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Note

Preparative routes to methyl 2-acetamido-2,6-dideoxy-α-D-glucopyranoside*

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2-Amino-2,6-dideoxy-D-glucose (quinovosamine) is a component residue[1] of the O-chain polysaccharide in the lipopolysaccharide antigens[2] of *Pseudomonas aeruginosa*, Fisher immunotypes 3, 4, and 5. In connection with synthesis of artificial antigens and immunoadsorbents based on oligosaccharide segments[3] of the O-chains, a convenient preparative route to quinovosamine was of interest. This amino sugar has been synthesized from derivatives of 2-amino-2-deoxy-D-glucose by way of selective 6-*O*-monosulfonylation[4,5], and subsequently obtained by several other routes[6,7]; a preparative route employed in this laboratory[1] was based on *N*-bromosuccinimide-mediated ring-opening of a 4,6-benzylidene acetal[8].

The objective of the present work was to improve the net yield in preparation of the title glycoside from 2-amino-2-deoxy-D-glucose. This was accomplished in two routes, one a modification of the method[8] based on the 4,6-benzylidene acetal, and the second, judged superior overall, on selective C-6 monobromination by the action of carbon tetrabromide–triphenylphosphine[9]. Concurrently, Anderson and coworkers[10] have prepared the title glycoside, having physical constants in good agreement with those reported here, by a C-6 monobromination step employing *N*-bromosuccinimide–triphenylphosphine[11]; their report is published simultaneously with this one.

Glycosidation of 2-acetamido-2-deoxy-D-glucose with methanol in the presence of cation-exchange resin[1,12] gave, in 91% yield, methyl 2-acetamido-2-deoxy-α,β-D-glucopyranoside (**1**) as a cocrystallized, 5:1 α,β mixture, $[\alpha]_D$ +98°, and this was treated in pyridine at 60–65° with 2 equivalents of triphenylphosphine and 1 equivalent of carbon tetrabromide to give, in 46% yield, crystalline methyl 2-acetamido-6-bromo-2,6-dideoxy-α-D-glucopyranoside (**2**). Hydrogenolysis of the bromide **2** in the presence of Raney nickel gave crystalline methyl 2-acetamido-2,6-dideoxy-α-D-glucopyranoside (**3**) in essentially quantitative yield. Recrystallized from isopropyl alcohol, compound **3** had a m.p. in agreement with the litera-

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ture[10,13]. The foregoing simple, three-step synthesis thus affords the title glycoside **3** in 38% net yield from 2-acetamido-2-deoxy-D-glucose, which is commercially available or may be readily prepared[14], in 95% yield, from the inexpensive 2-amino-2-deoxy-D-glucose hydrochloride.

The net yield of **3** compares favorably with the previous preparation[1], which involves more steps and afforded the 4-benzoate of glycoside **3** in 15% overall yield from 2-acetamido-2-deoxy-D-glucose. That route was re-evaluated in the present work and several procedural improvements were made. Benzylidenation of the glycoside mixture **1** by a scaled-up, improved procedure gave 86% of the 4,6-benzylidene acetal[15], which was acetylated to give 90% of crystalline methyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[16] (**4**). *N*-Bromosuccinimide in carbon tetrachloride converted **4** into methyl 2-acetamido-3-*O*-acetyl-4-*O*-benzoyl-6-bromo-2,6-dideoxy-α-D-glucopyranoside (**5**), isolated crystalline in 79% yield, and hydrogenolysis of the bromo derivative **5** with subsequent *O*-deacylation gave the title glycoside in 70% yield. The yield of **3** from 2-acetamido-2-deoxy-D-glucose by this sequence was thus 43%, comparable to that obtained *via* compound **2**, but the route was procedurally rather less convenient because more steps are required, and the final product **3** was contaminated with some methyl benzoate. Noteworthy, however, is the high yield (79%) on the bromination step (**4** → **5**) through use of the 3-*O*-acetyl precursor **4**. The modest (44%) yield in the corresponding conversion[1] of the 3-hydroxyl analog may be attributed to the low solubility of this hydroxylated precursor in the reaction medium.

The structures of all products and intermediates were affirmed by appropriate conversions, and ^{1}H-n.m.r. (see Tables I and II), ^{13}C-n.m.r., and mass spectrometry (see Experimental section). Acetylation of bromide **2** gave the known[17] crystalline diacetate **13**, and likewise acetylation of the title glycoside **3** gave the known[13,18] diacetate **6** in 82% yield. The primary bromo derivative **2** showed a characteristic high-field triplet (δ 34.9) for C-6 in the off-resonance ^{13}C-n.m.r. spectrum, and the mass spectrum showed glycosyl cation peaks at *m/z* 267 and 269 indicative of monosubstitution by bromine; weak molecule-ion peaks were also observed.

The scope of the direct bromination reaction **1**→**2** with respect to an aglycon subsequently removable under mild conditions was evaluated by use of benzyl 2-acetamido-2-deoxy-D-glucopyranoside, prepared in 63% yield as an ~7:3 α,β-mixture (**7**) through direct glycosidation of 2-acetamido-2-deoxy-D-glucose with benzyl alcohol by the method of Gross and Jeanloz[19]. Conditions satisfactory for the conversion of **1** into **2** gave only incomplete reaction with **7**, but doubling the quantities of carbon tetrabromide and triphenylphosphine led to complete reaction, and benzyl 2-acetamido-6-bromo-2,6-dideoxy-α-D-glucopyranoside (**8**) was isolated in crystalline form in 44% yield; it was characterized by analytical and spectroscopic data and also by conversion into the known[20], crystalline diacetate **14**. Again, the simplicity of the sequence leading to **8** commends the route as a preparative method, as hydrogenolysis of **8** would afford free *N*-acetylquinovosamine directly.

TABLE I

PROTON CHEMICAL-SHIFTS FOR COMPOUNDS **4–6** AND **9–14**

	Chemical shifts (δ)										
Compound[a]	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*N-H*	OCH_3	*OAc*	*NAc*
4[b]	4.71d	4.32m	5.30t	3.77m	4 32m	←——3.77m—→		5.80d	3.40s	2.06s	1.96s
5[c]	4.81d	4 42ddd	5.41t	5 23	4.09dq	←——3.48m—→		5.71d	3.50s	1.90s	1.97s
6	4 65d	4.30ddd	5.16t	4.85t	3.82sex	←——1.19d—→		5.67d	3.38	2.01s,2.03s	1.94s
9	6.18d	4.50ddd	←——5.22t—→		4 00m	4.25q	4.06q	5.57d		2.04s,2.05s,2.10s,2.20s	1.93s
10[d]	5.66d	4.33dd	5.50t	5.23t	3.65dq	3.30q	3 09q	5.53d	1.74s	1.74s,2.02s,2.15s	1.92s
11	5.71d	4.28dd	←——5.14m—→		←————8.66m————→			5.67d		2.05s,2.06s,2.11s	1.93s
12	4.75d	4.32ddd	5.20t	5 12t	3 93dq	4.24q	4.11q	5.69d	3 43s(α),3 49(β)	2.00s,2.02s,2.10s	1.95s
13	4.75d	4.30ddd	5 30t	4.98t	3.94dq	←——3 45m—→		5 65d	3.45s	2.01s,2.05s	1.95s
14[b]	4 95d	4.38ddd	5 25t	5 00t	4.05dq	←——3.40m—→		5.65d		2.00s,2.05s	1.90s

[a]All spectra were recorded at 200 MHz for solutions in $CDCl_3$ with Me_4Si as an internal standard. Multiplicities are designated: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; sex, sextet, and m, multiplet. [b]δ 5.52s (C_6H_5CH) and 7.33–7.47 (Ar). [c]δ 7.40–8 00m (Ar). [d]δ 7.17–7.59 (Ar) [e]δ 4.82d, 4 52d ($C_6H_5CH_2$), and 8.25–8.50m (Ar).

Although methyl aldosides may be converted into 1-*O*-acetylaldoses by acetolysis [as demonstrated (see Experimental section) in the conversion of glycoside **1** into 2-acetamido-1,3,4-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose[21] (**9**)], the severe conditions required for acetolysis may not be compatible with syntheses in which sensitive functional groups are involved.

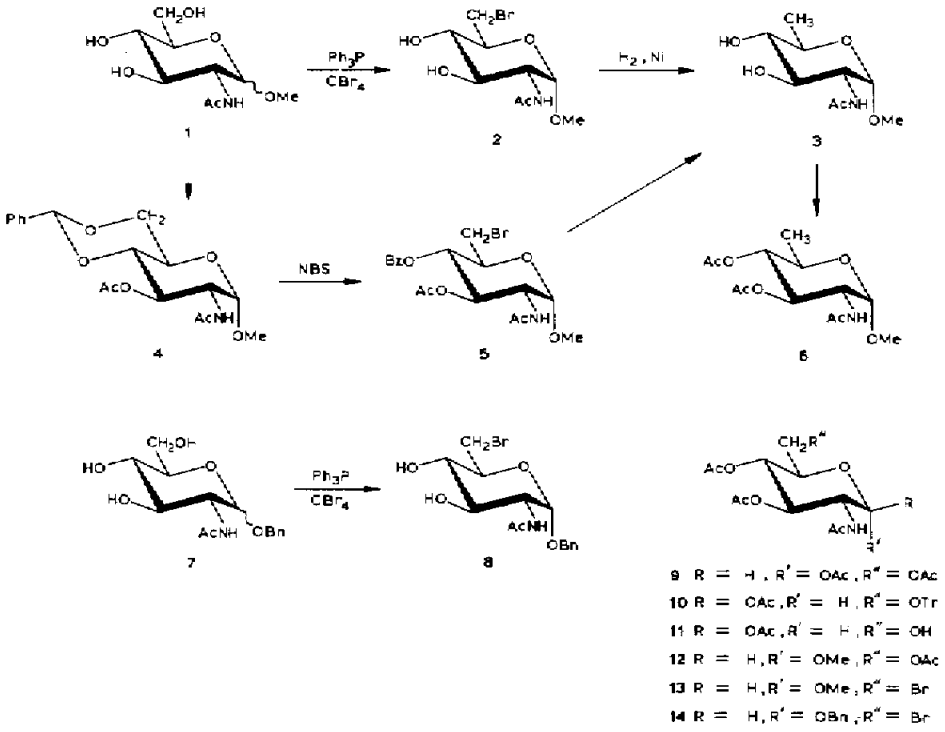

TABLE II

FIRST-ORDER PROTON–PROTON COUPLING CONSTANTS FOR COMPOUNDS **4–6** AND **9–14**

	Coupling constants (Hz)							
Compound[a]	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{2,NH}$
4	3.7	9.8	9.8	[b]	[b]	[b]	[b]	9.3
5	3.7	9.5	9.5	10.4	←7.8,2.6→			9.8
6	3.7	9.5	9.5	9.5	6.3			9.0
9	3.7	9.5	9.5	9.5	3.9	2.2	12.2	8.5
10	8.5	9.3	9.5	9.5	4.3	2.3	10.6	9.3
11	8.5	8.5	[b]	[b]	[b]	[b]	[b]	8.5
12	3.7	9.8	9.8	9.8	4.5	2.4	12.1	9.0
13	3.7	10.0	10.0	9.7	←7.2,2.7→			9.3
14[c]	3.9	9.8	9.8	9.8	←7.9,2.6→			9.3

[a]All spectra were recorded at 200 MHz for solutions in $CDCl_3$. [b]Not obtainable on first-order basis. [c]J_{AB} ($C_6H_5CH_2$) 11.5 Hz.

The ^{1}H-n.m.r. spectral data recorded in Tables I and II include data for the fully protected intermediates and products **4–6, 13,** and **14**, together with comparative data for peracetylated 2-acetamido-2-deoxy-α-D-glucopyranose (**9**), for 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-trityl-α-D-glucopyranose[22] (**10**) and its 6-hydroxyl analog[22] (**11**), and for methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside[23] (**12**). A large-scale preparation of compound **11** by way of **10** had been developed[7] in connection with synthetic routes to the lipid A component of the *Pseudomonas* antigens[2], and the n.m.r.-spectral data for **10** and **11** provided useful correlation with values reported in Tables I and II for the other derivatives of 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-D-glucopyranose.

The crystalline, direct-glycosidation product **1** is a 5:1 α,β-anomeric mixture, and the practical utility of the sequence **1**→**2**→**3** is greatly enhanced by the fact that the crystalline, isolated intermediate **2** is exclusively the α anomer, as is, consequently, the product **3**. Direct separation of the anomers of **1** is very difficult, being best accomplished by way of the 3,4,6-tri-*O*-acetyl derivatives[23], and avoidance of this separation is a major procedural convenience. Likewise, in the alternative route to **3** *via* **4** and **5**, compound **4** was obtained in crystalline form from **1** as the pure α anomer. The anomeric compositions of **1** and the derivatives prepared from it are readily monitored and approximately quantitated by inspection of the C-1 signals in ^{13}C-n.m.r., and the OCH_3 and NHCOCH_3 signals in the ^{1}H-n.m.r. spectra. Similar n.m.r.-spectral monitoring showed that the benzyl glycoside **7** was an α,β mixture and that the derived, crystalline 6-bromo derivative **8** was the pure α anomer.

The 200-MHz ^{1}H-n.m.r. spectral data (Tables I and II) confirm and extend generalizations earlier advanced[24,25] for 60-MHz spectra of related compounds. Spin-coupling values and H-1 chemical shifts are all consistent with expectations. As previously noted[25], the H-2 signals of these 2-acetamido-2-deoxyglucose derivatives are found consistently near δ 4.35, upfield of the H-3 and -4 signals in *O*-acetylated derivatives and readily recognized by their multiplicity through coupling to H-1, H-3, and NH (collapsed to doublets of doublets by NH→ND exchange); the appearance of the H-2 signal immediately further confirms the assigned anomeric configuration. Although H-3 generally resonated at lower field than H-4, the reverse was true for the trityl ether **10**; this may be attributed to anisotropy of the trityl group, as already observed[25] with the α anomer of **10**. The trityl group also caused a substantial upfield shift of the H-6,6′ signals and a change in the C-5–C-6 rotameric populations as a consequence of the bulky trityloxy group.

EXPERIMENTAL

General methods. — Evaporations were performed under diminished pressure at 40–50°. Optical rotations were recorded with a Perkin–Elmer model 141 polarimeter. Melting points are uncorrected. ^{1}H-N.m.r. spectra were recorded by Dr. Ole Mols at 200 MHz with a Bruker WP 200 spectrometer. ^{13}C-N.m.r. spectra

were recorded by David Riley at 20 MHz with a Bruker WP 80 spectrometer; tetramethylsilane was the internal standard. T.l.c. was performed on commercially prepared plates, Silica gel 60 F-254 (E. Merck, Darmstadt, Germany). Developing solvents were: *A*, 3:1 chloroform–methanol; *B*, ethyl acetate; *C*, 6:1 chloroform–methanol; and *D*, 1:1 ethyl acetate–hexane; all v/v. Detection was effected by charring with sulfuric acid, except for the 6-bromo derivatives, where 40% aqueous hydrobromic acid and u.v. light were more satisfactory. Column chromatography was performed on Silica gel G (Merck, 0.040–0.063 mm, 230–400 mesh). Microanalyses were performed by Dr. O. Mols and Galbraith Laboratories, Inc., Knoxville, Tennessee. Mass spectra were recorded by C. R. Weisenberger (The Ohio State University) with an AEI MS-902 mass spectrometer at an ionizing potential of 70 eV, an accelerating potential of 8 kV, and a direct-insert source temperature of 150°.

Methyl 2-acetamido-2-deoxy-α,β-D-glucopyranoside (**1**). — In a modification of the earlier procedure[1,12], a solution of 2-acetamido-2-deoxy-D-glucose (5.0 g, 23 mmol) in anhydrous methanol (120 mL) was boiled for 6 h under reflux with cation-exchange resin (Dowex 50W-X8, 11 g). The resin was filtered off and rinsed well with methanol. The filtrate was evaporated and the solid residue dried *in vacuo* at 40° to give **1** as a white powder containing the α- and β-D anomers in ~5:1 ratio; yield 4.82 g (91%), m.p. 184–185°, $[\alpha]_D^{26}$ +98° (*c* 1, water) [lit.[12] m.p. 187–189°, $[\alpha]_D$ +106.9° (*c* 1.12, water)]; ^{13}C-n.m.r. (D_2O): δ 22.7 (CH_3 of NAc), 54.4 (OCH_3), 56.0 (C-2), 61.4 (C-6), 70.8, 72.0 72.5 (C-3,4,5), 98.8 (C-1 of α anomer), and 170.0 (CO of NAc). Minor resonances for the β anomer were observed (δ 101.1 p.p.m. for C-1β).

Methyl 2-acetamido-6-bromo-2,6-dideoxy-α-D-glucopyranoside (**2**). — Compound **1** (2.35 g, 10 mmol) was added to a solution of triphenylphosphine (5.20 g, 20 mmol) in pyridine (50 mL). The solution was cooled, carbon tetrabromide (3.50 g, 11 mmol) was added, and the solution was heated for 30 min at 60–65°. Methanol (20 mL) was added and heating was continued for 20 min at 60–65°. The solution was evaporated to an oil that solidified on repeated evaporation of toluene from it. The residue was applied to a column (90 × 4 cm) of silica gel (200 g) that was eluted with 30:1 (v/v) ethyl acetate–methanol. Chromatographically pure **2** was obtained as a white powder; yield 1.37 g (4.6 mmol, 46%), m.p. 172–173°. The product was recrystallized once from chloroform–methanol–hexane to give white needles, m.p. 175–176°, $[\alpha]_D^{26}$ +125° (*c* 0.1, methanol); R_f 0.48 (solvent *C*); ^{13}C-n.m.r. (MeSO-d_6): δ 22.5 (CH_3 of NAc), 34.9 (C-6), 53.5 (C-2), 54.5 (OCH_3), 70.3, 71.0, 72.7 (C-3,4,5), 98.0 C-1), and 169.5 ($NHCOCH_3$); m.s. (relative intensity): *m/z* 297 (0.5), 299 (0.5).

Anal. Calc. for $C_9H_{16}BrNO_5$: C, 36.25; H, 5.41; Br, 26.80; N, 4.70. Found: C, 36.12; H, 5.24; Br, 26.66; N, 4.78.

Acetylation of **2** with acetic anhydride–pyridine gave, in 78% yield, *methyl 2-acetamido-3,4-di-O-acetyl-6-bromo-2,6-dideoxy-α-D-glucopyranoside* (**13**), recrys-

tallized from chloroform–hexane; m.p. 168–169°, $[\alpha]_D^{26}$ +85°(*c* 0.4, chloroform); [lit.[17] m.p. 164–165°, $[\alpha]_D^{25}$ +89.5° (*c* 1.4), chloroform].

*Methyl 2-acetamido-2,6-dideoxy-α-*D*-glucopyranoside* (**3**). — Chromatographically pure **2** (1.00 g, 3.4 mmol) was dissolved in anhydrous methanol (150 mL). Anion-exchange resin (CO_3^{2-}) and Raney nickel catalyst (No. W-2, 0.30 g) were added. The suspension was shaken for 16 h under 0.4 MPa of hydrogen. The mixture was filtered (Celite) and the filtrate evaporated to give crude **3**; yield 0.77 g (3.4 mmol, 100%). Recrystallization from isopropyl alcohol gave **3** as a white powder; m.p.172–173°, $[\alpha]_D^{26}$ +117° (*c* 0.1, methanol) [lit.[13] m.p. 172–174°, $[\alpha]_D^{25}$ +115° (*c* 2.0, water) and[10] m.p. 168–170° (hemihydrate), $[\alpha]_D$ +138° (methanol)]; R_F 0.40 (solvent *C*); ^{13}C-n.m.r. (Me_2SO-d_6): δ 18.0 (C-6), 22.5 ($NCOCH_3$), 54.0 (C-2), 54.5 (OCH_3), 67.0, 70.0, 76.0 (C-2,3,4), 98.0 (C-1α), and 169.7 ($NCOCH_3$).

*Methyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranoside* (**4**). — In a modification of the procedure of Neuberger[15], finely powdered compound **1** (53.0 g, 225 mmol, pulverized in a blender) was shaken for 24 h with a mixture of fused zinc chloride (53.0 g) and freshly distilled benzaldehyde (150 mL). The clear syrup was poured into 5% aqueous sodium hydrogensulfite (1 L)*. The product solidified immediately and the suspension was mechanically stirred for 3 h. This mixture was filtered and the filter cake washed well with water. The filter cake was reprocessed with hydrogensulfite solution until the odor of benzaldehyde was not evident. The solid was dried at 50° to give methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside as a white powder; yield 62.53 g (193 mmol, 85.7%), m.p. 249–255°, $[\alpha]_D^{26}$ +19.0° (*c* 0.1, ethanol) [lit.[15] m.p. 255°, $[\alpha]_D$ +19°.

A solution of the foregoing acetal (27.0 g, 84 mmol) in pyridine (400 mL) was cooled to 0° and acetic anhydride (200 mL) was added. After the initial reaction had subsided, the clear solution was stirred for 24 h at room temperature. The mixture was then poured into ice–water and mechanically stirred for 3 h, during which time some crystallization occurred. The mixture was filtered and the filtrate extracted with dichloromethane (2 × 200 mL). The filter cake was dissolved in the organic extract and dried (magnesium sulfate). The solution was evaporated and the last trace of pyridine was azeotropically evaporated with toluene until the syrup solidified. The solid was dried at 50° to give **4** as a white powder; yield 27.55 g (90%). Recrystallized from chloroform–hexane, compound **4** had m.p. 211–212°, $[\alpha]_D^{25}$ +31.0°, (*c* 0.5, chloroform) [lit.[16] m.p. 209–210°, $[\alpha]_D^{30}$ +38° (*c* 0.047, chloroform)].

*Methyl 2-acetamido-3-*O*-acetyl-4-*O*-benzoyl-6-bromo-2,6-dideoxy-α-*D*-glucopyranoside* (**5**). — Compound **4** (5.00 g, 14 mmol) was dissolved with heating in 5:1 (v/v) carbon tetrachloride–1,1,2,2-tetrachloroethane (600 mL). Barium carbonate (4.00 g) was added, followed by *N*-bromosuccinimide (2.80 g, 16 mmol), and the mixture was boiled under reflux for 1.5 h. After this time, t.l.c. indicated the reaction to be complete; one major product (**5**, R_F 0.57) was detected. The hot mixture

*This procedure was suggested by Mr. T. F. Gallagher.

was filtered and the filtrate evaporated to an oil that was dissolved in chloroform (250 mL). This solution was washed with 5% aqueous sodium hydrogensulfite (3 × 100 mL), sodium hydrogencarbonate (100 mL), and then dried (magnesium sulfate). The organic phase was evaporated to an oil that solidified by repeated trituration with petroleum ether (b.p. 30–65°). The crude material was an off-white powder; yield 4.83 g (11 mmol, 79%). A small additional amount (~0.2 g) of **5** crystallized from the trituration solvent upon cooling; m.p. 123–124°. The crude product (1.00 g) was eluted from silica gel (100 g) by 2:1 (v/v) ethyl acetate–hexane. The resultant product was homogeneous by t.l.c. and was recrystallized from acetone–hexane to give pure **5** as white crystals; m.p. 131–132°, $[\alpha]_D^{26}$ +20.0° (*c* 0.1, chloroform); m.s. (relative intensity): *m/z* 261 (10), 263 (10), 383 (4), 385 (4), 412 (0.5), 414 (0.5), 443 (0.5), and 445 (0.5).

Anal. Calc. for $C_{18}H_{22}BrNO_7$: C, 48.66; H, 4.99; Br, 17.99; N, 3.15. Found: C, 48.84; H, 5.00; Br, 17.27; N, 3.05.

Conversion of **5** *into methyl 2-acetamido-2,6-dideoxy-α-*D*-glucopyranoside* (**3**). — Compound **5** (1.00 g, 2 mmol) was dissolved in methanol (40 mL) and triethylamine (6 mL). Raney nickel catalyst (W-2, 0.5 g) was added and the mixture was shaken for 16 h under 0.4 MPa of hydrogen. The mixture was filtered (Celite) and the filtrate evaporated. The solution was diluted with dichloromethane (50 mL) and extracted with dilute aqueous hydrochloric acid (3 × 20 mL). The combined organic extracts were dried (magnesium sulfate) and evaporated to a syrup that was homogeneous by t.l.c. (R_F 0.60, solvent *B*). The syrup was dissolved in anhydrous methanol (20 mL) and a small shaving of metallic sodium was added to this solution. The solution was stirred for 3 h and then made neutral with cation-exchange resin (Dowex 50W-X8). The resin was filtered off and the solution evaporated to a syrup that solidified upon trituration with abs. ether to give crude **3**, contaminated with some methyl benzoate; yield 0.30 g (1.4 mmol, 70%). This product was purified by recrystallization from isopropyl alcohol; m.p. 170–171°, $[\alpha]_D^{26}$ +117° (*c* 0.1, methanol), R_F 0.40 (solvent *C*); ^{1}H-n.m.r., i.r., and mass-spectral data for this product were identical in all respects with those of **3** prepared from compound **2**.

Acetylation of **3** with acetic anhydride–pyridine gave, in 82% yield, *methyl 2-acetamido-3,4-di-*O*-acetyl-2,6-dideoxy-α-*D*-glucopyranoside* (**6**), m.p. 149–150°, $[\alpha]_D^{26}$ +108° (*c* 0.4, chloroform); lit.[18] m.p. 150–151°, $[\alpha]_D$ +111.1° (*c* 1.07, chloroform).

*Benzyl 2-acetamido-2-deoxy-α,β-*D*-glucopyranoside* (**7**). — Prepared by the method of Gross and Jeanloz[19], this product was recrystallized several times from ethanol to give white crystals of a ~7:3 α,β anomeric mixture; yield 65%, m.p. 177–178°, $[\alpha]_D^{27}$ +104° (*c* 0.25, methanol); lit.[19] α anomer, m.p. 187–189°, $[\alpha]_D^{23}$ +170°, (*c* 0.9, water); β anomer, m.p. 207–208°, $[\alpha]_D^{26}$ −48° (*c* 1.0, water).

*Benzyl 2-acetamido-6-bromo-2,6-dideoxy-α-*D*-glucopyranoside* (**8**). — Compound **7** (0.50 g, 1.6 mmol) was added to a solution of triphenylphosphine (1.68 g, 6.4 mmol) in pyridine (20 mL). The solution was cooled, carbon tetrabromide (1.2

g, 3,2 mmol) was added, and the solution was heated for 45 min at 60–65°. Methanol (5 mL) was added and heating was continued for 20 min at 60–65°. The solution was evaporated to an oil that solidified when toluene was evaporated from it. The residue was applied to a column (90 × 4 cm) of silica gel (100 g) that was eluted with 30:1 (v/v) chloroform–methanol. The chromatographically pure **8** was an off-white powder; yield 0.25 g (0.7 mmol, 44%). Further purification of **5** by recrystallization from chloroform–methanol–petroleum ether gave fluffy, white needles; m.p. 184–185°, $[\alpha]_D^{26}$ +100° (*c* 0.16, methanol); R_F 0.25 (solvent *C*); ^{13}C-n.m.r. (Me_2SO-d_6): δ 22.3 ($NHCOCH_3$), 34.9 (C-6), 53.5 (C-2), 68.1, 70.1, 71.2 (C-3,4,5), 72.7 ($C_6H_5CH_2$), 96.0 (C-1), 127.5, 128.2, 137.6 (arom.), and 169.6 ($NHCOCH_3$); m.s. (relative intensity): *m/z* 255 (7), 257 (7), 266 (5), 268 (3), 281 (3), and 282 (2).

Anal. Calc. for $C_{15}H_{20}BrNO_5$; C, 48.14; H, 5.39; Br, 21.35; N, 3.74. Found: C, 47.94; H, 5.25; Br, 21.56; N, 3.74.

Acetylation of **8** with acetic anhydride–pyridine gave 75% of *benzyl 2-acetamido-3,4-di-*O*-acetyl-6-bromo-2,6-dideoxy-α-*D*-glucopyranoside* (**14**), recrystallized from chloroform–hexane, m.p. 133–134°, $[\alpha]_D^{28}$ +118° (*c* 0.1, chloroform); lit.[20] m.p. 134–135°, $[\alpha]_D^{20}$ +120° (*c* 0.2, chloroform).

*2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-*D*-glucopyranose* (**9**) *by acetolysis of* **1**. — A solution of **1** (0.50 g, 2 mmol) in acetic anhydride (15 mL), acetic acid (10 mL), and concentrated sulfuric acid (0.2 mL) was stirred for 71 h; after this time one major and two minor products were detected by t.l.c. (solvent *C*). Chloroform was added and acids were removed by cold, aqueous sodium hydrogencarbonate (with back-extraction by chloroform to retain the appreciably water-soluble product) to give **9** as a thick syrup that crystallized from chloroform–hexane; m.p. 135–137°, $[\alpha]_D^{26}$ +88° (*c* 0.7, chloroform); lit.[21] m.p. 139°, $[\alpha]_D^{26}$ +92° (chloroform).

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