **8a**. Fraction E (Nos. 43—46) was 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranose (**5**) (192.6 mg, 25.6%); mp 150—154 °C [lit,[9] mp 154—156 °C].

A portion of Fraction B was purified by means of TLC to give a glass of **6**; $[\alpha]_D+128°$ (*c* 0.7, $CHCl_3$). Found:

C, 55.16; H. 4.56; N, 3.49%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%. The rest of Fraction B was treated with a solution of sodium methoxide in methanol (0.05 M, 25 ml) overnight, followed by neutralization with acetic acid and chromatography (Solvent-BB, 10:1→1:1, gradient), to give unchanged **2** (240.4 mg, 22.2%) and the pure de-*O*-acetate of **6** (563.9 mg, 35% from **2**). This was agitated for 5 h in aq acetone (80%, 50 ml) in which Dowex 1×2 (OH-form, 15 ml) has been suspended. After filtration and evaporation, chromatography using Solvent-BE (10:1→5:1, gradient) gave a colorless mass (388.2 mg). This was hydrogenated over palladium black (390 mg) in acetic acid (10 ml) at 340 kPa overnight. After the removal of the catalyst, followed by concentration, the residue obtained was chromatographed on Dowex 1×2 (OH-form, 20×1ϕ cm, 5-ml fraction) developed with water; each fraction was examined by paper chromatography. Fraction Nos. 10—20 gave a ninhydrin-positive, homogeneous glass of **17** (106.3 mg, 19% from **2**); $[\alpha]_D$+198° (*c* 1.0, H_2O). Found: C, 40.79; H, 6.85; N, 3.79%. Calcd for $C_{12}H_{23}NO_{10}\cdot 0.75H_2O$: C, 40.69; H, 6.96; N, 3.95%.

The treatment of this (14 mg) with a mixture of acetic anhydride (2 ml) and pyridine (2 ml) for 4 d gave the acetate (**29**) (25 mg, 94%); mp 222—223 °C, $[\alpha]_D$+181° (*c* 0.3, $CHCl_3$), IR(KBr)ν: 1745 (OAc), 1645, 1545 (NHAc), NMR ($CDCl_3$, TMS) δ: 2.01 (3H, s, $NHCOCH_3$), 2.03, 2.04, 2.05, 2.09, 2.17 (3H, 6H, 3H, 6H, 3H, $OCOCH_3$), 6.20 (1H, d, *J*=8.0 Hz, NHAc). Found: C, 49.93; H, 5.95; N, 1.97%. Calcd for $C_{28}H_{39}NO_8$: C, 49.63; H, 5.80; N, 2.07%.

The purification of Fraction C gave **8** (163.0 mg, 9%); mp 79—80 °C, $[\alpha]_D$+70° (*c* 0.9, $CHCl_3$). Found: C, 54.90; H, 4.79; N, 3.98%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%. This was treated with a dil solution of sodium methoxide in methanol and then with Dowex resin in aq acetone and successively hydrogenated to afford glass of **19** (26 mg); $[\alpha]_D$+117° (*c* 0.4, H_2O). Found: C, 41.91; H, 7.03; N, 4.09%. Calcd for $C_{12}H_{23}NO_{10}$: C, 42.23; H, 6.79; N, 4.10%.

A sample of (≈30 mg) of Fraction D was purified by TLC to furnish **7**; mp 74—77 °C, $[\alpha]_D$−11° (*c* 0.9, $CHCl_3$). Found: C, 54.43; H, 4.73; N, 4.18%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%. The rest of Fraction D was treated with a dil solution of sodium methoxide in methanol and chromatographed as described above to furnish the de-*O*-acetate of **7** (238.9 mg, 15% from **2**) and then that of **8a** (52.4 mg, 3% from **2**). The former compound was treated with Dowex resin in aq acetone and then hydrogenated to afford **18** (55.3 mg); $[\alpha]_D$+93° (*c* 0.4, H_2O). Found: C, 40.84; H, 6.92; N, 3.81%. Calcd for $C_{12}H_{23}NO\cdot 0.75H_2O$: C, 40.62; H, 6.96; N, 3.95%. The latter compound was subjected to the same deprotection process to afford **20** (7 mg); $[\alpha]_D$−19° (*c* 0.3, H_2O). Found: C, 41.43; H, 7.02; N, 3.91%. Calcd for $C_{12}H_{23}NO_{10}\cdot 0.5H_2O$: C, 41.14; H, 6.91; N, 4.00%.

α-D-*Mannopyranosyl 2-Amino-2-deoxy-*α-D-*glucopyranoside (**21**) and Its Isomers (**22**, **23**, and **24**).* A mixture of **1** (854 mg, 1.6 mmol), **3** (1085 mg, 1.6 mmol), silver perchlorate (331 mg, 1.6 mmol), and tribenzylamine (459 mg, 1.6 mmol) in benzene (8 ml) was stirred in the dark for 24 h. The subsequent chromatography of the reaction mixture (silica gel (30 g) and Solvent-BB (100:1→5:1, gradient, 10-ml fraction)) gave five fractions: A (Nos. 17 and 18), B (Nos. 22—29), C (No. 30), D (Nos. 31—35), and E (Nos. 38—41).

Fraction A gave **33** (59.3 mg, 5.5%), which was identified with the sample prepared alternatively as below.

A small portion of Fraction B was purified by TLC to furnish **9**; $[\alpha]_D$+104° (*c* 0.8, $CHCl_3$). Found: C, 55.92; H, 4.91; N, 3.49%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%. The rest of Fraction B was treated with a dil solution of sodium methoxide in methanol, followed by chromatography, to afford unchanged **3** (382.6 mg, 30%) and the yellow de-*O*-acetate of **9** (496.5 mg, 31% from **3**). This was treated with Dowex resin in aq acetone to give a colorless mass of **15** (303.2 mg); mp 149—153 °C, $[\alpha]_D$+53° (*c* 0.2, MeOH). Found: C, 56.38; H, 5.11; N, 1.57%. Calcd for $C_{40}H_{41}Cl_4NO_{10}\cdot H_2O$: C, 56.15; H, 5.06; N, 1.64%. Compound **15** was then hydrogenated and deionized to afford **21** (94.0 mg 16% from **3**); $[\alpha]_D$ +141° (*c* 0.4, H_2O). Found: C, 40.46; H, 6.74; N, 3.91%. Calcd for $C_{12}H_{23}NO_{10}\cdot 0.75H_2O$: C, 40.62; H, 6.96; N, 3.95%.

An aqueous solution of this (32 mg) was acidified with hydrochloric acid (35%) to pH 3 and then freeze-dried to give crystals. Recrystallization from methanol containing acetone afforded needles of **31** (*ca.* 20 mg); mp 194—195 °C (dec), $[\alpha]_D$ +110° (*c* 0.5, H_2O) [lit,[3a] mp 230 °C (dec), $[\alpha]_D^{23}$ +91.3° (*c* 2, H_2O)], NMR (D_2O, ext. TMS) δ: 5.64 (1H, d, *J*=1.9 Hz, H-1′), 5.90 (1H, d, *J*=3.8 Hz, H-1′). Found: C, 37.07; H, 6.32; N, 3.37%. Calcd for $C_{12}H_{23}NO_{10}\cdot HCl\cdot 0.5H_2O$: C, 37.26; H, 6.52; N, 3.62%.

The treatment of **9** (22 mg) with pyridine and acetic anhydride afforded octaacetate, **30** (38.2 mg, 87%); mp 90—93 °C, $[\alpha]_D$ +106° (*c* 1.0, $CHCl_3$) [lit,[3a] mp 91.5—93 °C]; IR(KBr)ν: 1745 (OAc), 1660, 1540 (NHAc); NMR ($CDCl_3$, TMS) δ: 1.97 (3H, s, $NHCOCH_3$), 2.03, 2.05, 2.07, 2.08, 2.16 (3H,6H,6H,3H,3H, $OCOCH_3$), 6.25 (1H, d, *J*=8 Hz, NH). Found: C, 49.49; H, 5.89; N, 1.97%. Calcd for $C_{28}H_{39}NO_{18}$: C, 49.63; H, 5.80; N, 2.07%.

Fraction C was **11** (200.3 mg, 11% from **3**); mp 77—79 °C, $[\alpha]_D$ −1° (*c* 1.0, $CHCl_3$). Found: C, 55.13; H, 4.50; N, 3.61%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%. Removal of the protecting groups from **11** furnished **23** (38.4 mg); $[\alpha]_D$ +71° (*c* 1.0, $CHCl_3$). Found: C, 40.81; H, 6.68; N, 3.89%. Calcd for $C_{12}H_{23}NO_{10}\cdot 0.75H_2O$: C, 40.62; H, 6.96; N, 3.95%.

A portion of Fraction D was purified by means of TLC to give **10**; mp 70—73 °C, $[\alpha]_D$ −49° (*c* 1.0, $CHCl_3$) (Found: C, 55.29; H, 4.03; N, 3.76%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%) and **12**; mp 74—75 °C, $[\alpha]_D$ −55° (*c* 1.0, $CHCl_3$) (Found: C, 54.99; H, 4.40; N, 3.72%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%). The rest of Fraction D was treated with a dil solution of sodium methoxide in methanol, followed by chromatography, to afford the de-*O*-acetate of **10** (394.4 mg, 25% from **3**) first and then that of **12** (54 mg, 3.3% from **3**). These compounds were subsequently subjected to the de-protection processes to give **22** (82.1 mg); $[\alpha]_D$ +34° (*c* 1.0, H_2O) (Found: C, 41.18; H, 6.82; N, 3.90%. Calcd for $C_{12}H_{23}NO_{10}\cdot 0.5H_2O$: C, 41.14; H, 6.91; N, 4.00%) and **24** (9.2 mg), $[\alpha]_D$ −71° (*c* 0.1, H_2O) (Found: C, 39.85, H, 6.61; N, 3.64%. Calcd for $C_{12}H_{23}NO_{10}\cdot H_2O$: C, 40.11; H, 7.01; N, 3.90), respectively.

α-D-*Glucopyranosyl 2-Amino-2-deoxy-*α-D-*glucopyranoside (**25**) and Its Isomers (**26**, **27**, and **28**).* A mixture of **1** (1068 mg, 2.0 mmol), **4** (1356 mg, 2.0 mmol), silver perchlorate (414 mg, 2.0 mmol), and tribenzylamine (574 mg, 2.0 mmol) in benzene (10.6 ml) was vigorously stirred in the dark for 24 h. Chromatography on silica gel (50 g) with Solvent-BB (100:1→10:1, gradient, 15-ml fraction) gave five fractions: A (Nos. 17—20), B (Nos. 21—31), C (Nos. 32—36), D (Nos. 37—41) and E.

Fraction B (1335 mg) was composed of the fast-moving, major yellow band and unchanged **4**. A sample of Fraction B (≈50 mg) was subjected to TLC (25 mg/20×20×0.05 cm, developed with Solvent-BB (20:1), 15 times) to give two yellow products, **13a** (minor faster-moving) and **13** (major slower-moving); mp 125—130 °C, $[\alpha]_D$ +112° (*c* 0.9, $CHCl_3$). Found: C, 55.41; H, 4.66; N, 3.76%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.54; N, 3.71%. The rest of Fraction B was treated with a mixture of a methanolic solution of sodium methoxide (0.05 M, 34 ml) and 1,4-dioxane (10 ml), followed by neutralization with acetic acid and chromatography, to give a mixture (717 mg, 36% from **4**) of the de-*O*-acetates of **13** and **13a**. A portion of this was treated with Dowex resin in aq acetone, followed by chromatography (Solvent-BE) and recrystallization from diisopropyl ether containing ethanol, to give **16**; mp 153—156 °C; $[\alpha]_D$ +108° (*c* 0.3, MeOH). Found: C, 56.58; H, 5.09; N, 1.53%. Calcd for $C_{40}H_{41}Cl_4NO_{10}\cdot0.5H_2O$: C, 56.75; H, 5.00; N, 1.65%. The mixture (*ca.* 650 mg) of the de-*O*-acetates of **13** and **13a** was subjected to the deprotecting processes as described above to afford a free base whose ^{13}C NMR (D_2O) showed the presence of **25** and **27** (*ca.* 3:1). The free base (110 mg) was then dissolved in water (6 ml), and to the mixture 2,4-dinitrofluorobenzene (Wako, 70 mg), sodium hydrogencarbonate (45 mg) and ethanol (3 ml) were added. After this mixture had been stirred for 2 d, a yellow mixture was acidified and evaporated to give a residue which was further treated with pyridine and acetic anhydride. The yellow product (230 mg) composed of two compounds (R_f=0.55 (major) and 0.45, ethyl acetate-1,2-dichloroethane (1:3)) gave a homogeneous faster-moving compound (>126 mg) after preparative TLC. The treatment of this with a dil solution of sodium methoxide in methanol and then Dowex resin in aq acetone, followed by passing it through a little column of the resin, afforded $[\alpha]_D$ +183° (*c* 0.9, H_2O). Found: C, 40.66; H, 6.81; N, 3.87%. Calcd for $C_{12}H_{23}NO_{10}\cdot0.75H_2O$: C, 40.62; H, 6.96; N, 3.93%.

The treatment of this with acetic anhydride and pyridine gave octaacetate of **25**; mp 98—100 °C, $[\alpha]_D$ +151° (*c* 0.5, $CHCl_3$) [lit, mp 100—102 °C,[1] 99 °C,[3] $[\alpha]_D$ +163.5° ($CHCl_3$),[1] +152° (*c* 1.08, $CHCl_3$, at 25 °C)[3]].

The slower-moving, yellow band obtained by preparative TLC mentioned just above furnished a homogeneous glass (≈45 mg) which was later converted into **27** (15 mg); $[\alpha]_D$ +111° (*c* 0.4, H_2O). Found: C, 41.30; H, 7.19; N, 3.87%. Calcd for $C_{12}H_{23}NO_{10}\cdot0.5H_2O$: C, 41.14; H, 6.91; N, 4.00%.

Fraction C (352.5 mg) was treated with a dil solution of sodium methoxide in methanol and chromatographed to give the de-*O*-acetate of **14a** (131.7 mg, 6.6% from **4**). This was then converted into **28** (29 mg), $[\alpha]_D$ −43° (*c* 0.3, H_2O). Found: C, 40.92; H, 7.09; N, 4.02%. Calcd for $C_{12}H_{23}NO_{10}\cdot0.5H_2O$: C, 41.14; H, 6.91; N, 4.00%.

Fraction D was purified by rechromatography to give **14** (581.7 mg, 26% from **4**); mp 73—75 °C, $[\alpha]_D$ −51° (*c* 0.3, $CHCl_3$). Found: C, 55.32; H, 4.81; N, 3.71%. Calcd for $C_{52}H_{51}Cl_4N_3O_{17}$: C, 55.18; H, 4.51; N, 3.71%. Fraction D was subjected to deprotection processes to furnish **26** (87 mg), $[\alpha]_D$ +81° (*c* 0.3, H_2O). Found: C, 40.64; H, 6.79; N, 3.85%. Calcd for $C_{12}H_{23}NO_{10}\cdot0.75H_2O$: C, 40.62; H, 6.96; N, 3.95%.

2,3,4,6-Tetra-O-(p-chlorobenzyl)-α-D-galactopyranosyl 2,3,4,6-Tetra-O-(p-chlorobenzyl)-α-D-galactopyranoside (***32***). A mixture of **2** (136 mg, 0.2 mmol), silver *p*-nitrobenzenesulfonate[20] (62 mg, 0.2 mmol), and diphenyldichlorosilane (21 μl, 0.1 mmol) in dichloromethane (0.7 ml) was stirred at 0 °C in the dark for 6 h. The subsequent chromatography of the reaction mixture using Solvent-BB on silica gel gave **32** (106.6 mg, 79%); $[\alpha]_D$ +81° (*c* 0.8, $CHCl_3$). Found: C, 61.30; H, 4.57%. Calcd for $C_{68}H_{62}Cl_8O_{11}$: C, 61.00; H, 4.64%.

The hydrogenation of **32** in acetic acid in the presence of palladium black gave α-D-galactopyranosyl α-D-galactopyranoside; mp 268—269 °C, $[\alpha]_D$ +211° (*c* 0.5, H_2O) [lit,[18] 264—267 °C, $[\alpha]_D^{20}$ +235° (*c* 0.35, H_2O)].

2,3,4,6-Tetra-O-(p-chlorobenzyl)-α-D-mannopyranosyl 2,3,4,6-Tetra-O-(p-chlorobenzyl)-α-D-mannopyranoside (***33***). Compound **3** (136 mg, 0.2 mmol) was similarly condensed to afford **33** (81.2 mg, 60%); $[\alpha]_D$ +21° (*c* 1, $CHCl_3$). Found: C, 60.62; H, 4.57%. Calcd for $C_{68}H_{62}Cl_8O_{11}$: C, 61.00; H, 4.67%.

The hydrogenolysis of **33** in acetic acid in the presence of palladium black furnished α-D-mannopyranosyl α-D-mannopyranoside; mp 245—246 °C, $[\alpha]_D$ +122° (*c* 0.3, H_2O) [lit,[21] mp 240—243 °C, $[\alpha]_D^{20}$ +124° (*c* 1, H_2O)], ^{13}C-NMR (D_2O, ext, TMS) δ: 96.4, 74.6, 71.4, 71.1, 67.8, 62.0.

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Note added in proof: A. A. Pavia, *et al.* describe and discuss about the ^{13}C chemical shifts of the anomeric carbons of the 1,1′-linked glycosyl glycosides in their latest paper (*Nouv. J. Chem.*, **5**, 101 (1981)).