and H-5'a,b), 6.20 (t, $J_{1',2'a} = J_{1',2'b} = 6.5$ Hz, 1 H, H-1'), 7.88 (s, 1 H, H-8).

Anal. Calcd for $C_{10}H_{14}N_6O_3$: C, 45.11; H, 5.30; N, 31.56. Found: C, 45.24; H, 5.42; N, 31.19.

9-(3-Acetylamino-2,3-dideoxy-β-D-ribofuranosyl)adenine (10). 9-(3-Amino-2,3-dideoxy-β-D-ribofuranosyl)adenine (**6**) (35 mg, 0.14 mmol) was dissolved in methanol (10 mL) and treated with acetic anhydride (0.03 mL, 0.3 mmol) and triethylamine (0.05 mL). The solution was stirred over night at room temperature and evaporated. The residue was dissolved in a minimal amount of 9% methanol–chloroform and applied to a column of silica gel (15 g) made up in chloroform and was eluted with 200 mL each of 9 and 15% methanol–chloroform, collecting 17.4-mL fractions. Fractions 17–21 contained a material which gave a single spot (R_f 0.41 in system B). These fractions were combined and evaporated to dryness. 9-(3-Acetylamino-2,3-dideoxy-β-D-ribofuranosyl)adenine (**10**) was crystallized as fine plates from methanol (33 mg, 81%): mp 235–237 °C; UV λ_{max} (H_2O) 259.5 (ε 15300) and (pH 1) 257 nm (ε 14800); CD λ_{max} 265 ([θ] −900), 226 ([θ] +1100), and 217 nm ([θ] −600); NMR (Me_2SO-d_6) δ 1.89 (s, 3 H, MeCO), 2.2–2.9 (m, 2 H, H-2'a,b), 3.64 (m, 2 H, H-5'a,b), 3.93 (m, 1 H, H-4'), 4.50 (m, 1 H, H-3'), 5.17 (brs, 1 H, OH-5'), 6.39 (t, 1 H, $J_{1',2'a} = J_{1',2'b} = 6.5$ Hz, H-1'), 7.31 (brs, 2 H, NH_2), 8.16, 8.38 (s, 2 H, H-2 and H-8), 8.41 (d, 1 H, $J_{3',NH} = 7$ Hz, NH-3').

Anal. Calcd for $C_{12}H_{16}N_6O_3$: C, 49.31; H, 5.52; N, 28.75. Found: C, 49.15; H, 5.56; N, 28.66.

Synthesis of Adenosine from 2',3',5'-Tri-*O*-acetyluridine (13). N^6-Octanoyladenine (**11**) (238 mg, 0.91 mmol) and 2',3',5'-tri-*O*-acetyluridine (**13**) (185 mg, 0.50 mmol) were suspended in acetonitrile (3 mL) and BSA (0.5 mL, 2.0 mmol) was added. The mixture was heated at reflux temperature for 15 min. Trimethylsilyl trifluoromethanesulfonate (0.11 mL, 0.65 mmol) was added to the clear solution. After heating at reflux temperature for 4 h, the reaction mixture was poured in 25 mL of ethanol–concentrated NH_4OH (4:1) with stirring. After 1 day at room temperature, the solution was evaporated and the residue was dissolved in 40 mL of 60% methanol–water and applied to a column of Dowex 1 × 4 (OH^-) (20 mL) which was eluted with 60% methanol–water (300 mL) and 75% methanol–water (150 mL). The main fractions containing adenosine were combined and evaporated to dryness. The residue was recrystallized from water (75 mg, 56%), mp 236–238 °C. This compound was found to be identical in all respects with an authentic sample.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft for financial support and one of us (M.I.) thanks the Alexander von Humboldt Stiftung for a fellowship. The measurement of the NMR spectra by Mr. B. Seeger is gratefully acknowledged. We also thank Dr. V. Armstrong for helping us with the writing of the manuscript.

Registry No.—**2,** 15981-92-7; **3a,** 66323-40-8; **3b,** 30516-87-1; **4a,** 66323-41-9; **4b,** 66323-42-0; **5a,** 66323-43-1; **5b,** 66323-44-2; **6,** 7403-25-0; **7a,** 66323-45-3; **7b,** 66323-46-4; **8a,** 66323-47-5; **8b,** 66323-48-6; **9,** 66323-49-7; **10,** 66323-50-0; **11,** 52854-12-3; **12,** 21047-87-0; **13,** 4105-38-8; adenosine, 58-61-7.

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(26) This spot was probably the α anomer (**4a**) of the starting material (**4b**) which was isolated in the synthesis of the guanine derivatives.
(27) This was confirmed by the alkaline hydrolysis of ethanolic extracts of these spots.
(28) All attempts to separate **8a** and **8b** were unsuccessful.

Aminoglycoside Antibiotics. 3.[1] Synthesis of a Furanosyl Isomer of Kanamycin B from a Protected 3-Amino-3-deoxyglucofuranosyl Chloride

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Received November 21, 1977

A new crystalline glycosylating agent, comprised of a mixture of α- and β-3-acetamido-2,5,6-tri-*O*-benzyl-3-deoxy-D-glucofuranosyl chlorides (**7a,b**), was synthesized. It was used to prepare, via a Koenigs–Knorr type condensation, the 2-deoxy-4-*O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)-6-*O*-(3-amino-3-deoxy-α- and β-D-glucofuranosyl)-D-streptamines, **1** and **2,** isomers of the antibiotic kanamycin B. The structure of α-glycoside **1** was confirmed by its ^{13}C NMR spectrum.

The aminoglycoside antibiotics have provided a versatile backbone for the organic chemist to construct analogues with improved antimicrobial properties.[2] While studies have concentrated on modifications of the 2-deoxystreptamine or on the aminosugar appended to its O-4 position, fewer analogues have appeared with modified sugars on the O-5 or O-6 positions. Usually in nature, there is a furanoside at the O-5 position or a pyranoside at the O-6 position, with the only reported O-6 furanosides being the relatively inactive 6-*O*-(β-D-ribofuranosyl)paromamine, synthesized by Hanessian et al.[3a] and the corresponding neamine derivative synthesized by Suami et al.[3b] As part of our program aimed at evaluating the antibacterial properties of pseudodisaccharides and pseudotrisaccharides derived from neamine, the α- and β-(*cis*

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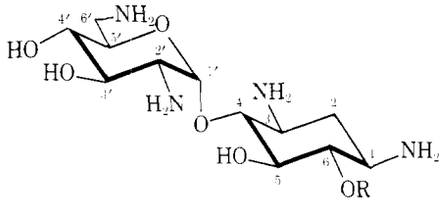
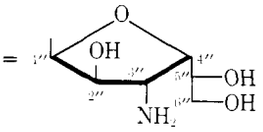
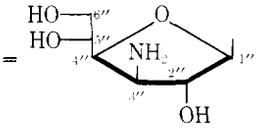
and *trans*)-aminofuranosylglycosides **1** and **2**, both isomers of kanamycin B,[4] **3**, were prepared. Although **1** and **2** would



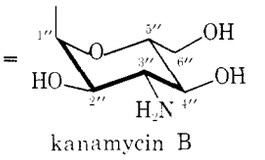
1, R =



2, R =



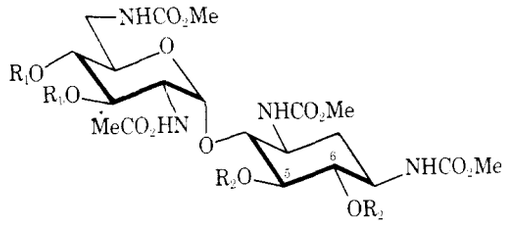
3, R =



kanamycin B

both be interesting to evaluate, the α-(*cis*)-glycoside, **1**, was expected to be the more desirable as it appears to be closer in structure, based on molecular models, to kanamycin B.

The pseudodisaccharide starting material, **6**, was obtained by acetylation and hydrolysis of the known diol **4**.[5] Although



4, R_1 = H; R_2 =

5, R_1 = $COCH_3$; R_2 =

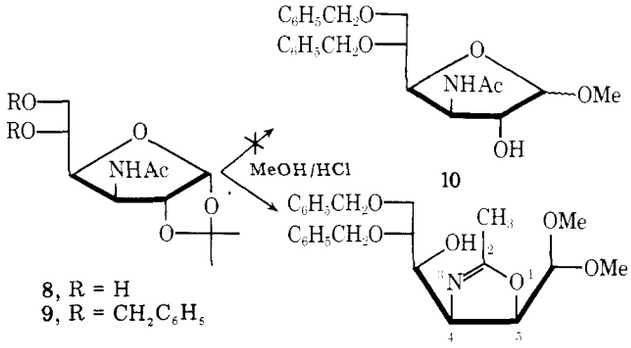
6, R_1 = $COCH_3$; R_2 = H

7a, α-chloride
b, β-chloride

two hydroxyls are present in **6**, adequate precedent exists in the literature[3a,6] to predict that a Koenigs–Knorr type condensation between it and a glycosyl chloride should give the desired O-6 substituted pseudotrisaccharide.

Although extensive efforts have been mounted to efficiently synthesize α-pyranosides,[7] spurred by the presence of such α linkages in many natural products, only a limited number of publications (excluding nucleoside work) have appeared on the stereospecific preparation of α-(1,2-*cis*)-furanosides.[8] The furanose system lacks the rigidity and anomeric effect of the pyranose ring, both useful in controlling glycosylations. In general, with a furanosyl halide, product control for glycosylation is determined by the type of substituent present at its 2 position. Thus, if the substituent is a participating group, such as an ester, *trans*-(β)-glycoside formation will be favored because of anchimeric assistance in the active intermediate. On the other hand, a nonparticipating group, such as a nitrate ester or a benzyl ether, will favor the formation of a *cis*-glycoside. This occurs by kinetic control, whereby the alcohol displaces, with inversion, the statistically more prevalent (sterically less hindered) *trans*-(β)-halide. Based on these considerations, tribenzyl chloride **7b** was chosen as the suitably protected glycosyl halide for the synthesis of **1** and **2**. In addition, α-glycoside formation might be further enhanced by anchimeric assistance[8c,9] from the 3-acetamido group present in **7b**.

In a first approach to **7b**, the known diol **8**,[10] readily available from diacetone glucose, was benzylated to give crystalline



8, R = H
9, R = $CH_2C_6H_5$

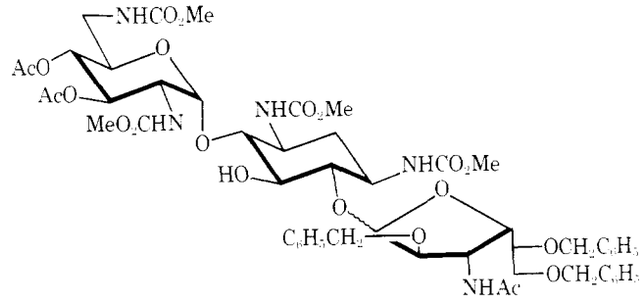
10

11

diether **9**. Acidic methanolysis of **9** under a variety of conditions yielded, instead of the desired methyl furanosides **10**, a complex mixture of products from which a crystalline oxazoline dimethylacetal was isolated. The product was tentatively assigned the *manno*-structure **11** based on spectral data and mechanistic considerations.

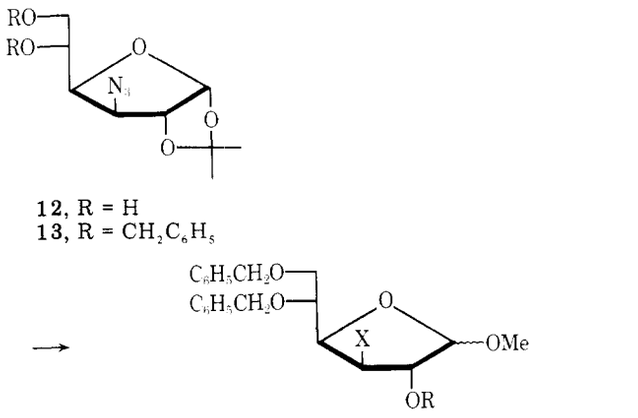
To avoid undesired oxazoline formation, the known azide **12**[10] was used as the starting material and was successfully converted to the desired new crystalline chlorides **7a** and **7b** as outlined in Scheme I. In carrying out this series of reactions, nearly all of the azido intermediates were oils and required chromatography for purification. In the preparative work, intermediates were not purified until the crystalline mixture of acetamides **16a** and **16b** was obtained. Acetylation of free sugar **17** gave β-(*trans*)-acetate **18**, which, on solvolysis in ethereal hydrogen chloride, yielded the mixture of chlorides **7a** and **7b**. The higher melting, more polar α-chloride [NMR ($CDCl_3$) δ 6.12 (d, 1 H, J = 4 Hz)] could be selectively crystallized from the mixture. However, it quickly reverted to the original anomeric mixture [δ 6.12 (d, ~½ H, J = 4 Hz), 6.02 (s, ~½ H)] on standing in deuteriochloroform solution. Because of this rapid equilibration, the anomeric mixture was used in the pseudotrisaccharide work.

The mixture of chlorides **7a** and **7b** was treated under anhydrous conditions for 5 days with an excess of diol **6** in dry methylene chloride containing pyridine and silver perchlorate. Chromatography of the crude product gave the desired crystalline α-glycoside, **19a**, in 12% yield and the β-glycoside, **19b**,



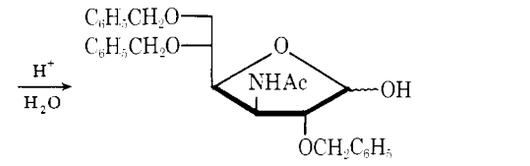
19a, α-glycoside
19b, β-glycoside

Scheme I



12, R = H
13, R = $CH_2C_6H_5$

14a+b, R = H; X = N_3; α- + β-glycosides
15a+b, R = $CH_2C_6H_5$; X = N_3; α- + β-glycosides
16a+b, R = $CH_2C_6H_5$; X = NHAc; α- + β-glycosides



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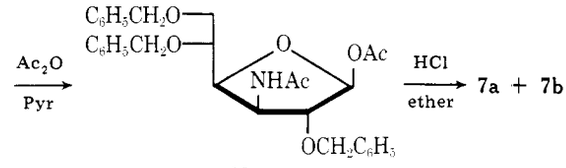

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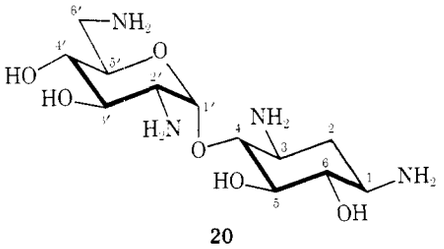
in 1.5% yield. In the absence of pyridine, several other products and higher amounts of **19b** were observed, resulting from anomerization and transglycosylation about the relatively acid-labile furanoside system. Although definitive structure assignments could not be made for **19a** or **19b** because of their complex NMR spectra, their structures were readily discerned from the simpler spectra of their respective deblocked final products **1** and **2**. Both **1** and **2** display a doublet at δ 5.5 (J = 4 Hz) from the α-pyranosyl anomeric proton present in the neamine precursor. In addition, **1** has a doublet at δ 5.8 (J = 5 Hz) indicative of a *cis*-(α)-anomeric furanosyl proton whereas **2** has a singlet at δ 5.3 indicative of a *trans*-(β)-furanoside.

As indicated in a previous paper in this series,[1a,11] the location of attachment of the new sugar can be readily confirmed with the aid of pH profile ^{13}C nuclear magnetic resonance (^{13}C NMR) spectra. Table I shows the ^{13}C NMR chemical shifts of synthetic α-glycoside **1**, neamine (**20**), and α-methylglycoside **21** at various pHs with tentative resonance



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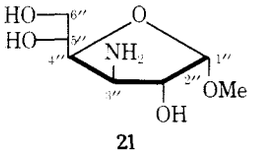

21

assignments. In addition, Figure 1 shows the pH profile of **1** in the region containing its C-4, C-5, and C-6 resonances (75–90 ppm). The fact that the two downfield peaks near 88 ppm both shift on protonation indicates that both glycosides are attached to carbons β to amino groups. Since one glycoside linkage (at C-4) was present in the starting neamine, the new linkage must be at C-6 which is β to the amino group on C-1.

In vitro antibacterial testing of **1** against several Gram-positive and Gram-negative organisms indicated it to have approximately 3% of the activity of kanamycin B whereas **2** had less than 1% the activity of kanamycin B. It is of interest that α-glycoside **1** is more active than β-glycoside **2** although it would appear that the overall structure perturbation in going from a 3-aminopyranoside to a 3-aminofuranoside is too large for maintenance of the desired biological activity.

Experimental Section

Column chromatography was carried out on J. T. Baker silica gel (60–200 mesh). Proton nuclear magnetic resonance spectra (NMR) were run on a Varian T-60 instrument using Me_4Si as standard. Mass spectra were obtained from a Perkin-Elmer RMU-6 or a Varian CH5 instrument. Infrared spectra were run on a Perkin-Elmer Infracord Model 137. Carbon magnetic resonance (^{13}C NMR) spectra were recorded on a Varian CFT-20 instrument and calibrated with an internal (~5%) dioxane standard set at 67.4 ppm. Samples for ^{13}C NMR spectra were decarbonated by passage through a short column of Amberlite IRA-400 (OH^-) resin and lyophilized. All manipulations, including neutralizations with 38% DCl, were performed in a CO_2-free, nitrogen atmosphere. pDs were measured with pHydrion papers (Micro Essential Laboratories, Brooklyn, N.Y.) and are uncorrected for D_2O. Melting points were taken in a Thomas-Hoover melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was run on Uniplate precoated silica gel plates, 250 or 1000 μm (Analtech, Inc., Newark, Del.). Organic extracts were dried over anhydrous sodium sulfate.

5,6-*O,O'*-Cyclohexylidene-2-deoxy-*N,N'*-bis(methoxycarbonyl)-4-*O*-[3,4-di-*O*-acetyl-2,6-dideoxy-2,6-bis[(methoxycarbonyl)amino]-α-D-glucopyranosyl]streptamine (5). To a chilled solution of acetic anhydride (50 mL) in pyridine (200 mL) was added 5,6-*O,O'*-cyclohexylidene-2-deoxy-*N,N'*-bis(methoxycarbonyl)-4-*O*-[2,6-dideoxy-2,6-bis[(methoxycarbonyl)amino]-α-D-glucopyranosyl]streptamine[5] (**4**) (100 g, 0.16 mol). The mixture was allowed to stand overnight at room temperature and concentrated in vacuo (0.1 mmHg). The residue was dissolved in methylene chloride (500 mL), washed with saturated aqueous sodium bicarbonate, dried, and concentrated in vacuo. The concentrate was triturated with ether and crude **5** (101 g, 88%) was collected.

For analysis, a sample was chromatographed on silica gel with chloroform–methanol (97:3) to yield pure **5** as a white amorphous solid: $[\alpha]^{25}_D$ +55.3° (c 1, $CHCl_3$); mass spectrum m/e 718 (M^+). Anal. Calcd for $C_{30}H_{46}N_4O_{16}$: C, 50.14; H, 6.45; N, 7.80. Found: C, 49.83; H, 6.47; N, 7.59.

2-Deoxy-*N,N'*-bis(methoxycarbonyl)-4-*O*-[3,4-di-*O*-acetyl-2,6-dideoxy-2,6-bis[methoxycarbonyl)amino]-α-D-glucopyranosyl]streptamine (6). To a solution of cyclohexylidene diacetate **5** (100 g, 0.14 mol) in methanol (300 mL) was added 3 N aqueous HCl (60 mL). The solution was allowed to stand for 6 h at room temperature, neutralized with aqueous sodium bicarbonate, and concentrated in vacuo. The residue was dissolved in methylene chloride (500 mL), washed with water, dried, and concentrated in vacuo to give a tan oil which was dissolved in hot ethyl acetate (500 mL) and added dropwise to ether (2 L) with vigorous stirring to yield **6** (65.5 g, 73%) as an amorphous hygroscopic solid: $[\alpha]^{25}_D$ +77.8 (c 1, $CHCl_3$); MS m/e 638 (M^+). Anal. Calcd for $C_{24}H_{38}N_4O_{16}$: C, 45.14; H, 6.00; N, 8.77. Found: C, 45.04; H, 6.29; N, 8.49.

3-Acetamido-5,6-di-*O*-benzyl-3-deoxy-1,2-*O,O'*-isopropylidene-α-D-glucofuranose (9). Benzyl chloride (3.4 g, 27.0 mmol) was added dropwise with stirring to a mixture of 3-acetamido-3-deoxy-1,2,-*O,O'*-isopropylidene-α-D-glucofuranose[10] (**8**) (870 mg, 3.3 mmol), crushed potassium hydroxide (3.7 g), and crushed Drierite (3.7 g) in DMF (20 mL). The reaction mixture was stirred at 65 °C for 2 h, allowed to cool, and filtered. The filtrate was concentrated in vacuo (0.1 mm) and the residual syrup was recrystallized from ether to give **9** (770 mg, 53%): mp 69–70 °C; $[\alpha]^{25}_D$ −27.4° (c 1, $CHCl_3$); IR ($CHCl_3$) 1670 and 1510 cm^{-1}; NMR ($CDCl_3$) δ 5.8 (1 H, d, J = 4 Hz), 1.75 (3 H, s), 1.50 (3 H, s), 1.30 (3 H, s); MS m/e 426 ($M - CH_3$)$^+$. Anal. Calcd for

Table I. The C^{13} Chemical Shifts of 20, 21, and 1 at pH (pD) 2 and 12 and Their Differences,[a] Δ

Carbon atom	20			21			1		
	pH 12	pH 2	Δ	pH 12	pH 2	Δ	pH 12	pH 2	Δ
1	51.17	50.64					(50.54)	(49.94)	
2	36.67	29.02	7.65				36.87	28.33	8.54
3	50.20	49.43					(50.10)	(49.17)	
4	88.30	78.16	10.14				(87.75)	78.24	9.51
5	76.79	75.95					75.40	74.97	
6	78.39	73.25	5.14				(87.41)	82.27	5.14
1′	101.72	96.47	5.25				101.37	96.79	4.58
2′	56.12	54.44					56.18	54.38	
3′	74.48	69.98	4.50				74.47	70.04	4.43
4′	72.26	71.55					72.28	71.49	
5′	74.04	69.03	5.01				74.08	69.03	5.05
6′	42.59	41.11					42.55	41.02	
1″				103.68	102.04		104.50	103.03	
2″				(78.32)	(75.38)	2.94	(78.70)	76.09	2.61
3″				58.46	57.79		57.92	56.66	
4″				(77.96)	(75.16)	2.80	(77.81)	74.79	3.02
5″				71.08	70.95		70.86	70.94	
6″				63.32	63.54		64.21	63.38	
OMe				56.55	56.03				

[a] Chemical shifts in ppm from Me_4Si. Shifts in parentheses were too close to be assigned unequivocally.

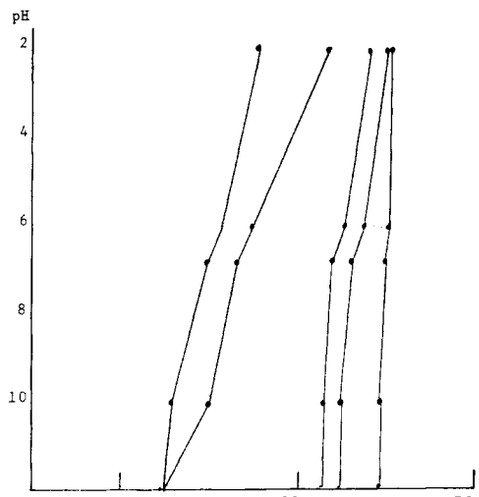

Figure 1. Change in chemical shifts (^{13}C NMR spectra) of 1 with deuterium ion concentration (75–90 ppm only).

$C_{25}H_{31}NO_6 \cdot H_2O$: C, 65.34; H, 7.24; N, 3.05. Found: C, 65.18; H. 6.97; N, 2.95.

2-Methyl[5,6-di-*O*-benzyl-2,3-dideoxy-D-mannose(glucose)][3′,2′:4,5]-2-oxazoline Dimethyl Acetal (11). A solution of isopropylidene ketal **9** (1.9 g, 4.3 mmol) in methanolic hydrogen chloride (30 mL, 5% w/v) was warmed at 60 °C for 3 h, quenched with aqueous sodium bicarbonate, and concentrated in vacuo. The residue was dissolved in chloroform, washed with aqueous sodium bicarbonate, dried, and evaporated under reduced pressure. Crystallization of the residue yielded oxazoline **11** (760 mg, 41%): mp 103–104.5 °C; $[\alpha]^{25}_D$ +80.6° (*c* 1, $CHCl_3$); IR ($CHCl_3$) 1670 cm^{-1}, no amide II band at 1510 cm^{-1}; NMR ($CDCl_3$) δ 3.46 (6 H, s), 1.98 (3 H, d, J = 1 Hz, five bond oxazoline coupling), acetal proton hidden; MS *m/e* 429 (M^+), 414 ($M - CH_3$)$^+$, 354 ($M - CH_3OCHOCH_3$)$^+$, 75 ($CH_3OCHOCH_3$)$^+$; mono-Me_4Si derivative, MS *m/e* 501 ($M + 1\ Me_4Si$)$^+$, 486 ($M + 1\ Me_4Si - CH_3$)$^+$, 426 ($M + 1\ Me_4Si - CH_3OCHOCH_3$)$^+$, 75 ($CH_3OCHOCH_3$)$^+$. Anal. Calcd for $C_{24}H_{31}NO_6$: C, 67.11; H, 7.27; N, 3.26. Found: C, 66.85; H. 7.40; N, 3.57.

Acetylation of **11** with acetic anhydride in pyridine yielded a monoacetate: NMR ($CDCl_3$) δ 5.15 (1 H, dd, J_1 = 4 Hz, J_2 = 8 Hz), 3.47 (3 H, s), 3.43 (3 H, s), 2.09 (3 H, s), 2.00 (3 H, d, J = 1 Hz), acetal proton hidden; IR ($CDCl_3$) 1740 and 1680 cm^{-1}, no NH or OH at 3000–4000 cm^{-1}, no amide II at 1510 cm^{-1}.

3-Azido-5,6-di-*O*-benzyl-3-deoxy-1,2-*O*,O′-isopropylidene-α-D-glucofuranose (13). This compound was made by the same procedure used to prepare **9** starting with 3-azido-3-deoxy-1,2-*O*,*O*′-isopropylidene-α-D-glucofuranose[10] (**12**) (17.3 g, 0.07 mol). Crude **13** was obtained as a syrup (29.5 g, 98%).

For characterization, a sample was purified by preparative TLC with ethyl acetate–hexane (1:9) to yield **13** as an oil: $[\alpha]^{25}_D$ −20.8° (*c* 1, $CHCl_3$); IR (film) 2110 cm^{-1} (azide); MS *m/e* 397 ($M - N_2$)$^+$, 382 ($M - N_2 - CH_3$)$^+$. Anal. Calcd for $C_{23}H_{27}N_3O_5$: C, 64.93; H, 6.40; N, 9.88. Found: C, 65.21; H, 6.46; N, 9.83.

Methyl 3-Azido-5,6-di-*O*-benzyl-3-deoxy-α- and -β-D-glucofuranosides (14a and 14b). A solution of crude isopropylidene ketal **13** (29 g, 0.07 mol) in methanolic hydrogen chloride (770 mL, 1.4 % w/v) was allowed to stand overnight at room temperature and slowly poured into 2 L of ice water containing sodium bicarbonate (40 g). The methanol was removed by concentration in vacuo and the aqueous suspension was extracted with methylene chloride. The extracts were dried and concentrated in vacuo to give a mixture of **14a** and **14b** (26 g, 93%).

For characterization a sample of the crude mixture was purified by preparative TLC (ethyl acetate–hexane, 1:4) to yield pure α-isomer **14a** as an oil: R_f 0.18 (ethyl acetate–hexane, 1:4); $[\alpha]^{25}_D$ +69.0° (*c* 0.5, $CHCl_3$); IR (CH_2Cl_2) 2110 cm^{-1}; NMR ($CDCl_3$) δ 4.9 (1 H, d, J = 4 Hz), 3.4 (3 H, s); MS *m/e* 370 ($M - N_2 - H$)$^+$. Anal. Calcd for $C_{21}H_{25}N_3O_5$: C, 63.15; H, 6.31; N, 10.52. Found: C, 63.33; H, 6.56; N, 10.29.

The β isomer, **14b,** was also obtained from the preparative TLC as an oil: R_f 0.14; $[\alpha]^{25}_D$ −55.0° (*c* 0.5, $CHCl_3$); IR (CH_2Cl_2) 2110 cm^{-1}; NMR ($CDCl_3$) δ 3.3 (3 H, s), anomeric proton hidden; MS *m/e* 370. Anal. Found: C, 63.56; H, 6.55; N, 10.42.

Methyl 3-Azido-2,5,6-tri-*O*-benzyl-3-deoxy-α- and -β-D-glucofuranosides (15a and 15b). The mixture of crude alcohols **14a** and **14b** (25 g, 0.062 mol) was benzylated in the same manner as used in the preparation of **9** to yield a mixture of crude **15a** and **15b** (33 g, 91%).

For characterization the mixture was chromatographed using ethyl acetate–petroleum ether (4:96) to yield crystalline α-isomer **15a:** mp 47.5–48° (ethanol–water); $[\alpha]^{25}_D$ + 48.1 (*c* 0.5, $CHCl_3$); IR (CH_2Cl_2) 2110 cm^{-1}; MS *m/e* 461 ($M - N_2$)$^+$ and 460 ($M - N_2 - H$)$^+$. Anal. Calcd for $C_{28}H_{31}N_3O_5$: C, 68.69; H, 6.36; N, 8.58. Found: C, 68.42; H, 6.62; N, 8.34.

The β isomer, **15b,** was obtained as a thermally labile oil: $[\alpha]^{25}_D$ −28.8° (*c* 0.5, $CHCl_3$); IR (film) 2110 cm^{-1}; MS *m/e* 461, 460. Anal. Found: C, 69.05; H, 6.92; N, 8.30.

Methyl 3-Acetamido-2,5,6-tri-*O*-benzyl-3-deoxy-α- and -β-glucofuranosides (16a and 16b). The crude mixture of tribenzyl azides **15a** and **15b** (11 g, 0.022 mol) was stirred with lithium aluminum hydride (1 g) in ether (200 mL) for 2 h. The excess reagent was destroyed by sequential addition of water (1 mL), 10% aqueous sodium hydroxide (1 mL), and water (3 mL) and the suspension was filtered and concentrated in vacuo. The residue was stirred overnight in acetic anhydride (20 mL) and pyridine (20 mL), concentrated in vacuo, and crystallized from ether–petroleum ether to yield a mixture of **16a** and **16b** (7.1 g, 64%).

For characterization, a sample was recrystallized from benzene–cyclohexane to yield the more polar α isomer, **16a:** mp 130–131 °C; R_f 0.35 (ethyl acetate–hexane, 1:3); $[\alpha]^{25}_D$ +63.3 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 1670 cm^{-1}; NMR ($CDCl_3$) δ 4.76 (1 H, d, J = 4 Hz), 3.40 (3 H, s), 1.67 (3 H, s); MS *m/e* 505 (M^+). Anal. Calcd for $C_{30}H_{35}NO_6$: C, 71.27; H, 6.98; N, 2.77. Found: C, 70.98; H, 7.04; N, 2.83.

The less polar, β isomer, **16b,** was isolated from the mother liquors: mp 104–105 °C (cyclohexane); R_f 0.48; $[\alpha]^{25}_D$ −36.7° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 1670 cm^{-1}; NMR ($CDCl_3$) δ 3.3 (3 H, s), 1.77 (3 H, s), 4.85 (1 H, s); MS *m/e* 505 (M^+). Anal. Found: C, 70.97; H. 7.03; N, 2.85.

3-Acetamido-2,5,6-tri-*O*-benzyl-3-deoxy-D-glucofuranose (17). A solution of the methylglycosides **16a** and **16b** (6 g, 0.012 mol) in acetic acid (55 mL) containing 3 N hydrochloric acid (8 mL) was stirred at 40 °C for 3 h. The solution was cooled and poured into ice–water containing excess sodium bicarbonate. The semisolid precipitate was collected and dissolved in methylene chloride and the solution was washed with aqueous sodium bicarbonate, dried, and concentrated in vacuo. The residue was recrystallized from benzene–cyclohexane to yield **17** (4.2 g, 73%): mp 104–105 °C; $[\alpha]_D^{25}$ −75.3° (*c* 0.5, $CHCl_3$); NMR ($CDCl_3$ + D_2O) δ 5.45 (~½ H, d, J = 4 Hz), 5.36 (~½ H, s), 1.68 and 1.76 (3 H, 2s); MS *m/e* 491 (M^+). Anal. Calcd for $C_{29}H_{33}NO_6$: C, 70.86; H, 6.77; N, 2.85. Found: C, 70.98; H, 7.02; N, 2.82.

3-Acetamido-1-*O*-acetyl-2,5,6-tri-*O*-benzyl-3-deoxy-β-D-glucofuranose (18). A solution of **17** (4.2 g, 8.5 mmol) in acetic anhydride (10 mL) and pyridine (50 mL) was left at room temperature for 3 h and then concentration in vacuo. The residue was evaporated several times with toluene and crystallized from benzene–cyclohexane to yield **18** (3.2 g, 71%): mp 88–89 °C; $[\alpha]^{25}_D$ −49.7° (*c* 0.5, $CHCl_3$); NMR ($CDCl_3$) δ 6.15 (1 H, s), 1.84 (3 H, s), 1.80 (3 H, s); IR (CH_2Cl_2) 1750 and 1665 cm^{-1}; MS *m/e* 533 (M^+). Anal. Calcd for $C_{31}H_{35}NO_7$: C, 69.78; H, 6.61; N, 2.62. Found: C, 69.74; H, 6.76; N, 2.54.

3-Acetamido-2,5,6-tri-*O*-benzyl-3-deoxy-α- and -β-D-glucofuranosyl Chlorides (7a and 7b). A solution of acetate **18** (3.2 g, 6 mmol) in dry saturated ethereal hydrogen chloride (200 mL) containing acetyl chloride (20 mL) was stirred overnight at room temperature during which time a white precipitate formed and redissolved. This was concentrated in vacuo and evaporated repeatedly with dry toluene to yield the anomeric mixture of chlorides **7a** and **7b** (3.0 g, 98%): mp 114–115.5 °C; $[\alpha]^{25}_D$ +114 → +66° (*c* 0.5, benzene); NMR ($CDCl_3$) δ 6.12 (~½ H, d, J = 4 Hz, α anomer), 6.02 (~½ H, s, β anomer), 1.74 (3 H, s); MS *m/e* 473 ($M - HCl)^+$; IR (CH_2Cl_2) 1670 cm^{-1}. Anal. Calcd for $C_{29}H_{32}ClNO_5$: C, 68.29; H, 6.32; Cl, 6.95; N, 2.75. Found: C, 68.40; H, 6.37; Cl, 6.71; N, 3.00.

Crystallization from benzene–cyclohexane gave the higher melting α anomer, **7a** [mp 120–121 °C; NMR ($CDCl_3$) δ 6.12 (1 H, d, J = 4 Hz)], which equilibrated overnight in $CDCl_3$ solution to the original anomeric mixture.

2-Deoxy-*N*-*N*′-bis(methoxycarbonyl)-4-*O*-[3,4-di-*O*-acetyl-2,6-dideoxy-2,6-bis[(methoxycarbonyl)amino]-α-D-glucopyranosyl]-6-*O*-(3-acetamido-2,5,6-tri-*O*-benzyl-3-deoxy-α- and -β-D-glucofuranosyl)streptamines (19a and 19b). A mixture of chlorides **7a** and **7b** (1.5 g, 2.9 mmol), the protected neamine **6** (3.6 g, 6.6 mmol), finely ground Drierite (10 g), and pyridine (0.25 mL) in dry methylene chloride (40 mL) was stirred with exclusion of moisture for 2 h and then anhydrous silver perchlorate (890 mg) was added. Stirring was continued in the dark for 5 days, after which the reaction was quenched with aqueous sodium bicarbonate and filtered. The filtrate was extracted several times with methylene chloride and the combined organic phases were dried and concentrated in vacuo. The residue (2.53 g) was chromatographed (chloroform–methanol, 98:2) to yield the more mobile β-isomer **19b** (55 mg, 1.5%): $[\alpha]^{25}_D$ −2° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 1730 and 1670 cm^{-1}; R_f (chloroform–methanol, 98:2) 0.54. Anal. Calcd for $C_{53}H_{69}N_5O_{21}$: C, 57.40; H, 6.00; N, 6.31. Found: C, 57.15; H, 6.21; N, 6.59.

Further elution yielded the more polar, crystalline α-isomer **19a** (407 mg, 12% based on **7a** and **7b**): mp 201–203 °C (toluene–methanol); $[\alpha]^{25}_D$ +63.6 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 1730 and 1670 cm^{-1}; R_f 0.39. Anal. Found: C, 57.14; H, 6.10; N, 6.18.

2-Deoxy-4-*O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)-6-*O*-(3-amino-3-deoxy-α-D-glucofuranosyl)streptamine (1). The recrystallized protected α-pseudotrisaccharide **19a** (465 mg, 0.4 mmol) in ethanol (20 mL) was hydrogenated at 60 psi over 10% palladium on charcoal (500 mg) for 16 h, after which the catalyst was removed by filtration and washed with excess ethanol. The filtrate was concentrated in vacuo and the residue was refluxed for 4 h in water (10 mL) containing barium hydroxide octahydrate (7.5 g). The solution was neutralized at 100 °C with carbon dioxide gas and filtered and the filtrate was neutralized to pH 6 with 0.5 N sulfuric acid. The barium sulfate was removed by filtration and the filtrate was charged onto a column of Amberlite IRC-50 ion exchange resin (20 mL) in the ammonium cycle. The column was eluted with an ammonia gradient (0 to 0.5 M) and the fractions containing **1** were concentrated in vacuo, neutralized to pH 6 with dilute sulfuric acid, and lyphilized to yield **1** as its sulfate salt (60 mg, 22%): $[\alpha]^{25}_D$ +88° (*c* 0.5, H_2O); NMR (D_2O) δ 5.8 (1 H, d, J = 4 Hz), 5.5 (1 H, d, J = 5 Hz). Anal. Calcd for $C_{18}H_{37}N_5O_{10}\cdot1.5H_2SO_4\cdot3H_2O$: C, 31.57; H, 6.77; N, 10.23; SO_4, 21.03. Found: C, 31.62; H. 6.20; N, 10.13; SO_4, 21.21.

2-Deoxy-4-*O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)-6-*O*-(3-amino-3-deoxy-β-D-glucofuranosyl)streptamine (2). A sample of the protected β isomer, **19b** (597 mg, 0.5 mmol), was deblocked in the same manner to yield **2** as its sulfate salt (258 mg, 55%): $[\alpha]^{25}_D$ +14.2° (*c* 0.5, H_2O); NMR (D_2O) δ 6.0 (1 H, d, J = 4 Hz), 5.3 (1 H, s). Anal. Calcd for $C_{18}H_{37}N_5O_{10}\cdot3H_2SO_4\cdot H_2O$: C, 27.17, H, 5.70; N, 8.80; SO_4^{2-}, 36.21. Found: C, 26.85; H, 5.65; N, 8.38; SO_4^{2-}, 37.61.

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Registry No.—1 sulfate salt, 66322-53-0; **2** sulfate salt, 66290-55-9; **4,** 35017-15-3; **5,** 57538-48-4; **6,** 57538-46-2; **7a,** 66290-72-0; **7b,** 66290-71-9; **8,** 14166-54-2; **9,** 66290-70-8; **11,** 66290-69-5; **11** monoacetate derivative, 66290-68-4; **11** mono Me_4Si derivative, 66290-67-3; **12,** 22169-71-7; **13,** 66290-66-2; **14a,** 66290-65-1; **14b,** 66290-64-0; **15a,** 66290-63-9; **15b,** 66290-62-8; **16a,** 66290-61-7; **16b,** 66290-60-6; **17,** 66290-59-3; **18,** 66290-58-2; **19a,** 66322-52-9; **19b,** 66290-57-1; **20,** 3947-65-7; **21,** 66290-56-0.

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