ethanol) [lit. $[\alpha]_D$ −128° (c 1.79, ethanol)].

Deuteriated Compounds. The ^1H NMR of some of the deuteriated intermediates have already been discussed.[1] Key differences in ^1H NMR signals from the undeuteriated to the deuteriated compounds are as follows: **1b** (R = ^2H, R′ = H), δ 2.20 (dd, J = 16, 7 Hz) has disappeared, and δ 2.80 (dd J = 16, 8 Hz) is a broad doublet (J = 8 Hz); **1c** (R = H, R′ = ^2H), δ 2.80 (dd, J = 16, 8 Hz) has disappeared, and δ 2.20 (dd, J = 16, 7 Hz) is a broad singlet; **4** (R = ^2H), δ 2.80 (dd J = 19, 12 Hz) has disappeared, and δ 1.35 (dd J = 19, 3 Hz) has become a broad singlet; **5** (R = ^2H), δ 2.69 (dd, J = 19, 12 Hz) has disappeared and δ 1.30 (dd, J = 19, 3 Hz) is a broad singlet; **6** (R = ^2H, R′ = H) and **6** (R = H, R′ = ^2H), δ 2.62 (m) has reduced intensity and is a broad singlet; **7** (R = ^2H, R′ = H) and **7** (R = H, R′ = ^2H), δ 2.15 (dd J = 9, 3 Hz) has disappeared, and δ 2.75 (dd, J = 9, 3 Hz) is a broad singlet; **11** (R = ^2H), δ 1.86 (m) has become reduced and converted into a broad doublet (J = 8 Hz).

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An Alternative Total Synthetic Approach toward Octosyl Acid A

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The naturally occurring nucleoside octosyl acid A (1) has been synthesized as its dimethyl ester, 2. Nitrooctose 5, prepared by a Henry reaction of the 5-nitro-D-ribose 3 with 2,3-*O*-isopropylidene-D-glyceraldehyde (4), has been converted to octosyl acid A dimethyl ester (2) by the following sequence: deoxygenation at C-6, interconversion of the 5-nitro group into an oxygen function, glycosylation with a uracil base, intramolecular cyclization to a bicyclic 3′,7′-anhydride, oxidation to obtain a carboxyl function at C-8′, and epimerization to the natural configuration at C-7′. Since 2 has already appeared in a total synthesis of octosyl acid A by the Danishefsky group, a formal total synthesis of the acid has been accomplished.

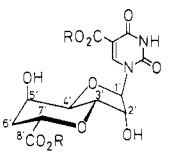
The octosyl acids were isolated from the culture filtrates of *Streptomyces cacaoi* var. *asoensis*. Although octosyl acid A itself does not possess any biological activity, its adenine analogue, readily obtained by transglycosylation, was shown to be an inhibitor of cyclic-AMP phosphodiesterase.[1] The structures were clarified as shown in Chart I by Isono et al.[2] A 3,7-anhydrooctofuranose skelton, a furanose to which a pyrane ring is trans-fused, is also found in the antifungal ezomycins.[3] Because of their unique structures, various synthetic approaches have been carried out and total synthesis of octosyl acid A has been reported by two groups.[4,5]

In our laboratory, a general synthesis of higher carbon carbohydrates has been developed by use of a fluoride anion catalyzed Henry reaction between a nitro sugar and a sugar aldehyde. We have reported syntheses of tunicamycins[6] and ezomycines[7] using this methodology. The present article describes a synthesis of octosyl acid A.

Results and Discussion

Octose construction was carried out by condensation of a C_5-nitrosugar and a C_3-aldehyde. A Henry reaction between 5-deoxy-1,2-*O*-isopropylidene-3-*O*-[(methylthio)-methyl]-5-nitro-α-D-ribofuranose (**3**)[7a,8] and 2,3-*O*-isopropylidene-D-glyceraldehyde (**4**) gave a diastereoisomeric mixture of 5-deoxy-5-nitrooctofuranose **5** in the presence of potassium fluoride–tetrabutylammonium iodide in toluene (Scheme I). Acetylation of **5** with acetic anhydride and pyridine, in the presence of 4-(dimethylamino)-pyridine, and successive treatment with sodium borohydride resulted in elimination of acetic acid to afford 45% (based on **3**) of the 6-deoxygenated compounds **6a** and **6b** as a diastereomeric mixture. The nitro group of the

Chart I



1: R = H
2: R = CH_3

mixture was hydrogenated with Raney nickel to give a single amino sugar **7** in 70% yield. Conversion of the amino group to a keto function was performed by Corey's method.[9] Thus, condensation of **7** with 3,5-di-*tert*-butyl-1,2-benzoquinone and subsequent hydrolysis of the resultant imine with oxalic acid afforded the ketone **8** in 65% yield. Other methods[10] for transforming **7** to **8** failed.

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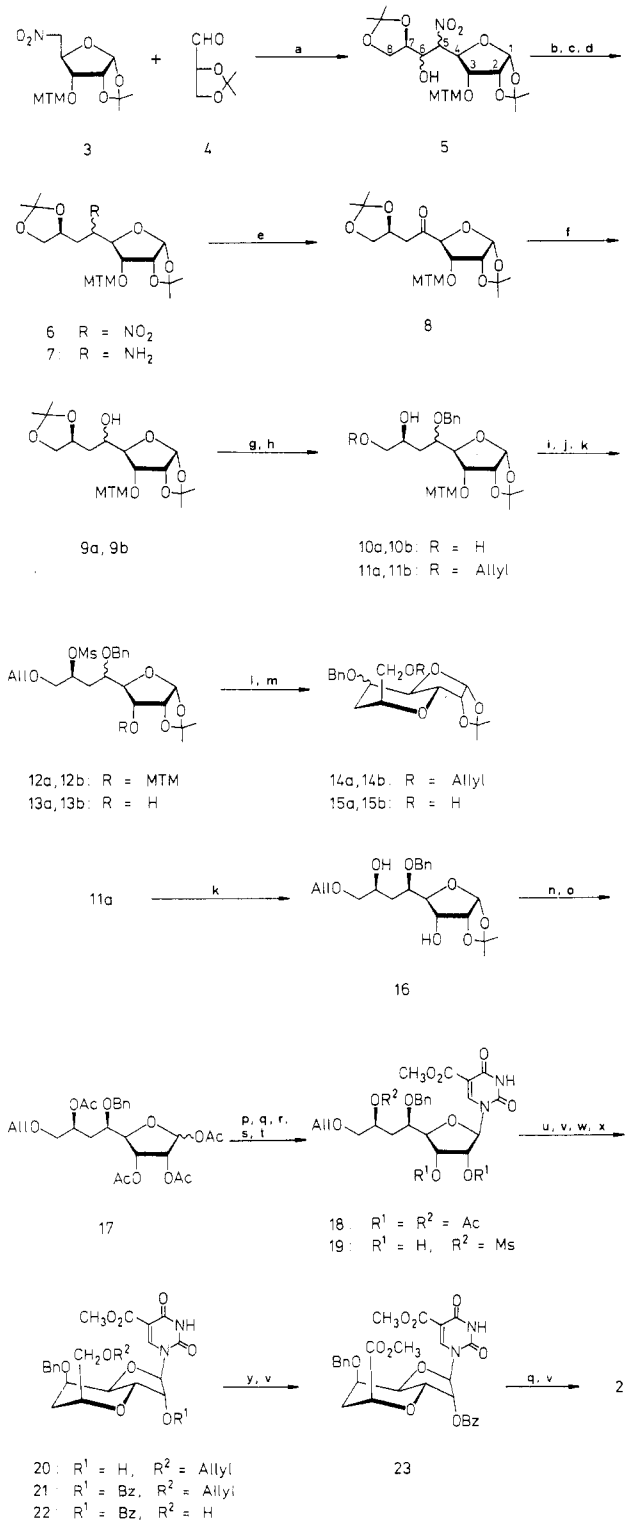
Scheme I[a]



[a] (a) KF, *n*-Bu_4NI in toluene; (b) Ac_2O, C_5H_5N, DMAP; (c) $NaBH_4$ (45% from **3**); (d) H_2, Raney Ni (70%); (e) 3,5-di-*tert*-butylbenzoquinone, then $(COOH)_2$ (66%); (f) $NaBH_4$ (**9a**, 55%; **9b** 32%); (g) $C_6H_5CH_2Br$, NaH, DMF; (h) aqueous HOAc (100%); (i) CH_2=$CHCH_2Br$, NaH, THF (**11a**, 72%; **11b**, 86%); (j) MsCl, C_5H_5N (**12a**, 99%; **12b**, 100%); (k) MeI, $NaHCO_3$, aqueous acetone; (l) NaH, DMF (**14a**, 89%; **14b**, 71%); (m) SeO_2, dioxane–HOAc (**15a**, 74%; **15b**, 91%); (n) 60% aqueous HOAc; (o) Ac_2O, C_5H_5N (96%, **17a**:**17b** = 1.3:1); (p) $Me_3SiOSO_2CF_3$, methyl 2,4-bis(trimethylsilyl)pyrimidine-5-carboxylate (80%); (q) NaOMe, MeOH; (r) 2,2-dimethoxypropane, TsOH, DMF; (s) MsCl, C_5H_5N; (t) aqueous CF_3CO_2H (81%); (u) NaH, DMSO; (v) MeOH, HCl (45%); (w) C_6H_5COCl, C_5H_5N (86%); (x) SeO_2, HOAc (86%); (y) CrO_3, acetone.

Reduction of **8** with sodium borohydride gave a diastereomeric mixture, which was readily separable by a silica gel column chromatography to give **9a** (55%) and **9b** (32%).

Both isomers were transformed to the bicyclic compounds **15a** and **15b** in order to establish the stereochemistry of the new chiral center introduced at C-5. O-Benzylation of **9a** with benzyl bromide and sodium hydride in *N*,*N*-dimethylformamide (DMF) and successive removal of the 7,8-*O*-isopropylidene group with aqueous acetic acid yielded the glycol **10a** quantitatively. Preferential O-allylation of the primary 8-OH in **10a** with allyl bromide and sodium hydride in tetrahydrofuran (THF) gave the allyl ether **11a** in 72% yield. O-Mesylation of **11a** with mesyl chloride in pyridine afforded the mesylate **12a** quantitatively. Deprotection of the (methylthio)methyl group with iodomethane in the presence of sodium hydrogen carbonate in aqueous acetone[11] provided **13a** (50% yield), a substrate for an intramolecular etheration. Compound **13a** was treated with sodium hydride in DMF to afford the 3,7-anhydride **14a** as expected in 77% yield. Removal of the allyl group of **14a** with selenium dioxide in dioxane containing acetic acid[12] gave alcohol **15a** in 74% yield. Compound **15b** could similarly be derived from **9b**. The ^1H NMR spectra of **15a** and **15b** showed $J_{4,5}$ to be 2.5 Hz and 9.5 Hz, respectively, indicative of the ae and aa couplings. Since the $J_{4',5'}$ value of natural octosyl acid A was 2.5 Hz, the C-5 configuration of **15a** was shown to correspond to that on C-5′ of the natural product.

Simultaneous removal of the 1,2,3-O-protective groups in **11a** under the acidic conditions[7c] gave **16** in poor yield. Therefore, the 3-*O*-(methylthio)methyl group of **11a** was first removed as mentioned above to afford **16** in 80% yield. Next the 1,2-*O*-isopropylidene group was removed with acetic acid and conventional acetylation then gave the tetraacetates **17a** and **17b** as an anomeric mixture in 96% yield. The intact anomeric mixture was directly glycosylated with methyl 2,4-bis(trimethylsilyl)uracil-5-carboxylate in the presence of trimethylsilyl trifluoromethanesulfonate in 1,2-dichloroethane[13] to give the β-glycoside **18** in 80% yield. O-Deacetylation of **18** with methanolic sodium methoxide, O-isopropylidenation with 2,2-dimethoxypropane and *p*-toluenesulfonic acid in DMF, 7′-O-mesylation, and de-O-isopropylidenation with aqueous trifluoroacetic acid were successively carried out to give the mesylate **19** in 81% yield from **18**. Cyclization of **19** to the 3′,7′-anhydride **20** was effected with sodium hydride in dimethyl sulfoxide (DMSO). The product contaminated with the deesterified compound was retreated with methanolic hydrogen chloride to give **20** in 45% yield based on **19**. When **19** was treated to the same conditions as used to cyclize **13a** into **14a**, **20** was obtained in a poor yield. O-Benzoylation of **20** with benzoyl chloride in pyridine gave 87% of the benzoate **21**. Removal of the allyl group with selenium dioxide afforded alcohol **22** in 77% yield. Jones' oxidation of **22** yielded the uronic acid, which was successfully esterified with methanolic hydrogen chloride to give the diester **23** in 67% yield. Treatment of **23** with sodium methoxide in boiling methanol resulted in epimerization at C-7′ and removal of all protecting groups gave the diacid, which was characterized by being reesterified with methanolic hydrogen chloride to afford diester **2** (62%), whose ^1H NMR (250 MHz) spectral data were identical with those of an authentic sample syn-

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thesized by Danishefsky et al.

Experimental Section

Melting points were determined on a Büchi 510 capillary apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-4 polarimeter. IR spectra were recorded on a Hitachi 225 spectrometer. ^{1}H NMR spectra were recorded with a Varian EM-390 (90 MHz) or a JEOL FX-200 (200 MHz) spectrometer with reference to tetramethylsilane as an internal standard. Mass spectra were recorded with a Hitachi M-80B spectrometer. Analytical TLC was performed on Merck silica gel 60 F-254 plates (Art. 5715). Spots were visualized by UV and/or spraying with 10% H_2SO_4 followed by heating on a hot plate. Column chromatography and preparative TLC were performed by using Katayama silica gel 60 (70–230 mesh) and Merck silica gel 60 F-254 plates (Art. 11798), respectively. After workup solutions were dried over anhydrous sodium sulfate and concentrated under reduced pressure below 40 °C.

5,6-Dideoxy-1,2:7,8-di-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-5-nitro-α-D-*glycero*-D-*allo* (and L-*talo*)-octofuranose-(1,4) (6a,b). To a solution of **3** (1.50 g, 5.38 mmol) in toluene (4.5 mL) were added **4** (2.10 g, 16.2 mmol), anhydrous potassium fluoride (0.38 g), and tetra-*n*-butylammonium iodide (1.11 g), and the mixture was stirred for 2 h at room temperature. The reaction mixture was diluted with ethyl acetate, and the mixture was repeatedly washed with water, dried, and concentrated. The residue was dissolved in dichloromethane (30 mL), and to the solution was added pyridine (3.5 mL), acetic anhydride (5.3 mL), and 4-(dimethylamino)pyridine (0.21 g). After 1 h at room temperature, the mixture was washed successively with aqueous sodium hydrogen carbonate and water, dried, and concentrated to a small volume. The concentrate was diluted with THF (15 mL), and sodium borohydride (0.25 g) and water (15 mL) were added with cooling. After 12 h at room temperature, the solution was deionized with Amberlite IR-120 (H^+) and then concentrated. The residue was chromatographed on a silica gel column (10:1 (v/v) toluene–ethyl acetate) to give 0.95 g (45% from **3**) of **6a,b** as a diasteromeric mixture. The intact mixture was used in the next step. Careful chromatography allowed only the faster moving component to be isolated as crystals: R_f on TLC 0.39 (4:1 (v/v) toluene–ethyl acetate); mp 119.5–120.5 °C; $[\alpha]^{21.5}_D$ +78° (*c* 0.99, $CHCl_3$); IR (KBr) 1550, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 5.73 (d, 1 H, *J* = 4 Hz, H-1), 4.78 (s, 2 H, CH_2S), 2.20 (s, 3 H, SMe), 1.53, 1.38, 1.33, 1.30 (each s, each 3 H, CMe_2 × 2). Anal. Calcd for $C_{16}H_{27}NO_8S$: C, 48.85; H, 6.92; N, 3.56. Found: C, 48.92; H, 6.76; N, 3.36.

5-Amino-5,6-dideoxy-1,2:7,8-di-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-α-D-*glycero*-D-*allo* (or L-*talo*)-octofuranose-(1,4) (7). Compound **6a,b** (1.89 g) was dissolved in ethyl acetate (19 mL) and hydrogenated in the presence of Raney nickel T-4 under pressure of 55 psi for 48 h at room temperature. After the catalyst was filtered off, the filtrate was concentrated, and the residue was chromatographed on a silica gel column (5:1 (v/v) toluene–ethanol) to afford 1.22 g (70%) of **7** as a syrup homogeneous on TLC: R_f on TLC 0.48 (10:1 (v/v) dichloromethane–methanol); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 5.71 (d, 1 H, *J* = 4 Hz, H-1), 4.79, 4.63 (each d, each 1 H, *J* = 12 Hz, SCH_2), 2.20 (s, 3 H, SMe), 1.57, 1.40, 1.35 (each s, 3, 3, and 6 H, CMe_2 × 2).

6-Deoxy-1,2:7,8-di-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-5-oxo-α-D-*glycero*-D-*ribo*-octofuranose-(1,4) (8). To a solution of **7** (1.22 g) in methanol (12 mL) was added 3,5-di-*tert*-butyl-1,2-benzoquinone (0.89 g), and the mixture was stirred for 2 h at room temperature. The mixture was concentrated to dryness, and the residue was dissolved in a mixture of THF (40 mL) and water (10 mL). The mixture was adjusted to pH 2 with oxalic acid and stirred for 4 days at ambient temperature. After the solution was concentrated, the residue was dissolved in ethyl acetate and the mixture was washed successively with aqueous sodium hydrogen carbonate and water, dried, and concentrated. The residue was chromatographed on a silica gel column (4:1 (v/v) toluene–ethyl acetate) to give 0.54 g (66%) of **8** as pale yellow crystals. Recrystallization from hexane afforded an analytical sample: R_f on TLC 0.27 (4:1 (v/v) toluene–ethyl acetate); mp 63–64.5 °C; $[\alpha]^{18.5}_D$ +84° (*c* 1.01, $CHCl_3$); IR (KBr) 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 5.82 (d, 1 H, *J* = 4 Hz, H-1), 4.81, 4.67 (each d, each 1 H, *J* = 12 Hz, CH_2S), 3.10 (dd, 1 H, *J* = 6, 18 Hz, H-6), 2.73 (dd, 1 H, *J* = 7.5, 18 Hz, H-6), 2.15 (s, 3 H, SMe), 1.57, 1.39, 1.37, 1.33 (each s, each 3 H, CMe_2 × 2). Anal. Calcd for $C_{16}H_{26}O_7S$: C, 53.02; H, 7.23. Found: C, 53.06; H, 7.08.

6-Deoxy-1,2:7,8-di-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-α-D-*glycero*-D-*allo*-octofuranose-(1,4) (9a) and 6-Deoxy-1,2:7,8-di-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-α-D-*glycero*-L-*talo*-octofuranose-(1,4) (9b). To a solution of **8** (0.116 g) in a mixture of THF (1.2 mL) and water (1.2 mL) was added sodium borohydride (18 mg) under ice cooling. After 0.5 h the mixture was concentrated and the residue was partitioned between ethyl acetate and water. The organic layer was washed twice with water, dried, and concentrated. The residue was chromatographed on a silica gel column (2:1 (v/v) toluene–ethyl acetate) to give 0.063 g (55%) of **9a** and 0.037 g (32%) of **9b**. Recrystallization of **9b** from hexane afforded an analytical sample.

9a: R_f on TLC 0.31 (2:1 (v/v) toluene–ethyl acetate); $[\alpha]^{22}_D$ +149° (*c* 0.69, $CHCl_3$); IR ($CHCl_3$) 3520 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 5.79 (d, 1 H, *J* = 4 Hz, H-1), 4.89, 4.72 (each d, each 1 H, *J* = 11 Hz, CH_2S), 2.97 (br s, 1 H, OH), 2.21 (s, 3 H, SMe), 1.82 (t, 2 H, *J* = 6 Hz, H_2-6), 1.57, 1.42, 1.36 (each s, 3, 3, and 6 H, CMe_2 × 2). Anal. Calcd for $C_{16}H_{28}O_7S$: C, 52.73; H, 7.74. Found: C, 52.82; H, 7.67.

9b: R_f on TLC 0.22 (2:1 (v/v) toluene–ethyl acetate); mp 67.5–68 °C; $[\alpha]^{21}_D$ +146° (*c* 0.74, $CHCl_3$); IR ($CHCl_3$) 3570 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 5.78 (d, 1 H, *J* = 4 Hz, H-1), 4.79 (s, 2 H, CH_2S), 2.20 (s, 3 H, SMe), 1.83 (t, 2 H, *J* = 6 Hz, H_2-6), 1.57, 1.40, 1.36 (each s, 3, 3, and 6 H, CMe_2 × 2). Anal. Calcd for $C_{16}H_{28}O_7S$: C, 52.73; H, 7.74. Found: C, 52.92; H, 7.53.

5-*O*-Benzyl-6-deoxy-1,2-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-α-D-*glycero*-D-*allo*-octofuranose-(1,4) (10a) and 5-*O*-Benzyl-6-deoxy-1,2-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-β-D-*glycero*-L-*talo*-octofuranose-(1,4) (10b). To a solution of **9a** (1.66 g) in anhydrous DMF (17 mL) were added sodium hydride (60% dispersion in mineral oil, 274 mg) and benzyl bromide (0.704 mL) under ice cooling, and the mixture was stirred for 1 h under ice cooling. After addition of a small amount of methanol, the mixture was dissolved in ethyl acetate, and the solution was repeatedly washed with water. The organic layer was dried and concentrated. The residue was dissolved in 70% aqueous acetic acid (33 mL), and the solution was allowed to stand for 4 h at room temperature. The mixture was coevaporated with toluene, and the residue was chromatographed on a silica gel column (1:1 (v/v) toluene–ethyl acetate) to give 1.86 g (98% from **9a**) of **10a** as a syrup.

Compound **10b** (123 mg) could similarly be obtained from **9b** (134 mg) as crystals in a quantitative yield.

10a: R_f on TLC 0.14 (1:1 (v/v) toluene–ethyl acetate); $[\alpha]^{26}_D$ +121° (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 3490 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.34 (s, 5 H, Ph), 5.72 (d, 1 H, *J* = 4.5 Hz, H-1), 2.15 (s, 3 H, SCH_3), 1.55, 1.34 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{20}H_{30}O_7S$: C, 57.96; H, 7.30. Found: C, 57.80; H, 7.23.

10b: R_f on TLC 0.44 (ethyl acetate); mp 96–97 °C; $[\alpha]^{22}_D$ +71° (*c* 1.15, $CHCl_3$); IR (KBr) 3480 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.37 (s, 5 H, Ph), 5.81 (d, 1 H, *J* = 4 Hz, H-1), 4.70, 4.67 (each s, each 2 H, CH_2S, CH_2Ph), 2.17 (s, 3 H, SMe), 1.76 (t, 2 H, *J* = 6 Hz, H-6), 1.56, 1.34 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{20}H_{30}O_7S$: C, 57.96; H, 7.30. Found: C, 58.28; H, 7.27.

8-*O*-Allyl-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-α-D-*glycero*-D-*allo*-octofuranose-(1,4) (11a) and 8-*O*-Allyl-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-3-*O*-[(methylthio)methyl]-α-D-*glycero*-L-*talo*-octofuranose-(1,4) (11b). To a solution of **10a** (1.86 g, 4.5 mmol) in anhydrous THF (19 mL) was added sodium hydride (60% dispersion in mineral oil, 0.35 g) and allyl bromide (0.42 mL, 4.9 mmol) under ice cooling, and the mixture was stirred for 36 h at 5 °C. After addition of a small amount of methanol, the solution was concentrated, and the residue was dissolved in dichloromethane. The solution was washed with water, dried, and concentrated, and the residue was chromatographed on a silica gel column (2:1 (v/v) toluene–ethyl acetate) to give 1.08 g (72%, based on **10a** consumed) of **11a** as a syrup, and 0.49 g of **10a** was recovered.

Compound **11b** (1.15 g) could similarly be obtained from **10b** (1.73 g) as a syrup in 86% (based on **10b** consumed) yield, and 0.51 g of **10b** was recovered.

11a: R_f on TLC 0.48 (2:1 (v/v) toluene–ethyl acetate); $[\alpha]^{23}_D$ +112° (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) 3500 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.33 (s, 5 H, Ph), 5.95 (m, 1 H, allylic), 5.74 (d, 1 H, *J* = 3.5 Hz, H-1), 5.21 (m, 2 H, allylic), 3.26 (d, 2 H, *J* = 5 Hz, H-8), 2.95 (br d, 1 H, *J* = 2.5 Hz, OH), 2.13 (s, 3 H, SMe), 1.73 (m, 2 H, H-6), 1.54, 1.33 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{23}H_{34}O_7S$: C, 60.78; H, 7.54. Found: C, 60.91, H, 7.47.

11b: R_f on TLC 0.40 (2:1 (v/v) toluene–ethyl acetate); $[\alpha]^{22}_D$ +85° (*c* 0.67, $CHCl_3$); IR ($CHCl_3$) 3570 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.37 (s, 5 H, Ph), 5.80 (d, 1 H, *J* = 4 Hz, H-1), 5.25 (m, 2 H, allylic), 4.73, 4.67 (each s, each 2 H, CH_2S, CH_2Ph), 1.55, 1.34 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{23}H_{34}O_7S$: C, 60.77; H, 7.54. Found: C, 60.98; H, 7.53.

8-*O*-Allyl-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-7-*O*-(methylsulfonyl)-3-*O*-[(methylthio)methyl]-α-D-*glycero*-D-*allo*-octofuranose-(1,4) (12a) and 8-*O*-Allyl-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-7-*O*-(methylsulfonyl)-3-*O*-[(methylthio)methyl]-α-D-*glycero*-L-*talo*-octofranose-(1,4) (12b). To a solution of **11a** (147 mg) in dry pyridine (4 mL) was added mesyl chloride (50 μL) under ice cooling, and the mixture was stirred for 1 h at room temperature. After addition of a small amount of methanol, the mixture was coevaporated with toluene, and the residue was dissolved in ethyl acetate and washed three times with water. The organic layer was dried and concentrated, and the residue was chromatographed on a silica gel column (6:1 (v/v) toluene–ethyl acetate) to give 171 mg (99%) of **12a** as a syrup.

Compound **12b** (198 mg) could similarly be obtained from **11b** (168 mg) as a syrup in a quantitative yield.

12a: R_f on TLC 0.45 (toluene–ethyl acetate); $[\alpha]^{24}_D$ +124° (*c* 1.36, $CHCl_3$); IR ($CHCl_3$) 1350, 1170 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.33 (s, 5 H, Ph), 5.71 (d, 1 H, *J* = 4 Hz, H-1), 2.98 (s, 3 H, SO_2Me), 2.18 (s, 3 H, SMe), 1.57, 1.35 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{24}H_{36}O_9S_2$: C, 54.12; H, 6.81. Found: C, 54.72; H, 6.71.

12b: R_f on TLC 0.45 (3:1 (v/v) toluene–ethyl acetate); $[\alpha]^{22}_D$ +82.3° (*c* 0.72, $CHCl_3$); IR ($CHCl_3$) 1340, 1170 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.38 (m, 5 H, Ph), 5.80 (d, 1 H, *J* = 4 Hz, H-1), 5.25 (m, 2 H, allylic), 4.85, 4.70 (each d, each 1 H, *J* = 10 Hz, CH_2S), 4.73 (s, 2 H, CH_2Ph), 3.07 (s, 3 H, SO_2Me), 2.17 (s, 3 H, SMe), 1.57, 1.35 (each s, each 3 H, CMe_2).

8-*O*-Allyl-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-7-*O*-(methylsulfonyl)-α-D-*glycero*-D-*allo*-octofuranose-(1,4) (13a) and 8-*O*-Allyl-5-*O*-benzyl-6-deoxy-7-*O*-(methylsulfonyl)-α-D-*glyero*-L-*talo*-octofuranose-(1,4) (13b). To a solution of **12a** (171 mg) in 80% aqueous acetone (3.5 mL) were added sodium hydrogen carbonate (0.13 g) and methyl iodide (0.40 mL), and the mixture was heated in a sealed tube for 3 h at 75 °C. After cooling to room temperature, an insoluble material was filtered off, the filtrate was concentrated, and the residue was dissolved in ethyl acetate. The solution was repeatedly washed with water, dried, and concentrated. The residue was chromatographed on a silica gel column (3:1 (v/v) toluene–ethyl acetate) to give 66 mg (43%) of **13a** as a syrup.

Compound **13b** (137 mg) could similarly be obtained from **12b** (197 mg) in 78% yield.

13a: R_f on TLC 0.29 (2:1 (v/v) toluene–ethyl acetate); $[\alpha]^{24}_D$ +48° (*c* 1.32, $CHCl_3$); IR ($CHCl_3$) 3550, 1350, 1170 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.35 (s, 5 H, Ph), 5.75 (d, 1 H, *J* = 4 Hz, H-1), 5.22 (m, 2 H, allylic), 3.00 (s, 3 H, SO_2Me), 1.55, 1.36 (each s, each 3 H, CMe_2).

13b: R_f on TLC 0.20 (2:1 (v/v) toluene–ethyl acetate); $[\alpha]^{20}_D$ +9° (*c* 0.37, $CHCl_3$); IR ($CHCl_3$) 3570, 1340, 1170 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.36 (s, 5 H, Ph), 5.82 (d, 1 H, *J* = 4 Hz, H-1), 5.22 (m, 2 H, allylic), 3.08 (s, 3 H, SO_2Me), 1.56, 1.36 (each s, each 3 H, CMe_2).

8-*O*-Allyl-3,7-anhydro-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-L-*glycero*-D-*allo*-octofuranose-(1,4) (14a) and 8-*O*-Allyl-3,7-anhydro-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-L-*glycero*-L-*talo*-octofuranose-(1,4) (14b). To a solution of **13a** (25 mg) in anhydrous DMF (0.5 mL) was added sodium hydride (60% dispersion in mineral oil, 8.4 mg) under ice cooling, and the mixture was stirred for 1 h at room temperature. After addition of ice water, the mixture was dissolved in ethyl acetate, and the solution was thoroughly washed with water. The organic layer was dried and concentrated, and the residue was chromatographed on a silica gel column (5:1 (v/v) toluene–ethyl acetate) to afford 18 mg (89%) of **14a** as a syrup.

Compound **14b** (21 mg) could similarly be obtained from **13b** (34 mg) as a syrup in 71% yield.

14a: R_f on TLC 0.43 (2:1 (v/v) toluene–ethyl acetate); $[\alpha]^{26}_D$ −20° (*c* 0.50, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.33 (s, 5 H, Ph), 5.84 (m, 1 H, allylic), 5.82 (d, 1 H, *J* = 3.5 Hz, H-1), 5.20 (m, 2 H, allylic), 4.83, 4.63 (each d, each 1 H, *J* = 12 Hz, CH_2Ph), 2.09, 1.81 (each m, each 1 H, H-6), 1.61, 1.35 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 66.75; H, 7.35.

14b: R_f on TLC 0.49 (2:1 (v/v) toluene–ethyl acetate); $[\alpha]^{24}_D$ −37° (*c* 0.44, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.33 (m, 5 H, Ph), 5.84 (m, 1 H, allylic), 5.82 (d, 1 H, *J* = 4 Hz, H-1), 5.20 (m, 2 H, allylic), 4.83, 4.63 (each d, each 1 H, *J* = 12 Hz, CH_2Ph), 2.09, 1.81 (each m, each 1 H, H-6), 1.61, 1.35 (each s, each 3 H, CMe_2); MS calcd for $C_{21}H_{28}O_6$ *m/z* 376.1844, found 376.1889.

3,7-Anhydro-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-L-*glycero*-D-*allo*-octofuranose-(1,4) (15a) and 3,7-Anhydro-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-L-*glycero*-L-*talo*-octofuranose-(1,4) (15b). To a solution of **14a** (37 mg) in anhydrous dioxane (3.7 mL) were added selenium dioxide (12 mg) and acetic acid (7.9 μL), and the mixture was vigorously stirred for 0.5 h at reflux. The mixture was concentrated, and the residue was dissolved in dichloromethane. The solution was washed with water, dried, and concentrated. The residue was chromatographed on a silica gel column (1:1 (v/v) toluene–ethyl acetate) to give 24 mg (74%) of **15a** as white crystals.

Compound **15b** (57 mg) could similarly be obtained from **14b** (70 mg) as a syrup in 91% yield.

15a: R_f on TLC 0.45 (ethyl acetate); mp 113.5–115 °C; $[\alpha]^{26}_D$ −20° (*c* 0.50, $CHCl_3$); IR (KBr) 3450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.33 (s, 5 H, Ph), 5.84 (d, 1 H, *J* = 3.5 Hz, H-1), 4.82, 4.61 (each d, each 1 H, *J* = 10 Hz, CH_2Ph), 4.70 (t, 1 H, *J* = 4 Hz, H-2), 4.08 (dd, 1 H, *J* = 10 Hz, 4 Hz, H-3), 3.92 (dd, 1 H, *J* = 10 Hz, 2.5 Hz, H-4), 1.63, 1.38 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.07. Found: C, 63.97; H, 7.07.

15b: R_f on TLC 0.43 (ethyl acetate); $[\alpha]^{23}_D$ −59° (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 3570 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.33 (s, 5 H, Ph), 5.84 (d, 1 H, *J* = 3.5 Hz, H-1), 4.84, 4.62 (each d, each 2 H, *J* = 12 Hz, CH_2Ph), 4.67 (t, 1 H, *J* = 4 Hz, H-2), 3.93 (t, 1 H, *J* = 9.5 Hz, H-4), 3.38 (dd, 1 H, *J* = 4 Hz, 9.5 Hz, H-3), 1.64, 1.38 (each s, each 3 H, CMe_2).

8-*O*-Allyl-5-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*glycero*-D-*allo*-octofuranose-(1,4) (16). To a solution of **11a** (621 mg) in 80% aqueous acetone (12 mL) were added sodium hydrogen carbonate (576 mg) and methyl iodide (1.71 mL), and the mixture was heated in a sealed tube for 3 h at 75 °C. The reaction mixture was processed in a similar manner, and the product was chromatographed on a silica gel column (1:1 (v/v) toluene–ethyl acetate) to give 432 mg (80%) of **16**, which was recrystallized from cyclohexane to afford an analytical sample: R_f on TLC 0.29 (1:1 (v/v) toluene–ethyl acetate); mp 69–70.5 °C; $[\alpha]^{25}_D$ +37° (*c* 1.17, $CHCl_3$); IR ($CHCl_3$) 3560 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 7.27 (s, 5 H, Ph), 5.84 (m, 1 H, allylic), 5.66 (d, 1 H, *J* = 4 Hz, H-1), 5.16 (m, 2 H, allylic), 2.94 (br s, 1 H, OH), 2.70 (br d, 1 H, *J* = 9 Hz, OH), 1.81 (m, 2 H, H-6), 1.53, 1.32 (each s, each 3 H, CMe_2). Anal. Calcd for $C_{21}H_{30}O_7$: C, 63.95; H, 7.67. Found: C, 63.66, H, 7.43.

1,2,3,7-Tetra-*O*-acetyl-8-*O*-allyl-5-*O*-benzyl-6-deoxy-β-D-*glycero*-D-*allo*-octofuranose-(1,4) (17a) and 1,2,3,7-Tetra-*O*-acetyl-8-*O*-allyl-5-*O*-benzyl-6-deoxy-α-D-*glycero*-D-*allo*-octofuranose-(1,4) (17b). Compound **16** (444 mg) was dissolved in 60% aqueous acetic acid (13 mL), and the mixture was stirred for 25 min at 115 °C under reflux. The solution was coevaporated with toluene, and the residue was treated with a mixture of pyridine (4.4 mL) and acetic anhydride (4.4 mL) for 2 h at room temperature. The mixture was processed in the usual manner, and the product was chromatographed on a silica gel column (5:1 (v/v) toluene–ethyl acetate) to give a mixture of **17a** and **17b** (589 mg, 96% from **16**), which could be separated by repeating silica gel column chromatography (1.3:1 **17a**/**17b**). The intact mixture was used in the next step.

17a: R_f on TLC 0.62 (1:1 (v/v) toluene–ethyl acetate); $[\alpha]^{25}_D$ −14° (*c* 1.04, $CHCl_3$); IR ($CHCl_3$) 1740, 1220 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.34 (s, 5 H, Ph), 6.11 (s, 1 H, H-1), 4.62 (s, 2 H,

CH_2Ph), 4.23 (m, 1 H, H-4), 3.93 (m, 2 H, allylic), 3.71 (m, 1 H, H-5), 3.42 (d, 2 H, J = 5 Hz, H-8), 2.10, 2.01, 1.89 (each s, 3, 6, and 3 H, acetyl × 4). Anal. Calcd for $C_{26}H_{34}O_{11}$: C, 59.77; H, 6.56. Found: C, 59.61; H, 6.56.

17b: R_f on TLC 0.53 (1:1 (v/v) toluene–ethyl acetate); $[\alpha]^{25}_D$ +45° (c 1.03, $CHCl_3$); IR ($CHCl_3$) 1740, 1220 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.32 (s, 5 H, Ph), 6.37 (d, 1 H, J = 5 Hz, H-1), 5.91 (m, 1 H, allylic), 4.59 (s, 2 H, CH_2Ph), 4.32 (dd, 1 H, J = 5.5, 3 Hz, H-4), 3.93 (m, 2 H, allylic), 3.68 (m, 1 H, H-5), 3.42 (d, 2 H, J = 5 Hz, H-8), 2.10, 2.02, 2.00 (each s, 3, 6, and 3 H, acetyl × 4).

Methyl 1-[2,3,7-Tri-*O*-acetyl-8-*O*-allyl-5-*O*-benzyl-6-deoxy-β-D-*glycero*-D-*allo*-octofuranos-(1,4)-yl]uracil-5-carboxylate (18). A mixture of 1,1,1,3,3,3-hexamethyldisilazane (4.3 mL) and dry methyl 2,4-dihydroxypyrimidine-5-carboxylate (0.549 g) was stirred for 75 min under reflux. The mixture was concentrated, and the residue was dissolved in anhydrous dichloroethane (11 mL) containing trimethylsilyl trifluoromethanesulfonate (0.312 mL). The solution was added to a mixture of **17a** and **17b** (440 mg), and the mixture was stirred for 2 h at room temperature. To the mixture was added aqueous sodium hydrogen carbonate under ice cooling. The mixture was passed through a short silica gel column, and the filtrate was partitioned between ethyl acetate and water.

The organic layer was washed with water, dried, and concentrated. The residue was chromatographed on a silica gel column (1:1 (v/v) toluene–ethyl acetate) to give 409 mg (80%) of **18** as an amorphous solid: R_f on TLC 0.17 (1:1 (v/v) toluene–ethyl acetate); $[\alpha]^{25.5}_D$ −41° (c 0.72, $CHCl_3$); IR ($CHCl_3$) 3750, 1720, 1670, 1220 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 9.16 (br s, 1 H, NH-3), 8.52 (s, 1 H, H-6), 7.30 (m, 5 H, Ph), 6.13 (d, 1 H, J = 6.5 Hz, H-1′), 5.81 (m, 1 H, allylic), 4.73 (d, 2 H, J = 5.5 Hz, CH_2Ph), 4.34 (m, 1 H, H-4′), 3.94 (m, 2 H, allylic), 3.70 (m, 1 H, H-5′), 3.67 (s, 3 H, methyl ester), 3.44 (d, 2 H, J = 6 Hz, H-8′), 2.3–1.8 (m, 2 H), 2.12, 2.05, 2.04 (each s, each 3 H, acetyl × 3); MS calcd for $C_{30}H_{36}N_2O_{13}$ m/z 632.56, found (M + 1) 633.

Methyl 1-[8-*O*-Allyl-5-*O*-benzyl-6-deoxy-7-*O*-(methylsulfonyl)-β-D-*glycero*-D-*allo*-octofuranos-(1,4)-yl]uracil-5-carboxylate (19). Compound **18** (49.8 mg) was dissolved in ice-cooled 0.1 M methanolic sodium methoxide (1.0 mL), and the mixture was stirred for 1 h at room temperature. The mixture was deionized with Amberlite IR-120 (H^+) and concentrated to give a white solid. The residue was dissolved in anhydrous DMF (0.5 mL), and to this solution were added 2,2-dimethoxypropane (0.19 mL) and p-toluenesulfonic acid (3.0 mg). After 12 h at room temperature, the mixture was diluted with ethyl acetate, and the mixture was successively washed with aqueous sodium hydrogen carbonate and water, dried, and concentrated. The residue was treated with mesyl chloride (18 μL) in pyridine (0.5 mL) under ice cooling. After 0.5 h, the mixture was diluted with ethyl acetate, and a solution was washed successively with aqueous sodium hydrogen carbonate and water, dried, and concentrated to dryness. The residue was dissolved in 90% aqueous trifluoroacetic acid (1.0 mL), and the mixture was stirred for 0.5 h at room temperature. After coevaporation with toluene, the residue was chromatographed on a silica gel column (ethyl acetate) to give 37.2 mg (81%) of **19** as crystals. Recrystallization from ethyl acetate afforded an analytical sample: R_f on TLC 0.24 (ethyl acetate); mp 129.5–130 °C; $[\alpha]^{24.5}_D$ −22° (c 0.76, $CHCl_3$); IR (KBr) 3440, 3050, 1700, 1670, 1280, 1100 cm^{-1}; ^1H NMR (90 MHz, DMSO-d_6) δ 8.46 (s, 1 H, H-6), 7.35 (s, 5 H, Ph), 6.1–5.5 (m, 2 H), 5.5–3.8 (m, 7 H), 3.55 (s, 3 H, methyl ester), 3.55 (s, 1 H, H-1), 3.5 (m, 2 H), 3.10 (s, 3 H, SO_2Me), 2.00 (m, 2 H, OH × 2). Anal. Calcd for $C_{25}H_{32}N_2O_{12}S$: C, 51.37; H, 5.52; N, 4.79. Found: C, 51.48; H, 5.55; N, 4.88.

Methyl 1-[8-*O*-Allyl-3,7-anhydro-5-*O*-benzyl-6-deoxy-β-L-*glycero*-D-*allo*-octofuranos-(1,4)-yl]uracil-5-carboxylate (20). To a solution of **19** (266 mg) in anhydrous dimethylsulfoxide (8.0 mL) was added sodium hydride (60% dispersion in mineral oil, 91 mg), and the mixture was stirred for 2.5 h at 50 °C. The reaction mixture was poured into ice-cooled 0.1 M aqueous hydrochloric acid (27 mL) and extracted with dichloromethane. The extract was washed with water, dried, and concentrated. The residue was dissolved in 5% methanolic hydrochloride (13 mL), and the mixture was stirred for 0.5 h under reflux. The solution was coevaporated with methanol, and the residue was chromatographed on a silica gel column (30:1 (v/v) dichloromethane–methanol) to give 101 mg (45%) of **20** as white crystals: R_f on TLC 0.18 (ethyl acetate); mp 73–74 °C; $[\alpha]^{21}_D$ +4° (c 1.25, $CHCl_3$); IR (KBr) 3430, 3060, 1700 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.32 (s, 1 H, NH-3), 8.95 (s, 1 H, H-6), 7.34 (s, 5 H, Ph), 5.87 (m, 1 H, allylic), 5.82 (s, 1 H, H-1′), 5.20 (m, 2 H, allylic), 4.83, 4.74 (each d, each 1 H, J = 13 Hz, CH_2Ph), 4.5–3.4 (m, 9 H), 3.64 (s, 3 H, methyl ester), 2.04, 1.70 (each m, each 1 H, H-6′); MS calcd for $C_{24}H_{28}N_2O_9$ m/z 488.1792, found 488.1782.

Methyl 1-[8-*O*-Allyl-3,7-anhydro-2-*O*-benzoyl-5-*O*-benzyl-6-deoxy-β-L-*glycero*-D-*allo*-octofuranos-(1,4)-yl]uracil-5-carboxylate (21). To a solution of **20** (110 mg) in dry pyridine (2.2 mL) was added benzoyl chloride (0.047 mL) under ice cooling, and the mixture was stirred for 1 h under ice cooling. After addition of a small amount of methanol, the solution was coevaporated with toluene to dryness. The residue was dissolved in dichloromethane, and the mixture was washed successively with aqueous sodium hydrogen carbonate and water, dried, and concentrated. The residue was chromatographed on a silica gel column (2:1 (v/v) toluene–ethyl acetate) to give 115 mg (86%) of **21** as an amorphous solid: R_f on TLC 0.68 (ethyl acetate); $[\alpha]^{21.5}_D$ +1° (c 1.19, $CHCl_3$); IR ($CHCl_3$) 1720 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 9.20 (s, 1 H, NH-3), 8.87 (s, 1 H, H-6), 8.10, 7.46 (each m, total 5 H, COPh), 7.38 (s, 5 H, Ph), 5.90 (s, 1 H, H-1′), 5.8 (m, 1 H, allylic), 5.68 (d, 1 H, J = 5.5 Hz, H-2′), 5.16 (m, 2 H, allylic), 4.80 (s, 2 H, CH_2Ph), 4.4–3.4 (m, 8 H), 3.72 (s, 3 H, methyl ester), 2.3–1.5 (m, 2 H, H-6′). Anal. Calcd for $C_{31}H_{32}N_2O_{10}$: C, 62.84; H, 5.44; N, 4.73. Found: C, 63.04; H, 5.48; N, 4.29.

Methyl 1-[3,7-Anhydro-2-*O*-benzoyl-5-*O*-benzyl-6-deoxy-β-L-*glycero*-D-*allo*-octofuranos-(1,4)-yl]uracil-5-carboxylate (22). To a solution of **21** (28.6 mg) in anhydrous dioxane (0.29 mL) were added selenium dioxide (6.6 mg) and acetic acid (4.1 μL), and the mixture was vigorously stirred for 45 min under reflux. The reaction mixure was concentrated, and the residue was chromatographed on a silica gel column (1:2 (v/v) toluene–ethyl acetate) to give 20.6 mg (77%) of **22** as white crystals: R_f on TLC 0.45 (ethyl acetate); mp 117.5–121 °C; $[\alpha]^{20}_D$ −5° (c 0.88, $CHCl_3$); IR (KBr) 3460, 1710 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.38 (br s, 1 H, NH-3), 8.99 (s, 1 H, H-6), 8.44, 8.00 (each m, total 10 H, Ph × 2), 5.97 (s, 1 H, H-1′), 5.76 (d, 1 H, J = 4 Hz, H-2′), 4.89, 4.76 (each d, each 1 H, J = 13 Hz, CH_2Ph), 4.8 (m, 1 H), 4.54 (dd, 1 H, J = 4 Hz, 10 Hz, H-3′), 4.4–3.9 (m, 4 H), 3.70 (s, 3 H, methyl ester), 3.23 (m, 1 H), 3.00 (br s, 1 H, OH), 1.79 (m, 2 H, H-6′). Anal. Calcd for $C_{28}H_{28}N_2O_{10}$: C, 60.87; H, 5.11; N, 5.07. Found: C, 60.98; H, 5.24; N, 4.70.

Methyl 1-[Methyl 3,7-anhydro-2-*O*-benzoyl-5-*O*-benzyl-6-deoxy-β-L-*glycero*-D-*allo*-octofuranos-(1,4)-yluronate]uracil-5-carboxylate (23). To a solution of **22** (22 mg) in acetone (2.9 mL) was added Jones' reagent [0.22 mL, a solution of chromic trioxide (2.67 g) in sulfuric acid (2.3 mL) diluted with water to a volume of 10 mL] under ice cooling, and the mixture was stirred for 0.5 h at the same temperature. The reaction mixture was dissolved with dichloromethane, and the solution was washed with water, dried, and concentrated to dryness. The residue was heated with 2% methanolic hydrochloride (11 mL) for 50 min under reflux. The solution was coevaporated with methanol, and the residue was chromatographed on a silica gel column (1:1 (v/v) toluene–ethyl acetate) to afford 16 mg (67%) of **23** as white crystals: R_f on TLC 0.65 (ethyl acetate); mp 146–148 °C; $[\alpha]^{22.5}_D$ −31° (c 1.27, $CHCl_3$); IR ($CHCl_3$) 1720, 1260 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.85 (s, 1 H, H-6), 8.22 (br s, 1 H, NH-3), 8.09, 7.52 (each m, total 5 H, COPh), 7.33 (s, 5 H, Ph), 6.04 (s, 1 H, H-1′), 5.78 (d, 1 H, J = 5 Hz, H-2′), 4.77, 4.66 (each d, each 1 H, J = 12.5 Hz, CH_2Ph), 4.67 (dd, 1 H, J = 5 Hz, 11 Hz, H-3′), 4.47 (dd, 1 H, J = 7 Hz, ~2 Hz, H-7′), 4.31 (m, 1 H, H-5′), 4.07 (dd, 1 H, J = 11 Hz, 3 Hz, H-4′), 3.66, 3.63 (each s, each 3 H, methyl ester × 2), 2.76 (ddd, 1 H, J = 15 Hz, 4 Hz, ~2 Hz, H-6′e), 1.90 (ddd, 1 H, J = 15 Hz, 7 Hz, ~2 Hz, H-6′a); MS calcd for $C_{29}H_{28}N_2O_{11}$ m/z 580.49, found (M + 1) 581.

Methyl 1-[Methyl 3,7-anhydro-6-deoxy-α-D-*glycero*-D-*allo*-octofuranos-(1,4)-yluronate]uracil-5-carboxylate (2). Compound **23** (6.1 mg) was dissolved in 1 M methanolic sodium methoxide (0.6 mL), and the solution was stirred for 40 min under reflux. The mixture was deionized with Amberlite IR-120 (H^+) and concentrated to dryness. The residue was dissolved in 2% methanolic hydrogen chloride (0.6 mL), and the mixture was

stirred for 40 min under reflux. The solution was coevaporated with methanol, and the product was purified by a silica gel preparative TLC (10:1 (v/v) dichloromethane–methanol) to give 3.0 mg (62%) of **2** as white crystals: R_f on TLC 0.40 (10:1 (v/v) dichloromethane–methanol); $[\alpha]^{21}_D$ −8° (c 0.23, methanol); IR (KBr) 3430, 1710 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.93 (s, 1 H, H-6), 5.76 (s, 1 H, H-1′), 4.65 (m, 1 H, H-5′), 4.61 (dd, 1 H, J = 3 Hz, 12 Hz, H-7′), 4.31 (d, 1 H, J = 4.5 Hz, H-2′), 4.11 (dd, 1 H, J = 2 Hz, 10 Hz, H-4′), 3.94 (dd, 1 H, J = 10 Hz, 4.5 Hz, H-3′), 3.86, 3.78 (each s, each 3 H, methyl ester × 2), 2.22 (dt, 1 H, J = 15 Hz, 3 Hz, H-6′e), 1.83 (ddd, 1 H, J = 15 Hz, 13 Hz, 3 Hz, H-6′a); MS calcd for $C_{15}H_{18}N_2O_{10}$ m/z 386.26, found (M + 1) 387.

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Registry No. **1**, 55728-21-7; **2**, 101696-63-3; **3**, 106180-08-9; **4**, 15186-48-8; **6a**, 111689-96-4; **6b**, 111717-87-4; **7**, 111689-97-5; **8**, 111689-98-6; **9a**, 111689-99-7; **9b**, 111690-00-7; **10a**, 111690-01-8; **10b**, 111690-02-9; **11a**, 111690-03-0; **11b**, 111690-04-1; **12a**, 111690-05-2; **12b**, 111690-06-3; **13a**, 111690-07-4; **13b**, 111717-88-5; **14a**, 111690-08-5; **14b**, 111690-09-6; **15a**, 111690-10-9; **15b**, 111690-11-0; **16**, 111690-12-1; **17a**, 111690-13-2; **17b**, 111690-14-3; **18**, 111690-15-4; **19**, 111690-16-5; **20**, 111690-17-6; **21**, 111690-18-7; **22**, 111690-19-8; **23**, 111690-20-1; methyl 2,4-dihydroxypyrimidine-5-carboxylate, 42821-92-1.

Synthesis and Structural Revision of (7*E*)- and (7*Z*)-Punaglandin 4[1]

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A convergent synthesis of antineoplastic (7*E*)- and (7*Z*)-punaglandin 4 is described, dictating revision of the originally postulated structures, **1** and **2**, to the stereoisomers, **3** and **4**, respectively. Condensation of (*R*)-3-chloro-4-(*tert*-butyldimethylsiloxy)-2-cyclopentenone (**5**) and the organolithium derivative generated from 3-(trimethylstannyl)-1,2-octadiene (**27**) and methyllithium gives after desilylation the crystalline acetylenic diol **28**. Partial hydrogenation of the triple bond using Lindlar catalyst followed by oxidation of the secondary alcohol with pyridinium dichromate affords the hydroxy enone **31**. The whole punaglandin skeleton is constructed by aldol condensation of the silyl-protected hydroxycyclopentenone **32** and (2*R*,3*S*)-2,3-diacetoxy-6-carbomethoxyhexanal (**7**). Dehydration of the resulting aldol followed by removal of the silyl protective group leads to a mixture of **3** and **4**, identical with the naturally occuring sample in all respects. The enantiomers and some other stereoisomers exhibit similar inhibitory effects on L1210 leukemia cell proliferation.

Prostaglandin (PG) chemistry has now entered a new stage by adding newly discovered antineoplastic activity[2] to their properties as powerful local hormones maintaining the homeostasis of the human body. Punaglandins (PUGs), PUG 1–PUG 4, are halogenated eicosanoids first isolated from a Hawaiian octacoral, *Telesto riisei*.[3] PUG 1 and 2 are chlorinated cyclopentenone derivatives having the functionalized seven-carbon and unsaturated eight-carbon side chains. PUG 3 and 4 formally result from elimination of acetic acid from PUG 1 and 2, respectively, and possess the cross-conjugated dienone structures. Both 7*E* and 7*Z* isomers are natural products. PUG 3 and 4 among others have received particular attention because of the potent inhibitory effect on L1210 leukemia cell proliferation.[4] Their potency of IC_{50} 0.02 μg/mL[4] is 10- to 15-fold greater than that of the corresponding non-chlorinated compounds such as clavulone[5] (or claviridenone[6]), PGJ_2,[7] Δ^{12}-PGJ_2,[8] or Δ^7-PGA_1.[9] The relative configurations of these important materials have been postulated[3] on the basis of spectroscopic data and an assumed mechanism of chemical transformation, and the absolute configurations have been suggested by assuming stereochemical analogy of C-12 oxygenation with the related octacoral-derived clavulones[5] (or claviridenones[6]). However, because these grounds seemed not sufficiently

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