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Synthesis of dibekacin analogs containing 3-oxa- and 3-aza-2,3,4-trideoxy-D-*glycero*-hexopyranose

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Abstract

6-*O*-(3-Oxa-2,3,4-trideoxy-α-D-*glycero*-hexopyranosyl) derivatives (**10** and **17**) of both 3′,4′-dideoxyneamine and 5-epifluoro-5,3′,4′-trideoxyneamine have been prepared by coupling ethyl 6-*O*-benzyl-3-oxa-2,3,4-trideoxy-1-thio-D-*glycero*-hexopyranoside (**5**) with suitable aglycons. The corresponding 3″-aza derivative (**19**) of dibekacin (**6**) was prepared by oxidation of 1,3,2′,6′-tetra-*N*-tosyldibekacin (**7**) with $Pb(OAc)_4$ followed by treatment with NH_4OAc and reduction with $NaBH_3CN$. Related ring-opening compounds (**11** and **25**) were also prepared. © 1996 Elsevier Science Ltd.

Keywords: Aminoglycoside antibiotic; 5-Deoxy-5-fluorination; Glycosylation; $Pb(OAc)_4$ oxidation; Reductive amination; Na in liquid NH_3

1. Introduction

In a previous paper [1] we reported the synthesis of kanamycin A (KMA) analogs having new 1,4-dioxane rings, namely 6-amino-3-oxa-2,3,4,6-tetradeoxy-D- and -L-*glycero*-hexopyranoses, instead of the 6-amino-6-deoxy-D-glucose (6AG) moiety of KMA. By this synthesis, 6-azido-3-oxa-2,3,4,6-tetradeoxy-D- and -L-*glycero*-hexopyranoses underwent successful coupling, through their 1-(ethylthio) derivatives, to a protected pseudodisaccharide [1] of 6-*O*-(3-amino-3-deoxy-α-D-glucopyranosyl)-2-deoxystreptamine (3AD). However, these KM analogs were devoid of, or showed only slight, antibacterial activity. Since the other pseudodisaccharide moieties of KMA, kanamycin B (KMB), and 3′,4′-dideoxykanamycin B (dibekacin) {these being respec-

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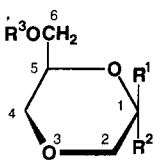
tively 4-*O*-(6-amino-6-deoxy-α-D-glucopyranosyl)-2-deoxystreptamine [2] (6AD), 4-*O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)-2-deoxystreptamine [neamine (NA)], and its 3′,4′-dideoxy analog (DDNA) [3]}, are considered essential for antibacterial activity [1], we tried to replace the 3-amino-3-deoxy-D-glucose (3AG) unit, the activity-enhancing portion, with a different one, to obtain derivatives of improved activity. Another aim of this synthesis is to examine the role of 3AG, and more precisely of its 3-amino group, for antibacterial activity, because α-anomeric attachment of 3AG to O-6 of 6AD, NA, or DDNA (to form KMA, KMB, and dibekacin, respectively) greatly enhances [4] the activities of the parent pseudodisaccharides. In this paper we describe the synthesis of dibekacin analogs bearing 3-oxa- and 3-aza-2,3,4-trideoxy-α-D-*glycero*-hexopyranoses attached at O-6 of the 2-deoxystreptamine unit, as well as structurally related ring-opened derivatives.

2. Results and discussion

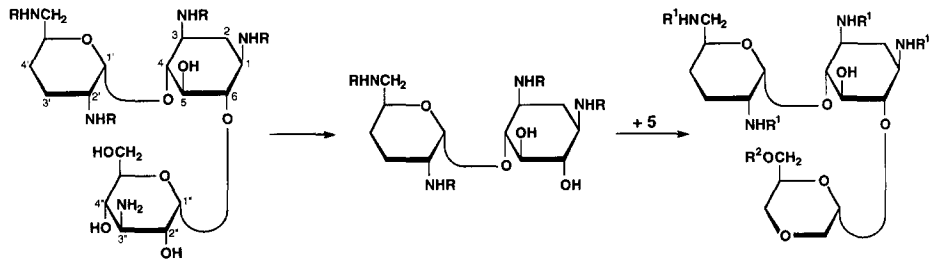
The required 6-*O*-benzyl-3-oxa-1-(ethylthio) glycoside **5** for coupling to tetra-*N*-tosyl-DDNA (**8**) was prepared from methyl 3-oxa-2,3,4-trideoxy-α-D-*glycero*-hexopyranoside (**1**) [1]. *O*-Benzylation (to give **2**) followed by acid-catalyzed hydrolysis gave the free sugar **3** in high yield, and this was then acetylated with Ac_2O in pyridine to give an anomeric mixture (~ 1:3) of 1-*O*-acetyl derivatives **4a** (α) and **4b** (β). Treatment of **4b** with $C_2H_5SSnBu_3$ in the presence of $CF_3SO_3Si(CH_3)_3$ [5] as described in a previous paper [1] gave an anomeric mixture of 1-(ethylthio) glycosides **5** in 80% yield.



	R^1	R^2	R^3
1	H	OCH_3	H
2	H	OCH_3	Bn
3	H, OH		Bn
4a	H	OAc	Bn
4b	OAc	H	Bn
5	H, SCH_2CH_3		Bn

Preparation of the condensing partner **8** was attempted by tosylation of DDNA, which was expected to be accessible by acid-catalyzed hydrolysis of dibekacin (**6**) or by periodate oxidation of the 3AG component of **6**. However, hydrolysis of **6** (aq 3–6 M HCl, 60–100 °C), unlike kanamycin B, was difficult and did not give DDNA effectively [6]; accompaniment by several undesirable mono- (including 2-deoxystreptamine) and

di-saccharides hampered the high-yield isolation of DDNA. Direct periodate oxidation of **6** also gave DDNA in poor yield. In searching for an alternative method, however, we found that tosylation of **6** gave rather preferentially a 1,3,2′,6′-tetra-*N*-tosyl derivative **7** with H_2N-3″ free. Successive treatment of **7** with $Pd(OAc)_4$, followed by $NaBH_4$, and hydrolysis readily gave **8** with removal of the 3AG moiety. The weak reactivity of H_2N-3″ group evidently results from the presence of the two electron-withdrawing 2″ and 4″ hydroxyl groups in **6**, which lowers the basicity as compared to those for the other amino groups (the pK_a values of the H_3N^+-1, 3, 2′, 6′, and 3″ groups were roughly estimated to be ~8.4 [7], ~8.4 [7], ~9.1 [8], ~9.7 [8], and ~8.1 [8], respectively). The structure of **7** was confirmed by its ^1H NMR spectrum, in which H-3″ resonated upfield by 1.05 ppm as compared to the resonance of H-3″ of the *N*-Boc derivative (**11**).

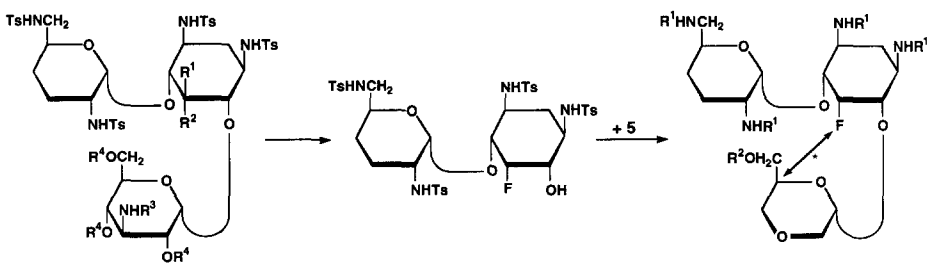


Dibekacin (6) R = H
7 R = Ts

8 R = Ts
DDNA R = H

9 R^1 = Ts, R^2 = Bn
10 $R^1 = R^2$ = H

Conventional [9] condensation of 1-thioglycoside **5** with **8** using *N*-iodosuccinimide (NIS) in a slightly acidic medium gave several products, and the desired 6-*O*-α-D-glycosyl derivative **9** was obtained in only 23% yield. Deprotection of **9** with sodium in liquid ammonia gave the final product **10**. The α-anomeric structure and the position of attachment (C-6 and not C-5 of 2-deoxystreptamine) were determined, respectively, by the small $J_{1'',2''}$ value and the HMBC method, which verified the H-6–C-1″ connection.



	R^1	R^2	R^3	R^4
11	OH	H	Boc	H
12	OH	H	Boc	Ac
13	H	F	Boc	Ac
14	H	F	H	H

15

	R^1	R^2
16	Ts	Bn
17	H	H

* Interspace coupling was observed in **17**

Table 1
^{13}C NMR chemical shifts (ppm) of **10**, **17**, **19**, **21**, **25**, and DDNA measured in 26% ND_3 in D_2O

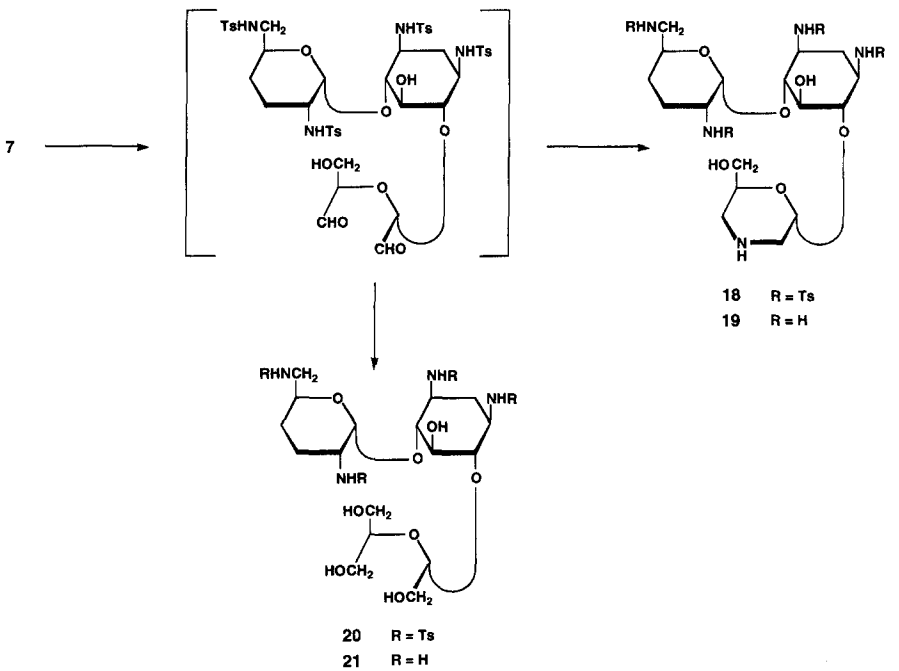
	10	**17** [a]	**19**	**21**	**25**	DDNA
C-1	50.79	47.83	50.29 [b]	51.03	50.10	51.14
C-2	36.56	36.31	36.55	36.73	36.73	36.61
C-3	50.28	47.58 d	50.64 [b]	50.20	50.80	50.35
C-4	88.14	79.06 d	87.95	88.52	84.81	88.34
C-5	75.53	90.74 d	75.63	75.94	76.31	76.74
C-6	87.36	84.07 d	87.29	85.38	88.67	78.30
C-1′	102.22	97.12	102.19	102.51	102.55	102.37
C-2′	50.75	50.14	50.73	50.61	50.53	50.60
C-3′	26.82	26.78	26.67	27.02	27.05	26.92
C-4′	28.32	28.17	28.29	28.33	28.28	28.30
C-5′	71.39	71.16	71.32	71.45	71.43	71.34
C-6′	45.91	45.70	45.87	45.94	45.88	45.88
C-1″	96.74	98.29	97.02	105.31	105.04	
C-2″	68.67	68.33	48.09	61.67	63.26	
C-3″					43.32	
C-4″	67.99	67.58	45.73	63.41 [c]	72.45	
C-5″	69.51	69.67 d	70.26	80.75	80.68	
C-6″	61.36	61.34	62.76	62.14 [c]	61.06	

[a] $J_{C,F}$ are $J_{C\text{-}1,F} \approx J_{C\text{-}3,F}$ 4, $J_{C\text{-}4,F} \approx J_{C\text{-}6,F}$ 17, $J_{C\text{-}5,F}$ 177, $J_{5'',F}$ 0.7 Hz; on weak irradiation of F-5 signals for C-3, 4, 6, and 5″ became singlets and C-5 became a doublet of smaller width.
[b,c] Interconvertible.

As the poor yield of **9** was attributed partly to the presence of vicinal diols [1,10] at C-5 and 6 in **8**, 5-epifluoro-1,3,2′,6′-tetra-*N*-tosyl-5,3′,4′-trideoxyneamine (**15**), lacking HO-5 was prepared. Another reason to choose **15** was based on the finding [7] that some 5-deoxy-5-epifluoro analogs of kanamycins had better antibacterial activities than the corresponding parent compounds. Compound **15** was prepared from **7**. *tert*-Butoxycarbonylation (to give **11**) followed by acetylation gave the tri-*O*-acetyl derivative **12** having HO-5 free; the inertness toward acetylation at this position is attributed to steric crowding near HO-5 [6,11]. Fluorination of **12** with *N*,*N*-diethylaminosulfur trifluoride [12] (DAST) gave the 5-epifluoro derivative **13** in high yield, which was deprotected (except for the *N*-tosyl groups) to give the 3″-amino-5-epifluorodibekacin derivative **14**. The 3AG portion was then cleaved in the manner described for **8** to give the 5-epifluoro analog (**15**) of **8**. Coupling of **5** with **15** was performed as described for **9**, and the 6-*O*-glycosyl derivative **16** was obtained in 57% yield. Deprotection of **16** gave the final product **17**. The α-anomeric structure and the position of attachment were confirmed based on ^1H and ^{13}C NMR data. It is noteworthy that a through-space coupling was observed between F-5 and C-5″ (see Table 1). This indicates that the 1,4-dioxane ring introduced occupies a conformation similar to that for the 3AG portion in kanamycin [13].

Next, a 3″-aza analog of **10** having a morpholine ring was prepared. The reaction intermediate obtained by oxidation of **7** (Solid A, see Experimental section) was utilized, and this was treated with NH_4OAc in methanol and reduced with $NaBH_3CN$ [14], whereupon a 3″-aza derivative **18** was obtained, albeit in poor yield. Attempts to

improve the yield were unsuccessful. Detosylation with Na in liquid ammonia gave the desired product **19**. The 3″-aza structure was confirmed by the upfield shifts of both H-2″ and 4″, and C-2″ and 4″ in the ^{1}H and ^{13}C NMR spectra, respectively, as compared to those for **10**. The α-anomeric structure and chair conformation were confirmed by the small $J_{1'',2''ax}$ and large $J_{4''ax,5''}$ values.



Compounds having an open-ring structure were also prepared. Reduction of solid A with $NaBH_4$ gave a tetraol **20** in 44% yield; the moderate yield suggests that the pure dialdehyde (and other acetal forms) in solid A comprised only about half the material. Detosylation of **20** gave the 6-*O*-tri(hydroxymethyl) derivative **21**. Another ring-opening compound bearing an amino group was also prepared. The free H_2N-3″ group of tetra-*N*-tosyldibekacin (**7**) was trifluoroacetylated with CF_3CO_2Et [15], and the 3-*N*-acyl derivative was protected with $PhCH(OMe)_2$ giving the 4″,6″-acetal **22**. Subsequent *N*-deacylation gave an amine **23**. Attempts to obtain **23** by direct benzylidenation of **7** were unsuccessful. It is noteworthy that the N*H*$COCF_3$ proton resonated downfield as compared to the N*H*Ts protons (see Experimental section). Cleavage of the amino alcohol **23** with $Pb(OAc)_4$ in pyridine, followed by reduction with $NaBH_4$ gave, after resin chromatography, an amine **24** in 26% yield. In this experiment, if the reduction was performed on the oxidized product obtained after conventional purification, no **24** was obtained. This suggests that the reaction intermediate formed just after oxidation (with an imine structure) is unstable. Deprotection of **24** with Na in liquid ammonia gave the free amine **25** in poor yield. As similar treatment of **9** and **16** gave DDNA and

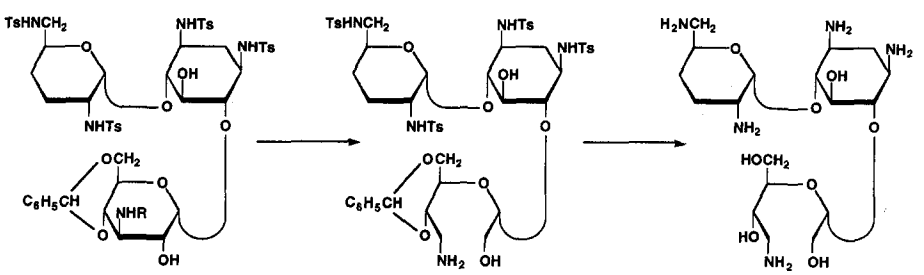
Table 2
Minimal inhibitory concentration[a] ($\mu g\ mL^{-1}$) of **10**, **17**, **19**, **21**, **25**, and DDNA

Test organism [b]	**10**	**17**	**19**	**21**	**25**	DDNA
St. a. FDA 209P	25	100	3.12	> 100	12.5	3.12
St. a. Ap01	> 100	> 100	> 100	> 100	> 100	50
St. e. 109	25	50	1.56	100	6.25	3.12
B. s. PCI219	12.5	25	0.78	100	3.12	1.56
E. c. K-12	25	50	12.5	> 100	50	6.25
E. c. K-12 ML1629	100	> 100	25	> 100	100	12.5
E. c. K-12 R5	> 100	> 100	> 100	> 100	> 100	> 100
E. c. J5R11-2	25	25	6.25	> 100	12.5	6.25
E. c. JR66/W677	100	> 100	25	> 100	> 100	25
K. p. PCI602	100	> 100	50	> 100	> 100	12.5
Ps. r. GN311	50	100	6.25	> 100	100	3.12
S. m.	> 100	> 100	> 100	> 100	> 100	50
Ps. a. A3	50	100	6.25	> 100	25	6.25
Ps. a. H9	> 100	> 100	100	> 100	> 100	25

[a] Judged by the agar dilution streak method (Mueller–Hinton agar, 17 h, 37 °C); the data for dibekacin (**6**) were as follows (in the order cited above): 0.2, > 100, 1.56, 0.1, 0.35, 0.78, > 100, 0.39, 25, 0.78, 0.2, 12.5, 0.2, 1.56.

[b] Strains selected are the same as those reported in a previous paper [1]. Abbreviations: *St. a.*, *Staphylococcus aureus*; *St. e.*, *Staphylococcus epidermidis*; *B. s.*, *Bacillus subtilis*; *E. c.*, *Escherichia coli*; *K. p.*, *Klebsiella pneumoniae*; *P. r.*, *Proteus rettgeri*; *S. m.*, *Serratia marcescens*; *Ps. a.*, *Pseudomonas aeruginosa*.

5-epifluoro-5,3′,4′-trideoxyneamine [16], respectively, treatment with Na may have led to partial cleavage of glycoside bonds by a radical mechanism. The presence of H_2N–C-3″ and the absence of connection between C-2″–C-3″ in **25** was confirmed by the ^1H and ^{13}C NMR spectra.



22 R = $COCF_3$
23 R = H
24
25

Antibacterial activities (Table 2) of **10**, **17**, **19**, **21**, and **25** showed that substitution of 3AG in dibekacin with a 3-oxaglycose (to give **10** and **17**) greatly lowered the activity

of DDNA, whereas substitution with a 3-azaglycose (to give **19**) led to retention of some activity, thus indicating the difference of O and NH groups in terms of activity.

3. Experimental

General methods.—Optical rotations were determined with a Perkin–Elmer 241 polarimeter. Mass spectra were recorded with a Jeol SX-102 spectrometer. NMR spectra (^{1}H at 250 and 500 MHz, ^{13}C at 125.8 MHz, ^{19}F at 235 and 470.5 MHz) were recorded with Bruker AC-250P and AMX-500 spectrometers, using Me_4Si or $CFCl_3$ (for ^{19}F) as the internal reference. Proton signals were mostly confirmed by ^{1}H–^{1}H COSY. TLC and preparative TLC was performed on Silica Gel 60 F_{254} (Merck 5715 and 5717), and detected under UV light at 254 nm, by charring with aq 50% H_2SO_4, by spraying 2.5% ammonium molybdate in aq 1.5 M H_2SO_4, or by 0.4% ninhydrin in pyridine. Column chromatography was performed on Wakogel C-300.

*Methyl 6-O-benzyl-3-oxa-2,3,4,-trideoxy-α-*D-glycero-*hexopyranoside* (**2**).—To an ice-cold solution of **1** [1] (1.48 g, 10 mmol) in THF (45 mL) was added NaH (0.48 g net in mineral oil, 12 mmol) and, after stirring for 10 min, $C_6H_5CH_2Br$ (1.78 mL, 15 mmol) was added, and the mixture was stirred for 6 h at room temperature. After benzene (300 mL) had been added, the organic solution was washed with water, dried (Na_2SO_4), and concentrated. Chromatography of the residue with 5:2 hexane–EtOAc gave **2** as a syrup (2.14 g, 90%), $[\alpha]_D^{23}$ +86° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.44 (s, 3 H, OCH_3), 3.45 and 3.51 (each dd of 1 H, H-6a,6b), 3.54 (dd, 1 H, H-4*ax*), 3.61 (dd, 1 H, H-2*ax*), 3.74 (d, 1 H, H-2*eq*), 3.83 (dd 1 H, H-4*eq*), 4.23 (ddt, 1 H, H-5), 4.56 (d, 1 H, H-1), 4.57 (br s, 2 H, C*H*$_2$Ph), 7.32 (m, 5 H, Ph); $J_{1,2ax}$ 2, $J_{2ax,2eq}$ 12, $J_{4ax,4eq}$ 11, $J_{4ax,5}$ 10.5, $J_{4eq,5}$ 3.2, $J_{5,6a} \approx J_{5,6b}$ 4.5, $J_{6a,6b}$ 10.5 Hz. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.22; H, 7.57.

The β anomer of **2** was obtained in a similar way, by treating an anomeric mixture [1] of **1** (1.58 g) with $C_6H_5CH_2Br$ followed by chromatography, as a syrup (0.49 g), $[\alpha]_D^{23}$ −85° (*c* 1, $CHCl_3$), together with **2** (1.93 g); ^{1}H NMR ($CDCl_3$): δ 3.21 (dd, 1 H, H-2*ax*), 3.32 (dd, 1 H, H-4*ax*), 3.51 (s, 3 H, OCH_3), 3.53 and 3.59 (each dd of 1 H, H-6a,6b), 3.76 (dd, 1 H, H-2*eq*), 3.78 (dd, 1 H, H-4*eq*), 3.92 (m, 1 H, H-5), 4.52 (dd, 1 H, H-1), 4.56 (s, 2 H, C*H*$_2$Ph), 7.33 (m, 5 H, Ph); $J_{1,2ax}$ 8, $J_{1,2eq}$ 3, $J_{2ax,2eq}$ 11, $J_{4ax,4eq}$ 9.5, $J_{4ax,5}$ 11.5, $J_{4eq,5}$ 3, $J_{5,6a}$ 4, $J_{5,6b}$ 5, $J_{6a,6b}$ 10 Hz. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.23; H, 7.56.

*6-O-Benzyl-3-oxa-2,3,4-trideoxy-*D-glycero-*hexopyranose* (**3**).—A solution of **2** (1.93 g, 8.1 mmol) in 1:1 AcOH–aq M HCl (20 mL) was heated for 8 h at 60 °C. After the addition of aq $NaHCO_3$ (saturated, 100 mL), the mixture was repeatedly extracted with CH_2Cl_2. Concentration of the solution gave a residue, which was chromatographed (2:1 CH_2Cl_2–EtOAc) to give **3** as a chromatographically homogeneous syrup ($\alpha/\beta \sim 1$, 1.63 g, 90%); $[\alpha]_D^{24}$ +4.3° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) (only selected signals are listed): α anomer, δ 3.36 (dd, 0.5 H, HO-1), 3.62 (dt, 0.5 H, H-2*ax*), 3.72 (d, 0.5 H, H-2*eq*), 5.06 (br dd, 0.5 H, H-1); $J_{1,OH}$ 6, $J_{1,2ax} \approx J_{2ax,OH}$ 2, $J_{2ax,2eq}$ 11 Hz; β anomer, 3.16 (dd, 0.5 H, H-2*ax*), 3.41 (d, 0.5 H, HO-1), 3.80 (dd, 0.5 H, H-2*eq*), 4.90 (ddd, 0.5 H, H-1); $J_{1,OH}$ 6, $J_{1,2ax}$ 8, $J_{1,2eq}$ 2.5, $J_{2ax,2eq}$ 11 Hz. Anal. Calcd for $C_{12}H_{16}O_4 \cdot 0.2H_2O$: C, 63.25; H, 7.26. Found: C, 63.30; H, 7.11.

*1-O-Acetyl-6-O-benzyl-3-oxa-2,3,4-trideoxy-α- and -β-*D-glycero-*hexopyranoses* (**4a** *and* **4b**).—A mixture of **3** (1.67 g, 7.33 mmol) and Ac_2O (1.77 mL, 14.9 mmol) in pyridine (17 mL) was kept for 3 h at room temperature. Methanol (1.2 mL) was added, and after 2 h, the mixture was diluted with CH_2Cl_2 (200 mL). The solution was washed with water and aq 10% $KHSO_4$, dried (Na_2SO_4), and concentrated. Chromatography (4:1 hexane–EtOAc) of the residue gave **4a** (0.47 g, 24%), TLC (2:1 hexane–EtOAc): R_f 0.25 and **4b** (1.39 g, 71%; R_f 0.3) as syrups. **4a**: $[\alpha]_D^{24}$ +49° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.14 (s, 3 H, Ac), 3.44 (dd, 1 H, H-6a), 3.51 (dd, 1 H, H-6b), 3.57 (dd, 1 H, H-4*ax*), 3.71 (dd, 1 H, H-2*ax*), 3.81 (d, 1 H, H-2*eq*), 3.91 (dd, 1 H, H-4*eq*), 4.30 (m, 1 H, H-5), 5.96 (br d, 1 H, H-1); $J_{1,2ax}$ 2, $J_{1,2eq}$ ~ 0 Hz. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.50; H, 7.06.

4b: $[\alpha]_D^{24}$ −54° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.09 (s, 3 H, Ac) 3.41 (dd, 1 H, H-2*ax*), 3.51 (dd, 1 H, H-4*ax*), 3.59 (d, 2 H, H-6a,6b), 3.80 (dd, 1 H, H-2*eq*), 3.81 (dd, 1 H, H-4*eq*), 4.02 (ddt, 1 H, H-5), 5.82 (dd, 1 H, H-1); $J_{1,2ax}$ 7, $J_{1,2eq}$ 2.5 Hz. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 62.97; H, 6.95.

*Ethyl 6-O-benzyl-3-oxa-1-thio-2,3,4-trideoxy-*D-glycero-*hexopyranoside* (**5**).—A solution of **4b** (493 mg, 1.85 mmol), $EtSSnBu_3$ (0.69 mL, 2.21 mmol), and $CF_3SO_3SiMe_3$ (0.36 mL, 1.85 mmol) in 1,2-dichloroethane (5 mL) was kept for 1 h at room temperature. After dilution with the same solvent (50 mL), the solution was washed with aq $NaHCO_3$ (saturated), dried (Na_2SO_4), and concentrated. The residue was chromatographed (10:1 → 5:1 hexane–EtOAc) to give **5** as a syrup (α/β ~ 1, 395 mg, 80%), $[\alpha]_D^{24}$ +47° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.30 (t, 3 H, SCH_2CH_3), 2.57–2.79 (m, 2 H, SCH_2CH_3), 3.91 (α anomer) and 3.37 (β-form) (each dd of 0.5 H, H-2*ax*), 3.78 (d, α anomer) and 3.84 (dd, β-form) (each 0.5 H, H-2*eq*), 3.55 (α) and 3.35 (β) (each dd of 0.5 H, H-4*ax*), 3.85 (dd 1 H, H-4*eq*), 5.16 (d, α-form) and 4.72 (dd, β-form) (each 0.5 H, H-1); $J_{1,2ax}$ 3.6 (α), 10.5 (β), $J_{1,2eq}$ 0 (α), 2.5 (β), $J_{2ax,2eq} \approx J_{4ax,4eq}$ 11.5, $J_{4ax,5}$ 10, $J_{4eq,5}$ 3 Hz. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.65; H, 7.51; S, 11.94. Found: C, 62.98; H, 7.51; S, 11.83.

*1,3,2′,6′-Tetra-*N*-tosyldibekacin* (**7**).—To a solution of **6** (2.18 g free base, 5.0 mmol) in 1:1 1,4-dioxane–H_2O (80 mL), TsCl (2.85 g, 15 mmol) and Na_2CO_3 (2.1 g, 20 mmol) were added, and the mixture was stirred for 4 h at room temperature, and then additional TsCl (0.76 g, 4 mmol) was added, and the reaction was continued for further 15 h. The mixture was poured into water (500 mL), and the resulting precipitate was filtered, washed with water, and dried (4.9 g). In TLC (5:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3), the solid showed three spots at R_f 0.25 (major, **7**), 0.5 (minor, penta-*N*-tosyldibekacin), and 0.7 (two close slight spots, over-*N*,*O*-tosylated products?). The solid dissolved in 2:1 THF–H_2O was charged on a column containing Dowex 50W-X2 resin (H^+ form, 200–400 mesh, 200 mL), and after the column was washed with the solvent mixture (fully-*N*-tosylated and over-tosylated derivatives were eluted out), elution with 2:1 THF–aq 3 M NH_3 gave **7** as monohydrate (4.13 g, 76%), $[\alpha]_D^{24}$ +32° (*c* 1, DMF); ^{1}H NMR (pyridine-d_5): δ 1.61 (q, 1 H, H-2*ax*), 1.66–1.78 (m, 2 H, H-4′a,4′b), 1.92 (m, 1 H, H-3′a), 2.14, 2.17, 2.29, 2.35 [each s of 3 H, 4 Ts(Me)], 2.28 (m, 1 H, H-3′b), 2.69 (dt, 1 H, H-2*eq*), 2.85 (ddd, 1 H, H-3 or 1), 3.21 (t, 1 H, H-5), 3.40 (dd, 1 H, H-6′a), 3.46 (dd, 1 H, H-6′b), 3.49 (t, 1 H, H-4 or 6), 3.50 (t, 1 H, H-3″), 3.54–3.63 [m, 2 H, H-1(or 3),2′], 3.66 (t, 1 H, H-6 or 4), 3.92 (t, 1 H, H-4″), 3.98 (dd, 1 H, H-2″),

4.26–4.31 (m, 2 H, H-5″,6″a), 4.58 (dd, 1 H, H-6″b), 4.98 (m, 1 H, H-5′), 5.15 (d, 1 H, H-1″), 5.49 (d, 1 H, H-1′); $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 12, $J_{1,2eq} \approx J_{2eq,3}$ 3.5, $J_{1,6} \approx J_{3,4} \approx J_{4,5} \approx J_{5,6}$ 9, $J_{1',2'}$ 3, $J_{6'a,6'b}$ 12.5, $J_{1'',2''}$ 4, $J_{2'',3''} \approx J_{3'',4''} \approx J_{4'',5''}$ 9.5, $J_{5'',6''b}$ 5, $J_{6''a,6''b}$ 13.5 Hz. Anal. Calcd for $C_{46}H_{61}N_5O_{16}S_4 \cdot H_2O$: C, 50.86; H 5.85; N, 6.45. Found C, 50.81; H, 6.16; N, 6.61.

3′,4′-Dideoxy-1,3,2′,6′-tetra-N-*tosylneamine* (**8**).—A mixture of **7** hydrate (2.58 g, 2.4 mmol) and $Pb(OAc)_4$ (2.14 g, 4.8 mmol) in pyridine (30 mL) was kept for 2 h at room temperature. Ethylene glycol (0.67 mL) was added, and after 2 h, the mixture was poured into water (500 mL). The resulting precipitate was filtered, washed with water thoroughly, and dried in vacuo to give a solid (Solid A, 2.64 g). To a solution of the solid in MeOH (60 mL), $NaBH_4$ (1.83 g, 48 mmol) was added, and after 1.5 h, excess reagent was decomposed by addition of acetone (35 mL). Aqueous 6 M HCl (45 mL) was added, and after 3 h, the solution was poured into water (800 mL). The resulting precipitate was filtered and dried to give a residue, which was chromatographed (10:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3) to give **8** as a solid (1.34 g, 62%), $[\alpha]_D^{23}$ +13° (*c* 1, $CHCl_3$); ^1H NMR (pyridine-d_5): δ 2.14, 2.15, 2.24, and 2.27 [each s of 3 H, 4 Ts(Me)], 5.59 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1′). Anal. Calcd for $C_{40}H_{50}N_4O_{12}S_4 \cdot 1/2H_2O$: C, 52.44; H, 5.61; N, 6.12. Found: C, 52.39; H, 5.81; N, 6.18.

6-O-*(6-O-Benzyl-3-oxa-2,3,4-trideoxy-α-*D-glycero-*hexopyranosyl)-3′,4′-dideoxy-1,3,2′,6′-tetra*-N-*tosylneamine* (**9**).—A mixture of **5** (70 mg, 0.26 mmol), **8** (180 mg, 0.20 mmol), and molecular sieves 4A (50 mg) in CH_2Cl_2 (2 mL) was stirred for 30 min, NIS (110 mg, 0.49 mmol) and trace amount of CF_3SO_3H (20 μL of 0.09 M CH_2Cl_2 solution) were added, and stirring was continued for 45 min at room temperature. After addition of CH_2Cl_2 (20 mL), the solution was washed successively with aq $NaHCO_3$ (saturated), aq 10% $Na_2S_2O_3$, aq NaCl (saturated), and dried (Na_2SO_4). In TLC (45:5:1 CH_2Cl_2–EtOAc–EtOH), the solution showed several spots at R_f 0.15 (**9**), 0.22 (**8**), 0.25, and 0.3 along with some faint spots. Evaporation of the solvent gave a residue (~ 270 mg), which was subjected to preparative TLC (4 times) to give **9** as a solid (52 mg, 23%) together with **8** (78 mg) recovered. **9**: $[\alpha]_D^{23}$ +24° (*c* 1, $CHCl_3$); ^1H NMR (pyridine-d_5): δ 1.60–1.72 (m, 3 H, H-2*ax*,4′*ax*,4′*eq*), 1.79 (m, 1 H, H-3′*ax*), 2.12 (m, 1 H, H-3′*eq*), 2.13, 2.16, 2.24, and 2.26 [each s of 3 H, 4 Ts(Me)], 2.25 (m, 1 H, H-2*eq*), 3.43 (m, 2 H, H-6′a,6′b), 3.60 (br d, 1 H, H-2″*ax*), 3.66 (m, 1 H, H-2′), 3.67 (dd 1 H, H-4″*ax*), 3.65–3.73 (m, 2 H, H-6″a,6″b), 3.76 (m, 2 H, H-1,3), 3.88 (d, 1 H, H-2″*eq*), 3.93 (dd, 1 H, H-4″*eq*), 4.72 (m, 1 H, H-5′), 5.04 (m, 1 H, H-5″), 5.45 (d, 1 H, H-1′), 5.56 (br s, 1 H, H-1″), 8.30 (d, 1 H, TsN*H*-3), 8.49 (t, 1 H, TsN*H*-6′), 8.73 (br s, 1 H, TsN*H*-2′), 9.16 (d, 1 H, TsN*H*-1). Anal. Calcd for $C_{52}H_{64}N_4O_{15}S_4$: C, 56.10; H, 5.79; N, 5.03; S, 11.52. Found: C, 56.08; H, 5.69; N, 4.97; S, 11.02.

3′,4′-Dideoxy-6-O-*(3-oxa-2,3,4-trideoxy-α-*D-glycero-*hexopyranosyl)neamine* (**10**).—To a solution of **9** (58.8 mg, 0.053 mmol) in liquid NH_3 (~ 5 mL) at −55 °C, Na (~ 30 mg) was added, and the deep-blue solution was kept for 15 min at the same temperature. Methanol was added until the solution become colourless, NH_3 was gently evaporated under warming, and finally the solvent was removed under diminished pressure. The residue was dissolved in H_2O and neutralized with Dowex 50W-X2 resin (H^+ form, 200–400 mesh, ~ 3 mL). The whole mixture was poured into a column containing the same fresh resin (NH_4^+ form, 8 mL), and after washing the column with water, products

were eluted with aq 0.5 → 0.75 → 1 M NH_3 to give DDNA (3.5 mg) and **10** as its carbonate · 1/4 hydrate (14.6 mg, 58%), $[\alpha]_D^{23}$ +81° (*c* 1.5, H_2O); ^1H NMR (26% ND_3 in D_2O): δ 1.24 (q, 1 H, H-2*ax*), 1.39 (m, 1 H, H-4′*ax*), 1.62 (dq, 1 H, H-3′*ax*), 1.70–1.78 (m, 2 H, H-3′*eq*,4′*eq*), 1.97 (dt, 1 H, H-2*eq*), 2.63 (dd, 1 H, H-6′a), 2.67 (dd, 1 H, H-6′b), 2.81–2.88 (m, 3 H, H-1,3,2′), 3.310 and 3.325 (each dd of 1 H, H-4,6), 3.56 (dd, 1 H, H-4″*ax*), 3.57 (dd, 1 H, H-6″a), 3.59 (dd, 1 H, H-6″b), 3.62 (t, 1 H, H-5), 3.70 (dd, 1 H, H-2″*ax*), 3.83 (m, 1 H, H-5′), 3.87 (dd, 1 H, H-4″*eq*), 3.91 (d, 1 H, H-2″*eq*), 4.37 (m, 1 H, H-5″), 5.03 (br s, 1 H, H-1″), 5.12 (d, 1 H, H-1′); $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 12.5, $J_{1,2eq} \approx J_{2eq,3}$ 4, $J_{3,4} \approx J_{1,6}$ 8, $J_{4,5} \approx J_{5,6}$ 9.5, $J_{1',2'}$ 4, $J_{2',3'ax} \approx J_{3'ax,3'eq} \approx J_{3'ax,4'ax} \approx J_{4'ax,4'eq}$ 13, $J_{3'ax,4'eq}$ 4, $J_{5'6'a}$ 7, $J_{5',6'b}$ 4, $J_{6'a,6'b}$ 13, $J_{1'',2''ax}$ 4, $J_{1'',2''eq} \sim 0$, $J_{2''ax,2''eq} \approx J_{4''ax,4''eq}$ 12, $J_{4''ax,5''}$ 10, $J_{4''eq,5''}$ 3, $J_{5'',6''a}$ 5, $J_{5'',6''b}$ 8, $J_{6''a,6''b}$ 11.5 Hz. Anal. Calcd for $C_{17}H_{34}N_4O_7 \cdot H_2CO_3 \cdot 1/4H_2O$: C, 45.70; H, 7.78; N, 11.84. Found: C, 45.64; H, 7.70; N, 11.80.

*3″-*N*-t-Butyloxycarbonyl-1,3,2′,6′-tetra-*N*-tosyldibekacin* (**11**).—To a solution of **7** (1.55 g, 1.45 mmol) in 3:1 THF–H_2O (12 mL), (*t*-BuOCO)$_2$O (0.51 g, 2.32 mmol) and Et_3N (0.8 mL) were added, and the mixture was stirred for 1.5 h at 50 °C. The upper THF layer separated was poured into water (300 mL), and the resulting precipitate was washed thoroughly with water, and dried to give **11** as a solid (1.69 g, quant.), $[\alpha]_D^{24}$ +42° (*c* 1, $CHCl_3$); ^1H NMR (pyridine-d_5): δ 1.39 (s, 9 H, Boc), 2.14, 2.17, 2.37, and 2.39 [each s of 3 H, 4 Ts(Me)], 2.64 (br t, 1 H, H-1 or 3), 3.35–3.51 (m, 4 H, H-3 or 1, H-6 or 4, and H-6′a,6′b), 3.58–3.66 (m, 2 H, H-4 or 6, and H-2′), 4.55 (q, 1 H, *J* 10 Hz, H-3″), 5.25 (d, 1 H, H-1″), 5.56 (d, 1 H, H-1′). Anal. Calcd for $C_{51}H_{69}N_5O_{18}S_4$: C, 52.42; H, 5.95; N, 5.99. Found: C, 52.85; H, 6.14; N, 5.91.

*3″-*N*-t-Butyloxycarbonyl-1,3,2′,6′-tetra-*N*-tosyl-2″,4″,6″-tri-*O*-acetyldibekacin* (**12**).—To an ice-cold solution of **11** (1.20 g, 1.03 mmol) in pyridine (15 mL), AcCl (0.29 mL, 4.08 mmol) was added, and the turbid solution was stirred for 1 h, then the clear solution was kept for 15 h at room temperature. Water (0.7 mL) was added, and after 1 h, the solution was concentrated to give a gummy residue, which was thoroughly washed with water to afford a solid (1.41 g), which was chromatographed (50:1 → 40:1 $CHCl_3$–MeOH) to give **12** as a solid (1.18 g, 89%), $[\alpha]_D^{25}$ +42° (*c* 1, $CHCl_3$); ^1H NMR (pyridine-d_5): δ 1.49 (s, 9 H, Boc); 2.00 (3 H), 2.02 (3 H), 2.17 (6 H), 2.34 (6 H) and 2.43 (3 H) [each s, 3 Ac, 4 Ts(Me)], 3.43 (m, 2 H, H-6′a,6′b), 3.50–3.70 (m, 4 H, H-1,3,5,2′), 4.64 (m, 2 H, H-6″a,6″b), 4.78–5.01 (m, 3 H, H-5′,3″,5″), 5.53 (d, 1 H, H-1′), 5.60 (t, 1 H, H-4″), 5.64 (dd, 1 H, $J_{1'',2''}$ 11 Hz, H-2″), 5.89 (d, 1 H, H-1″). Anal. Calcd for $C_{57}H_{75}N_5O_{21}S_4$: C, 52.88; H, 5.84; N, 5.41; S, 9.91. Found: C, 52.47; H, 5.97; N, 5.29; S, 9.74.

*3″-*N*-t-Butyloxycarbonyl-5-deoxy-5-epifluoro-1,3,2′,6′-tetra-*N*-tosyl-2″,4″,6″-tri-*O*-acetyldibekacin* (**13**).—To an ice-cold solution of **12** (634 mg, 0.49 mmol) in CH_2Cl_2 (10 mL), DAST (0.13 mL, 0.98 mmol) was added, and the solution was kept for 1 h at room temperature. After addition of aq 5% $NaHCO_3$ (7.5 mL) followed by stirring for 10 min, the organic solution (after addition of CH_2Cl_2, 60 mL) was washed with water, dried (Na_2SO_4), and concentrated to give a residue, which was chromatographed (30:1 $CHCl_3$–MeOH) to give **13** as a solid (623 mg, 97% as monohydrate), $[\alpha]_D^{24}$ +53° (*c* 1, $CHCl_3$); ^1H NMR (pyridine-d_5): δ 1.40–1.70 (m, 12 H, Boc, H-3′*ax*,4′*ax*,4′*eq*), ~2.20 (m, 1 H, H-3′*eq*), 1.95 (3 H), 1.99 (3 H), 2.19 (3 H), 2.20 (3 H), 2.23 (3 H), and 2.31 (6

H) [each s, 3 Ac, 4 Ts(Me)], 5.49 (d, 1 H, H-1′), 5.53–5.69 (m, 3 H, H-1″,2″,4″), 5.85 (br d, 1 H, *J* 53 Hz, H-5). ^{19}F NMR (pyridine-d_5): δ −212.69 (dt, $J_{4(6),F}$ 29, $J_{5,F}$ 53 Hz, F-5). Anal. Calcd for $C_{57}H_{74}FN_5O_{20}S_4 \cdot H_2O$: C, 52.08; H, 5.83; N, 5.33; S, 9.76. Found: C, 51.98; H, 5.90; N, 5.21; S. 9.72.

5-Deoxy-5-epifluoro-1,3,2′,6′-tetra-N-*tosyldibekacin* (**14**).—To a solution of **13** (535 mg, 0.41 mmol) in MeOH (10 mL), 28% NaOMe in MeOH (0.25 mL) was added. The mixture was kept for 30 min and then concentrated. The residue was dissolved in 9:1 CF_3CO_2H–H_2O (5 mL), and after 30 min, the solution was concentrated (de-*t*-butyloxycarbonylation) to give a residue, which was thoroughly washed with cyclohexane. To the resulting syrup, aq 0.5 M NH_3 (15 mL) was added, and the insoluble matter was filtered off. The mass obtained was dissolved in 3:1 THF–H_2O, Dowex 50W-X2 (H^+ form, 200–400 mesh, 4 mL) was added, and, after shaking the mixture for a while, the resin was collected, and charged on a column containing the same fresh resin (25 mL). Elution with 3:1 THF–aq 4 M NH_3 gave **14** as a solid (359 mg, 81% as monohydrate), $[\alpha]_D^{25}$ +49° (*c* 1, DMF); ^{1}H NMR (pyridine-d_5): δ 2.16, 2.20, 2.21, and 2.28 [each s of 3 H, 4 Ts(Me)], 5.32 (d, 1 H, H-1″), 5.44 (d, 1 H, H-1′), 5.92 (br d, 1 H, *J* 52 Hz, H-5). ^{19}F NMR (pyridine-d_5): δ −212.76 (dt, $J_{4(6),F}$ 26.5, $J_{5,F}$ 53 Hz, F-5). Anal. Calcd for $C_{46}H_{60}FN_5O_{15}S_4 \cdot H_2O$: C, 50.76; H, 5.74; N, 6.44. Found: C, 50.77; H, 5.71; N, 6.24.

5-Epifluoro-1,3,2′,6′-tetra-N-*tosyl-5,3′,4′-trideoxyneamine* (**15**).—Compound **14** (319 mg, 0.29 mmol) in pyridine (3.5 mL) was successively oxidized [$Pb(OAc)_4$, 2.90 mg, 0.65 mmol], reduced ($NaBH_4$, 265 mg, 7 mmol), and treated with aq 6 M HCl (6.5 mL) in a manner described for **8** to give, after chromatography (25:1 $CHCl_3$–MeOH), **15** as a solid (138 mg, 51% as hemihydrate), $[\alpha]_D^{25}$ +37° (*c* 1, $CHCl_3$); ^{1}H NMR (pyridine-d_5): δ 1.53–1.68 (m, 3 H, H-3′*ax*,4′*ax*,4′*eq*), 1.77 (q, 1 H, H-2*ax*), 2.14, 2.20, 2.21, and 2.24 [each s of 3 H, 4 Ts(Me)], 2.20 (m, 1 H, H-3′*eq*), 2.66 (dt, 1 H, H-2*eq*), 3.25 (dt, 1 H, H-6′a), 3.33 (dd, 1 H, H-6′b), 3.72 (ddd, 1 H, H-6), 3.73 (m, 1 H, H-2′), 3.91 (m, 1 H, H-1), 4.02 (ddd, 1 H, H-4), 4.27 (m, 1 H, H-3), 4.79 (m, 1 H, H-5′), 5.24 (br dt, 1 H, H-5), 5.26 (d, 1 H, H-1′), 8.58 (t, 1 H, TsN*H*-6′), 8.92 (d, 1 H, TsN*H*-3), 9.10 (d, 1 H, TsN*H*-1), 9.17 (d, 1 H, TsN*H*-2′); distinctions between H-1 and 3, and between H-4 and 6 were performed by combination of ^{13}C NMR, HMQC, and HMBC methods; $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 12, $J_{1,2eq} \approx J_{2eq,3}$ 4, $J_{1,6} \approx J_{3,4}$ 10.5, $J_{4,5} \approx J_{5,6}$ 2, $J_{4,F} \approx J_{6,F}$ 27, $J_{5,F}$ 52, $J_{1',2'}$ 4, $J_{5',6'a}$ 6, $J_{5',6'b}$ 4, $J_{6'a,6'b}$ 12.5, $J_{6'a,NH} \approx J_{6'b,NH}$ 6 Hz. ^{19}F NMR (pyridine-d_5): δ −212.63 (dt, F-5). Anal. Calcd for $C_{40}H_{49}FN_4O_{11}S_4 \cdot 1/2H_2O$: C, 52.33; H, 5.50; N, 6.10; S, 13.97. Found: C, 52.35; H, 5.92; N, 6.25; S, 13.77.

*6-O-(6-O-Benzyl-3-oxa-2,3,4-trideoxy-α-*D-glycero-*hexopyranosyl)-5-epifluoro-1,3,2′,6′-tetra*-N-*tosyl-5,3′,4′-trideoxyneamine* (**16**).—A mixture of **5** (41 mg, 0.15 mmol), **15** (94.6 mg, 0.103 mmol), and molecular sieves 4A (40 mg) in CH_2Cl_2 (1 mL) was stirred for 30 min, NIS (58.5 mg, 0.26 mmol) and trace amounts of CF_3SO_3H (40 μL of 0.09 M CH_2Cl_2 solution) were added, and stirring was continued for 30 min. In TLC (45:5:1 CH_2Cl_2–EtOAc–EtOH), the solution showed a major spot at R_f 0.22 accompanied by several minor and faint spots. Subsequent work-up as described for **9** gave, after chromatography (the same solvent system for TLC was used), **16** as a solid (65.4 mg, 57%), $[\alpha]_D^{21}$ +45° (*c* 1, $CHCl_3$); ^{1}H NMR (pyridine-d_5): δ 2.203, 2.207, 2.211, and 2.218 [each s of 3 H, 4 Ts(Me)], 4.65 and 4.71 (each d of 1 H, PhCH_2), 5.03 (br s, 1 H, H-1″), 5.46 (d, 1 H, H-1′), 5.84 (br dt, 1 H, $J_{5,F}$ 51.5 Hz, H-5). ^{19}F NMR

(pyridine-d_5): δ −213.43 (dt, $J_{4(6),F}$ 26, $J_{5,F}$ 52 Hz, F-5). Anal. Calcd for $C_{52}H_{63}FN_4O_{14}S_4$: C, 56.00; H, 5.69; N, 5.02; S, 11.50. Found: C, 55.85; H, 5.90; N, 4.64; S, 11.08.

*5-Epifluoro-6-O-(3-oxa-2,3,4-trideoxy-α-*D-erythro-*hexopyranosyl)-5,3′,4′-trideoxyneamine* (**17**).—Compound **16** (49.1 mg, 0.044 mmol) was treated with Na in the manner described for **10** to give, after resin chromatography, **17** as its carbonate · 1/2 hydrate (14.6 mg, 69%) together with a minor product (~ 2 mg, 5-epifluoro-5,3′,4′-trideoxyneamine [12]). Compound **17**, TLC (2:4:7:7 $CHCl_3$–PrOH–EtOH–aq 17% NH_3): R_f 0.65 (cf. DDNA [3]: R_f 0.45), $[\alpha]_D^{23}$ +109° (*c* 1, H_2O); ^{1}H NMR (26% ND_3 in D_2O): δ 1.13 (q, 1 H, H-2*ax*), 1.34 (dq, 1 H, H-4′*ax*), 1.60 (dq, 1 H, H-3′*ax*), 1.64–1.72 (m, 2 H, H-3′*eq*,4′*eq*), 2.01 (dt, 1 H, H-2*eq*), 2.57 (dd, 1 H, H-6′a), 2.62 (dd, 1 H, H-6′b), 2.75 (dt, 1 H, H-2′), 3.06 (m, 1 H, H-1), 3.10 (m, 1 H, H-3), 3.41 (t, 1 H, H-4″*ax*), 3.46 (dd, 1 H, H-6″a), 3.46 (ddd, 1 H, H-6), 3.48 (ddd, 1 H, H-4), 3.54 (dd, 1 H, H-6″b), 3.62 (dd, 1 H, H-2″*ax*), 3.75 (m, 1 H, H-5′), 3.78 (dd, 1 H, H-4″*eq*), 3.86 (d, 1 H, H-2″eq), 4.22 (m, 1 H, H-5″), 4.90 (d, 1 H, H-1′), 4.95 (br s, 1 H, H-1″), 5.29 (dt, 1 H, H-5); $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 12, $J_{1,2eq} \approx J_{2eq,3}$ 4.5, $J_{1,F} \approx J_{3,F}$ ~ 1.5, $J_{3,4} \approx J_{1,6}$ 9.5, $J_{4,5} \approx J_{5,6}$ ~ 2, $J_{4,F} \approx J_{6,F}$ ~ 27, $J_{5,F}$ 52.5, $J_{1',2'} \approx J_{2',3'eq}$ 3.5 $J_{2',3'ax} \approx J_{3'ax,3'eq} \approx J_{3'ax,4'ax} \approx J_{4'ax,5'}$ 12, $J_{3'eq,4'ax}$ 4, $J_{5',6'a}$ 7, $J_{5',6'b}$ 4, $J_{6'a,6'b}$ 13, $J_{1'',2''ax}$ 2, $J_{1'',2''eq}$ ~ 0, $J_{2''ax,2''eq}$ 12.5, $J_{4''ax,4''eq}$ 11.5, $J_{4''ax,5''}$ 11, $J_{4''eq,5''}$ 3, $J_{5'',6''a}$ 7, $J_{5'',6''b}$ 3, $J_{6''a,6''b}$ 12.5 Hz. ^{19}F NMR (pyridine-d_5): δ −214.24 (dt, $J_{4(6),F}$ 29, $J_{5,F}$ 52.5 Hz). Anal. Calcd for $C_{17}H_{33}FN_4O_6 \cdot H_2CO_3 \cdot 1/2H_2O$: C, 45.08; H, 7.57; N, 11.69. Found: C, 45.21; H, 7.24; N, 11.63.

*6-O-(3-Aza-2,3,4-trideoxy-α-*D-glycero-*hexopyranosyl)-3′4′-dideoxy-1,3,2′,6′-tetra-*N-*tosylneamine* (**18**).—To a solution of freshly prepared Solid A (described in **8**, 518 mg) in MeOH (6 mL), NH_4OAc (193 mg, 2.5 mmol) was added, and the mixture was stirred for 2 h at room temperature, then $NaBH_3CN$ (157 mg, 2.5 mmol) in MeOH (4 mL) was added, and the reaction was continued under stirring overnight. In TLC (5:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3), a spot initially tailed [R_f 0.4–0.6 having an intense head at ~ 0.6, the shape did not change substantially throughout the reaction] began to show a minor, but clear spot at R_f 0.5). After concentration, the residue was dissolved in $CHCl_3$ (40 mL), washed with water, dried (Na_2SO_4), and concentrated. The residue (~ 580 mg) was chromatographed (10:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3) to give **18** as a solid (69.8 mg, 14% based on **7**), $[\alpha]_D^{23}$ +31° (*c* 1, $CHCl_3$); ^{1}H NMR (pyridine-d_5): δ 1.60–1.75 (m 3 H, H-2*ax*,4′*ax*,4′*eq*), 1.82 (m, 1 H, H-3′*ax*), ~ 2.2 (m, H-3′*eq*), 2.15, 2.17, 2.26, and 2.27 [each s of 3 H, 4 Ts(Me)], 2.48 (dt, 1 H, H-2*eq*), 2.78 (dd, 1 H, H-2″*ax*), 2.91 (dd, 1 H, H-4″*ax*), 3.01 (d, 1 H, H-2″*eq*), 3.19 (dd, 1 H, H-4″*eq*), 3.38–3.51 (m, 2 H, H-6′a,6′b), 3.52 (m, 1 H, H-1), 3.65 (m, 1 H, H-2′), 3.71 (t, 1 H, H-6), 3.78–3.85 (m, 3 H, H-3,4,5), 3.88 (dd, 1 H, H-6″a), 3.94 (dd, 1 H, H-6″b), 4.54 (m, 1 H, H-5″), 4.86 (m, 1 H, H-5′), 5.39 (br s, 1 H, H-1″), 5.53 (d, 1 H, H-1′), 8.45 (t, 1 H, TsN*H*-6′), 8.61 (d, 1 H, TsN*H*-3), 9.26 (d, 1 H, TsN*H*-1); $J_{1'',2''ax}$ 2, $J_{1'',2''eq}$ ~ 0, $J_{2''ax,2''eq}$ 12, $J_{4''ax,4''eq}$ 12.5, $J_{4''ax,5''}$ 11, $J_{4''eq,5''}$ 2, $J_{5'',6''a} \approx J_{5'',6''b}$ 5, $J_{6''a,6''b}$ 11.5, $J_{1,NH}$ 7, $J_{3,NH} \approx J_{6',NH}$ 6 Hz. ^{13}C NMR (pyridine-d_5): 21.15, 21.17, 21.24, and 21.28 [4 Ts(CH_3)], 25.57 (C-3′), 27.91 (C-4′), 36.04 (C-2), 47.72 (C-6′), 48.04 (C-4″), 48.05 (C-2″), 53.50 (C-3), 53.95 (C-1), 54.01 (C-2′), 63.74 (C-6″), 67.86 (C-5′), 70.78 (C-5″), 76.86 (C-5), 80.79 (C-6), 82.73 (C-4), 96.77 (C-1″), 100.33 (C-1′). Anal. Calcd for

$C_{45}H_{59}N_5O_{14}S_4 \cdot H_2CO_3$: C, 50.95; H, 5.67; N, 6.45; S, 11.83. Found: C, 50.81; H, 5.63; N, 6.80; S, 11.90.

*6-O-(3-Aza-2,3,4-trideoxy-α-*D-glycero-*hexopyranosyl)-3′,4′-dideoxyneamine* (**19**).—Compound **18** (74.7 mg, 0.069 mmol) was detosylated with Na in liquid NH_3 as described for **10** to give a mixture of **19** and DDNA (minor). In TLC with 2:4:7:7 $CHCl_3$–PrOH–EtOH–aq 17% NH_3, the mixture showed two spots at R_f 0.45 (DDNA) and 0.75 (**19**). The products were separated by chromatography with CM-Sephadex C-25 (3 mL) using 0 → 0.15 → 0.2 M aq NH_3 as the eluents to give **19** as a solid (15.5 mg, 50%), $[\alpha]_D^{23}$ +88° (*c* 1, H_2O); *m/z* 406.3 (M^+ + 1); Calcd for $C_{17}H_{35}N_5O_6$: *m/z* 405.3 for M^+; ^{1}H NMR (26% ND_3 in D_2O): δ 1.19 (q, 1 H, H-2*ax*), 1.35 (m, 1 H, H-4′*ax*), 1.57 (dq, 1 H, H-3′*ax*), 1.66–1.73 (m, 2 H, H-3′*eq*,4′*eq*), 1.92 (dt, 1 H, H-2*eq*), 2.56 (dd, 1 H, H-4″*ax*), 2.59 (dd, 1 H, H-6′a), 2.63 (dd, 1 H, H-6′b), 2.77–2.85 (m, 5 H, H-1,3,2′,2″*ax*,4″*eq*), 2.94 (d, 1 H, H-2″*eq*), 3.26 (t, 2 H, H-4,6), 3.48 (dd, 1 H, H-6″a), 3.53 (dd, 1 H, H-6″b), 3.58 (t, 1 H, H-5), 3.80 (m, 1 H, H-5′), 4.18 (m, 1 H, H-5″), 4.97 (br s, 1 H, H-1″), 5.08 (d, 1 H, H-1′); $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 12.5, $J_{1,2eq} \approx J_{2eq,3}$ 4, $J_{3,4} \approx J_{4,5} \approx J_{5,6} \approx J_{1,6}$ 9.5, $J_{1',2'}$ 4, $J_{2',3'ax} \approx J_{3'ax,3'eq} \approx J_{3'ax,4'ax}$ 12.5, $J_{3'ax,4'eq}$ 4, $J_{4'ax,5'}$ 12, $J_{4'eq,5'}$ 2, $J_{5',6'a}$ 7, $J_{5',6'b}$ 5, $J_{6'a,6'b}$ 13, $J_{1'',2''ax} \sim 2$, $J_{1'',2''eq} \sim 0$, $J_{2''ax,2''eq} \approx J_{4''ax,4''eq}$ 13, $J_{4''ax,5}$ 11, $J_{4''eq,5''}$ 3, $J_{5'',6''a}$ 6, $J_{5'',6''b}$ 4, $J_{6''a,6''b}$ 12 Hz. Anal. Calcd for $C_{17}H_{35}N_5O_6 \cdot 1/2H_2CO_3 \cdot H_2O$: C, 46.24; H, 8.43; N, 15.41. Found: C, 46.47; H, 8.27; N, 15.59.

*3′,4′-Dideoxy-6-O-[(1*S*)-2-hydroxy-1-[2-hydroxy-1-(hydroxymethyl)ethoxy]ethyl]-1,3,2′,6′-tetra-*N*-tosylneamine* (**20**).—To a solution of Solid A (see **8**, 800 mg, ~ 0.77 mmol) in MeOH (12 mL), $NaBH_4$ (580 mg, 15 mmol) was added, and the solution was kept for 18 h at room temperature. Acetone (4.5 mL) was added and, after 3 h, the mixture was poured into water (150 mL), and the resulting precipitate was filtered off, washed with water, and dried. In TLC (5:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3), the solid showed a major spot at R_f 0.65 (**20**) accompanied by several minor ones, most of which show tailing in shape, although some of them had the same R_f values as those for **8**). Chromatography (8:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3) of the solid gave **20** as a solid (359 mg, 44% based on **7**), $[\alpha]_D^{20}$ +24° (*c* 1, $CHCl_3$); ^{1}H NMR (pyridine-d_5): δ 1.58–1.79 (m, 3 H, H-2*ax*,4′*ax*,4′*eq*), 1.85 (m, 1 H, H-3′*ax*), 2.17 and 2.28 [each s of 6 H, 4 Ts(Me)], 2.19 (m, 1 H, H-3*eq*), 2.57 (dt, 1 H, H-2*eq*), 3.28–3.45 [m, H-3(or 1),6′a,6′b], 3.62–3.93 [m, 5 H, H-1(or 3),4,5,6,2′], 3.96 (d, 2 H, *J* 5.5 Hz, H-6″a,6″b or H-4″a,4″b), 4.05 (d, 2 H, *J* 5.5 Hz, H-4″a,4″b or H-6″a,6″b), 4.13 (m, 2 H, H-2″a,2″b), 4.39 (m, 1 H, H-5″), 4.84 (m, 1 H, H-5′), 5.54 (t, 1 H, *J* 5.5 Hz, H-1″), 5.61 (d, 1 H, *J* 3 Hz, H-1′). Anal. Calcd for $C_{45}H_{60}N_4O_{16}S_4 \cdot H_2O$: C, 51.02; H, 5.90; N, 5.29; S, 12.11. Found: C, 51.04; H, 5.99; N, 5.24; S, 12.21.

*3′,4′-Dideoxy-6-O-[(1*S*)-2-hydroxy-1-[2-hydroxy-1-(hydroxymethyl)ethoxy]ethyl]neamine* (**21**).—Compound **20** (193 mg) was detosylated as described for **10** and, after resin chromatography (Dowex 50W-X2, NH_4^+ form, aq 0.5 → 0.75 M NH_3), the ninhydrin-positive fractions were collected and concentrated. An aq solution of the residue was chromatographed with CM Sephadex C-25 with aq 0 → 0.15 M NH_3 to give **21** as a solid (36.1 mg, 38% as $1.5H_2CO_3$ salt) along with DDNA (18 mg), **21**, TLC: R_f 0.55 (1:4:3 $CHCl_3$–MeOH–aq 17% NH_3), $[\alpha]_D^{22}$ +35° (*c* 1, H_2O); ^{1}H NMR (26% ND_3 in D_2O): δ 1.23 (q, 1 H, H-2*ax*), 1.39 (dq, 1 H,

H-4′*ax*), 1.62 (dq, 1 H, H-3′*ax*) 1.69–1.78 (m, 2 H, H-3′*eq*,4′*eq*), 1.98 (dt, 1 H, H-2*eq*), 2.63 and 2.67 (each dd of 1 H, H-6′a,6′b), 2.78–2.88 (m, 3 H, H-1,3,2′), 3.28 (t, 1 H, H-4), 3.31 (t, 1 H, H-6), 3.58 (t, 1 H, H-5), 3.59 (dd, 1 H, H-2″a), 3.62 (dd, 1 H, H-2″b), 3.64–3.72 (m, 4 H, H-4″a,4″b,6″a,6″b), 3.84 (m, 1 H, H-5′), 3.98 (m, 1 H, H-5″), 4.97 (t, 1 H, H-1″), 5.09 (d, 1 H, H-1′); $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 12, $J_{1,2eq} \approx J_{2eq,3}$ 4, $J_{3,4} \approx J_{4,5} \approx J_{5,6} \approx J_{6,1}$ 9, $J_{1',2'}$ 4, $J_{2',3'ax} \approx J_{3'ax,3'eq} \approx J_{3'ax,4'ax} \approx J_{4'ax,4'eq} \approx J_{4'ax,5'}$ 12, $J_{3'ax,4'eq} \approx J_{3'eq,4'ax}$ 4, $J_{5',6'a}$ 7, $J_{5',6'b}$ 4.4, $J_{6'a,6'b}$ 13, $J_{1'',2''a} \approx J_{1'',2''b}$ 5, $J_{2''a,2''b}$ 12. Anal. Calcd for $C_{17}H_{36}N_4O_8 \cdot 1.5H_2CO_3$: C, 42.93; H,7.56; N, 10.83. Found: C, 42.90; H, 7.18; N, 10.84.

4″,6″-O-*Benzylidene-1,3,2′,6′-tetra*-N-*tosyl-3″*-N-*trifluoroacetyldibekacin* (**22**).—To a solution of **7** (3.21 g, 3.0 mmol) in DMF (30 mL), CF_3CO_2Et (1.05 mL, 8.8 mmol; 0.65 mL initially, and 0.2 mL each after 1.5 and 3 h) was added, and the solution was kept for 4.5 h at room temperature. Excess reagent and the solvent were evaporated in vacuo with toluene to give a syrup (~ 4.5 g), which showed, in TLC (5:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3), a single spot at R_f 0.3 (*cf* **7**: R_f 0.15). A mixture of the syrup, $PhCH(OMe)_2$ (1.35 mL, 9.0 mmol initially, and 0.23 mL after 3 h), and anhydrous TsOH (260 mg, 1.5 mmol) in DMF (30 mL) was kept for 5 h at 60 °C, poured into aq $NaHCO_3$ (saturated, 500 mL), and the resulting precipitate was collected and washed thoroughly with water. A solution of the solid in $CHCl_3$ was further washed with water, dried (Na_2SO_4), and concentrated to give **22** as a solid (3.76 g, quant.), TLC (with the same solvent system as described above): R_f 0.5, $[\alpha]_D^{23}$ +49° (*c* 1, $CHCl_3$); ^{1}H NMR (pyridine-d_5): δ 1.52–1.90 (m, 4 H, H-2*ax*,3′*ax*,4′*ax*,4′*eq*), 2.15, 2.17, 2.31, and 2.36 [each s of 3 H, 4 Ts(Me)], 2.25 (m, 1 H, H-3′*eq*), 2.67 (m, 1 H, H-2*eq*), 2.82 (t, 1 H, H-3 or 1), 3.17 (m, 1 H, H-5), 3.40–3.78 [m, 6 H, H-1(or 3),4,6,2′,6′a,6′b], 3.84 (t, 1 H, H-6″a), 4.12 (t, 1 H, H-4″), 4.46 (m, 1 H, H-5″), 4.65 (m, 1 H, H-2″), 4.83 (dd, 1 H, H-6″b), ~ 5.0 (m, 2 H, H-5′,3″), 5.40 (d, 1 H, H-1″), 5.59 (d, 1 H, H-1′), 5.66 (d, 1 H, HO-5), 5.70 (s, 1 H, PhC*H*), 8.34 (t, 1 H, TsN*H*-6′), 8.69 (d, 1 H, TsN*H*-2′), 9.18 (d, 1 H, TsN*H*-1 or 3), 9.37 (d, 1 H, HO-2″), 10.85 (d, 1 H, N*H*COCF$_3$). Anal. Calcd for $C_{55}H_{64}F_3N_5O_{17}S_4$: C, 52.74; H, 5.15; N, 5.59; S, 10.24. Found: C, 53.10; H, 5.28; N, 5.29; S, 9.88.

4″,6″-O-*Benzylidene-1,3,2′,6′-tetra*-N-*tosyldibekacin* (**23**).—A suspended mixture of **22** (1.25 g, 1.0 mmol) and K_2CO_3 (1.1 g, 1.0 mmol) in 4.5:1 MeOH–H_2O (22 mL) was stirred at 60 °C. The clear solution that resulted after 15 min was poured into water (200 mL), and the resultant precipitate was filtered off, washed with water, and dried. To the mass, pyridine (50 mL) was added, and after removal of a small insoluble residue by filtration, the solution was concentrated to dryness to give **23** as a solid (1.09 g, 95%), which was ninhydrin-positive, TLC (5:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3): R_f 0.55, $[\alpha]_D^{24}$ +23° (*c* 0.5, pyridine); ^{1}H NMR (pyridine-d_5): δ 1.62 (q, 1 H, H-2*ax*), 1.66–1.83 (m, 3 H, H-3′a,4′a,4′b), 2.16, 2.18, 2.28, 2.34 [each s of 3 H, 4 Ts(Me)], 2.26 (m, 1 H, H-3′b), 2.70 (dt, 1 H, H-2*eq*), 2.95 (m, 1 H, H-3 or 1), 3.32 (t, 1 H, H-5), 3.41–3.49 (m, 2 H, H-6′a,6′b), 3.51 (t, 1 H, H-3″), 3.58 (t, 1 H, H-4 or 6), 3.61 (t, 1 H, H-4″), 3.64–3.72 [m, 2 H, H-1 (or 3),2′], 3.71 (t, 1 H, H-6 or 4), 3.83 (t, 1 H, H-6″a), 3.98 (dd, 1 H, H-2″), 4.25 (dt, 1 H, H-5″), 4.72 (dd, 1 H, H-6″b), 4.98 (m, 1 H, H-5′), 5.21 (d, 1 H, H-1″), 5.58 (d, 1 H, H-1′), 5.72 (s, 1 H, PhC*H*), 8.30 (br s, 1 H, TsN*H*-6′), 8.55 (br s, 1 H, TsN*H*-2′), 9.09 (d, 1 H, TsN*H*-1 or 3); $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 13,

$J_{1,2eq} \approx J_{2eq,3}$ 4, $J_{3,4} \approx J_{4,5} \approx J_{5,6}$ 9.5, $J_{1',2'}$ 3, $J_{1'',2''}$ 4, $J_{2'',3''} \approx J_{3'',4''}$ 9.5, $J_{4'',5''}$ 10, $J_{5'',6''a} \approx J_{6''a,6''b}$ 10, $J_{5'',6''b}$ 4.5 Hz. Anal. Calcd for $C_{53}H_{65}N_5O_{16}S_4$: C, 55.05; H, 5.67; N, 6.06; S, 11.09. Found: C, 54.92; H, 5.82; N, 5.78; S, 10.85.

3',4'-Dideoxy-6-O-[(1S)-2-hydroxy-1-[(1R,2S)-3-amino-1a,2-O-benzylidene-2-hydroxy-1-(1a-hydroxymethyl)propoxy]ethyl]-1,3,2',6'-tetra-N-tosylneamine (**24**).—To a solution of **23** (580 mg, 0.50 mmol) in pyridine (10 mL), $Pb(OAc)_4$ (266 mg, 0.6 mmol) was added, and the solution was kept for 3.5 h at room temperature. In TLC (8:1:0.1 $CHCl_3$–MeOH–aq 28% NH_3), the solution showed a clear spot at the top with several minor spots (cf. **23**: R_f 0.25). To the clear solution, $NaBH_4$ (565 mg, 15 mmol) was added, and the black solution was kept for 1 h. Acetone (5.5 mL) was added, and after 30 min, the mixture was concentrated. To the residue, water (150 mL) was added, and after shaking vigorously for a while, the mixture was filtered with the aid of Celite. The whole mass obtained by filtration, after dryness in vacuo, was extracted with MeOH. In TLC, the solution showed a major spot (**24**, R_f 0.3) together with several minor spots. Concentration gave a residue, which was dissolved in 20:1 MeOH–H_2O and charged on a column of Dowex 50W-X2 (NH_4^+ form, 10 mL). Development with 9:1 MeOH–aq 14% NH_3 gave **24** as a solid (153 mg, 26%), $[\alpha]_D^{23}$ −5° (*c* 1, MeOH); *m/z* 1158.0 (M^+ + 1); Calcd for $C_{53}H_{67}N_5O_{15}S_4$: *m/z* 1157.35 for M^+; ^{1}H NMR (pyridine-d_5): δ 1.57 (q, 1 H, H-2*ax*), 1.62–1.85 (m, 3 H, H-3'*ax*,4'*ax*,4'*eq*), 2.20 (m, 1 H, H-3'*eq*), 2.11, 2.17, 2.24, and 2.29 [each s of 3 H, 4 Ts(Me)], 2.56 (m, 1 H, H-2*eq*), 3.17 (m, 1 H, H-1 or 3), 3.21 (dd, 1 H, H-3''a), 3.31 (br d, 1 H, H-3''b), 3.39 (dd, 1 H, H-6'a), 3.46 (dd, 1 H, H-6'b), 3.52–3.58 (m, 2 H, H-4,6), 3.60 (dt, 1 H, H-2'), 3.65–3.74 [m, 3 H, H-3(or 1),5,6''a], 3.81 (m, 1 H, H-4''), 3.87 (dd, 1 H, H-2''a), 3.98 (dd, 1 H, H-2''b), 4.51 (dd, 1 H, H-6''b), 4.92 (dt, 1 H, H-5''), 5.01 (m, 1 H, H-5'), 5.11 (dd, 1 H, H-1''), 5.56 (d, 1 H, H-1'), 5.68 (s, 1 H, PhC*H*); $J_{1'',2''a}$ 7, $J_{1'',2''b}$ 3, $J_{2''a,2''b}$ 11, $J_{3''a,3''b}$ 12, $J_{3''a,4''}$ 3, $J_{3''b,4''}$ ~ 0, $J_{4'',5''}$ 9, $J_{5'',6''a}$ ~ 9, $J_{5'',6''b}$ 5, $J_{6''a,6''b}$ 10 Hz. ^{13}C NMR (pyridine-d_5): d 21.16 (2 C), 21.22 and 21.31 [4 Ts(*C*H_3)], 25.71 (C-3'), 27.81 (C-4'), 36.41 (C-2), 40.62 (C-3''), 47.79 (C-6'), 53.28 (C-3 or 1), 53.52 (C-1 or 3), 53.84 (C-2'), 65.29 (C-2''), 67.59 (C-5'), 67.98 (C-5''), 70.17 (C-6''), 76.65 (C-6), 80.10 (C-4''), 81.77 (C-5), 82.84 (C-4), 99.93 (C-1'), 101.60 (Ph*C*H), 106.68 (C-1''). Anal. Calcd for $C_{53}H_{67}N_5O_{16}S_4$: C, 54.95; H, 5.83; N, 6.05; S, 11.07. Found: C, 54.87; H, 6.19; N, 5.73; S, 10.63.

3',4'-Dideoxy-6-O-[(1S)-2-hydroxy-1-[(1R,2S)-3-amino-2-hydroxy-1-(hydroxymethyl)propoxy]ethyl]neamine (**25**).—To a solution of **24** (424 mg, 0.37 mmol) in liquid NH_3 (~ 20 mL) at −55 °C, Na (~ 100 mg) was added, and the solution was kept for 15 min at the same temperature. After work-up as described for **10**, the crude products were roughly separated by resin chromatography (Dowex 50W-X2, NH_4^+ form, 10 mL) with aq 0.5 → 1 M NH_3 to give fraction 1 containing products of R_f 0.2 (major, DDNA), 0.38, and 0.65 in TLC (1:4:3 $CHCl_3$–MeOH–aq 28% NH_3), and fraction 2 containing products of R_f 0.13 (**25**), 0.3, and 0.6. The fraction 2 was concentrated and the residue was chromatographed with CM Sephadex C-25 (NH_4^+ form, 20 mL) with aq 0.2 → 0.3 M NH_3 (changed linearly) to give **25** as a solid (50.0 mg, 27%), $[\alpha]_D^{23}$ +33° (*c*1, H_2O); ^{1}H NMR (26% ND_3 in D_2O): δ 1.23 (q, 1 H, H-2*ax*), 1.39 (dq, 1 H, H-4'*ax*), 1.62 (dq, 1 H, H-3'*ax*), 1.73 (m, 1 H, H-4'*eq*), 1.76 (m, 1 H, H-3'*eq*), 1.98 (dt, 1 H, H-2*eq*), 2.63 (dd, 1 H, H-6'a), 2.67 (dd, 1 H, H-6'b), 2.72 (dd, 1 H, H-3''a), 2.75–2.83 (m, 2 H, H-1,3), 2.79 (dd, 1 H, H-3''b), 2.86 (dt, 1 H, H-2'), 3.27 (t, 2 H,

H-4,6), 3.59 (t, 1 H, H-5), 3.62–3.68 (m, 3 H, H-2″a,2″b,6″a), 3.74 (dd, 1 H, H-6″b), 3.77 (m, 1 H, H-4″), 3.84 (m, 1 H, H-5′), 4.01 (m, 1 H, H-5″), 4.98 (t, 1 H, H-1″), 5.09 (d, 1 H, H-1′); $J_{1,2ax} \approx J_{2ax,2eq} \approx J_{2ax,3}$ 12, $J_{1,2eq} \approx J_{2eq,3}$ 4, $J_{3,4} \approx J_{4,5} \approx J_{5,6} \approx J_{6,1}$ 9, $J_{1',2'}$ 4, $J_{2',3'ax}$ 12, $J_{2',3'eq}$ 4, $J_{1'',2''a} \approx J_{1'',2''b}$ 4.5, $J_{3''a,3''b}$ 13, $J_{3''a,4''}$ 7, $J_{3''b,4''}$ 4, $J_{4'',5''} \approx J_{5'',6''a}$ 6, $J_{5'',6''b}$ 4, $J_{6''a,6''b}$ 12 Hz. Anal. Calcd for $C_{18}H_{39}N_5O_8 \cdot H_2CO_3$: C, 44.26; H, 8.02; N, 13.58. Found: C, 44.46; H, 7.78; N, 13.25.

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