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Synthetic Approach toward Antibiotic Ezomycins. II. Synthesis of 5-Amino-3,7-anhydro-5-deoxy-octofuranose-(1,4) Derivatives

Osamu Sakanaka, Takashi Ohmori, Shuji Kozaki, and Tetsuo Suami*
Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Yokohama 223
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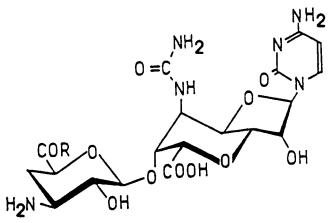
A conversion of 5-acetamido-5-deoxy-1,2:7,8-di-*o*-isopropylidene-3-*o*-methylthiomethyl-β-L-*erythro*-D-allo-octofuranose-(1,4) and -L-talooctofuranose-(1,4) to 5-amino-3,7-anhydro-5-deoxyoctofuranose-(1,4) derivatives has been investigated as a preliminary study for a synthesis of the octose moiety of ezomycins.

Nucleoside antibiotic ezomycins were discovered in a fermentation broth of a strain which was similar to Streptomyces Kitazawaensis.[1] They exhibit antimicrobial activity against limited species of phytopathogenic fungi, such as Sclerotinia and Botritis. Ezomycins A, B, and C comprise a unique bicyclic trans-fused octose derivative,[2-4] which is a target of our present studies. Although several studies related to synthesis of 3,7-anhydrooctofuranose-(1,4) derivatives have been described,[5-7] any derivatives with all functional groups have not yet been synthesized.

In the preceding paper,[8] a synthesis of 5-acetamido-5-deoxyoctofuranose-(1,4) derivatives has been described. A KF-catalyzed Henry reaction between 5-nitro-D-ribose derivative (**1**) and L-glyceraldehyde derivative (**2**) and successive hydrogenation followed by *N*-acetylation afforded three diastereomeric isomers (**3a**, **3b**, and **3c**). Also their absolute configurations of the newly introduced chiral centers on C-5 and C-6 have been established. The configurations of the major product **3a** were found to be identical with those of the octose part of ezomycins.

In the present article, we wish to report a synthesis of 5-amino-3,7-anhydro-5-deoxyoctofuranose-(1,4) derivatives from **3a** and **3b**.



Ezomycin

A_1

$R = NHCHCH_2CH_2SCH_2CHNH_2$ (COOH, COOH)

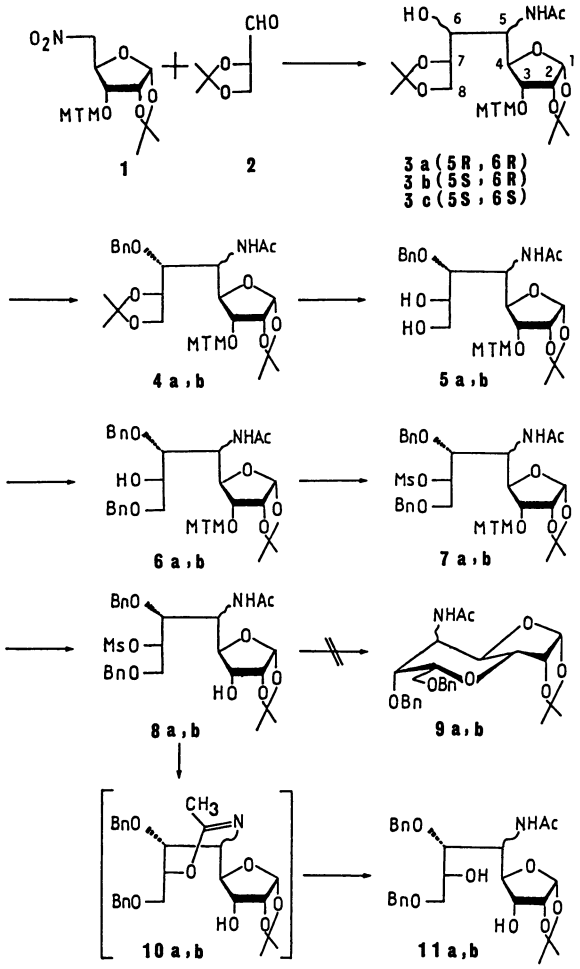
A_2

$R = OH$

Scheme 1.

Results and Discussion

O-Benzylation of an intact mixture (67% from 1) of **3a** and **3b**, which could not be separated chromatographically, with benzyl bromide and sodium hydride in *N,N*-dimethylformamide (DMF) gave the corresponding benzyl ethers (**4a** and **4b**), which could be isolated readily in 49 and 30% yield respectively.



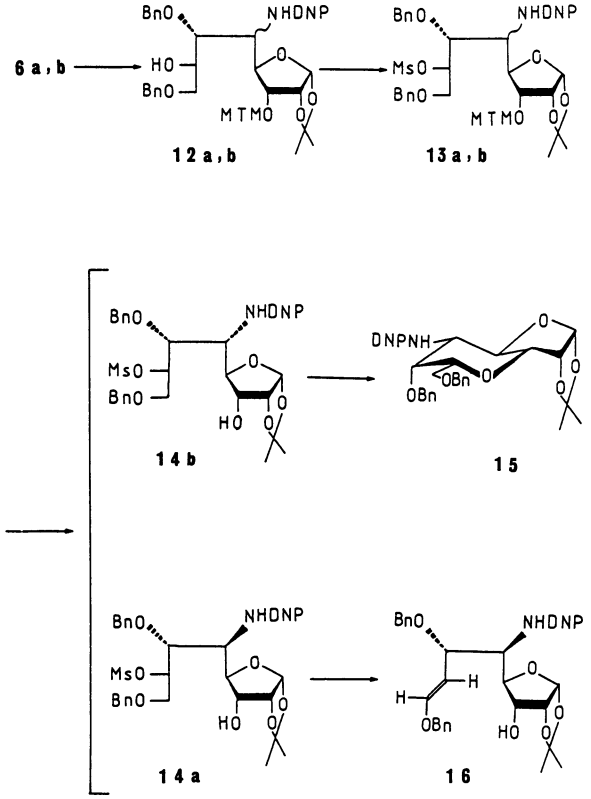
Bn benzyl
Ms methylsulfonyl
MTM methylthiomethyl

Scheme 2.

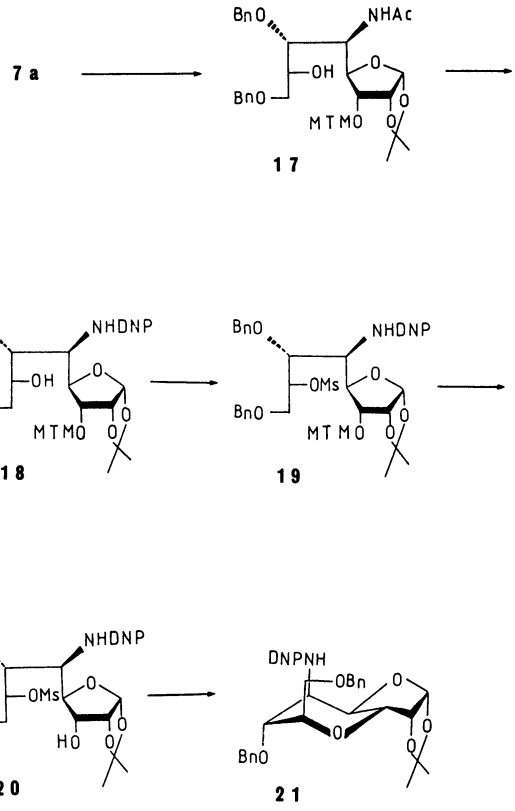
Selective removal of 7,8-*O*-isopropylidene group in **4a** with aqueous acetic acid afforded a diol (**5a**). Preferential 8-*O*-benzylation of **5a** with benzyl bromide and sodium hydride in tetrahydrofuran (THF) gave 6,8-di-*O*-benzyl compound (**6a**) in 49% yield. *O*-Mesylation of **6a** with methanesulfonyl chloride in pyridine afforded a mesylate (**7a**) in 78% yield. Treatment of **7a** with iodomethane in the presence of sodium hydrogencarbonate in aqueous acetone[9] gave 3-*O*-deprotected compound (**8a**) in 53% yield. Another benzyl ether (**5b**) was also converted to the corresponding compound (**8b**) by the analogous procedure. Cyclization of **8a** to a 3,7-anhydride with a base (NaH or *t*-BuOK) in various solvent systems have been attempted, but in vain. The product was treated with acetic anhydride in pyridine to give a diacetate, which was not an acetylated derivative of **5a**. Therefore, it was thought that an epimerization was caused by a participation of 5-acetamido group. The product derived from **8b** was also an epimerized diol (**9b**). Although a benzyloxycarbonyl or a phthaloyl group was used as protective group of the 5-amino group, a satisfactory result was not obtained.

Then, a 2,4-dinitrophenyl group was used as protective group. Hydrolysis of **6a** with sodium hydroxide in aqueous 2-methoxyethanol and successive treatment of the resultant amine with 2,4-dinitrofluorobenzene and triethylamine in THF afforded dinitrophenylamino compound (**12a**) in 75% yield. *O*-Mesylation of **12a** with methanesulfonyl chloride in pyridine yielded a mesylate (**13a**) quantitatively. Treatment of **13a** with iodomethane and sodium hydrogencarbonate in aqueous acetone gave 3-*O*-deprotected compound (**14a**) in 72% yield. Compound **6b** was also converted to the corresponding compound (**14b**) by the analogous procedure. Treatment of **14b** with NaH in DMF afforded the desired 3,7-anhydride (**15**) in 59% yield. However, attemps to cyclize **14a** with a base (NaH or *t*-BuOK) in various solvent systems were unsuccessful. The ^{1}H NMR spectrum of the main product showed a characteristic doublet at δ 6.64 (J=14 Hz), possibly a trans-olefin signal, and a doublet at δ 3.08 (J=6 Hz) assignable to 3-OH. Accordingly, the product is thought to have a structure **16**. The structure is also reasonable for all other signals. The other products were unable to isolate. The conformation of 7-mesyloxy group in **14a** might be unfavorable to a nucleophilic attack of a 3-oxido anion.

Therefore, the epimer of **14a** at C-7 was prepared as follows. Treatment of **7a** with NaH in DMF resulted in an attack of 5-acetamido group to C-7 as above-mentioned and successive acidic workup with silica gel afforded an epimeric product (**17**) in 92% yield. Compound **17** was converted to a mesylate (**20**) by the analogous procedure as described already. Treatment



Scheme 3.



Scheme 4.

of **20** with NaH in dimethyl sulfoxide (DMSO) afforded a bicyclic 3,7-anhydride (**21**) in 66% yield as expected. Since an attack of a 3-oxido anion to C-7 is an S_N2 type reaction, the stereochemistry is non-natural. However, if **21** can be oxidized to an uronic acid, it is expected that the configuration of C-7 can be reversed because of α-position of carboxyl function.

Experimental

Melting points were determined on a Büchi 510 capillary melting point 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 on a Varian EM-390 (90 MHz), a JEOL FX-200 (200 MHz), or a JEOL GX-400 (400 MHz) spectrometer with a reference to tetramethylsilane as an internal standard. Mass spectra were recorded on a Hitachi M-80B spectrometer. Solutions were dried over anhydrous sodium sulfate and concentrated below 35 °C. TLC was carried out on glass plates coated with Kieselgel 60 F_{254} (Merck Art. 5715), and compounds were detected by spraying with an H_2SO_4 followed by heating. Chromatography was performed on a silica gel (Merck Kieselgel 60 Art. 7734) column.

5-Acetamido-6-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-β-L-*erythro*-L-talooctofuranose-(1,4) (5b). Compound **4b** (104 mg) was dissolved in 70% aqueous acetic acid (2 ml) and the solution was allowed to stand for 14 h at room temperature. Coevaporation with toluene gave a pale yellow syrupy residue, which was chromatographed (chloroform–methanol (v/v) 30:1) to afford **5b** in an almost quantitative yield (95 mg) as crystals: R_f=0.35 on TLC (chloroform–methanol (v/v) 15:1); mp 136—138 °C; $[\alpha]_D^{21}$ +17.2° (*c* 1.06, $CHCl_3$); IR (KBr) 1650 cm^{-1} (NHCO); ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.32, 1.45 (3H×2, s×2, CMe_2), 1.97 (3H, s, NHAc), 2.14 (3H, s, SMe), 3.15 (1H, bs, OH), 5.77 (1H, d, *J*=4 Hz, H-1), 6.26 (1H, d, *J*=10 Hz, NH), 7.30 (5H, m, Ph).

Found: C, 55.78; H, 6.97; N, 3.13; S, 6.59%. Calcd for $C_{22}H_{33}NO_8S$: C, 56.04; H, 7.05; N, 2.97; S, 6.80%.

5-Acetamido-6,8-*O*-di-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-β-L-*erythro*-L-talooctofuranose-(1,4) (6b). To a chilled solution (−15 °C) of **5b** (163 mg) in anhydrous THF (4 ml) were added sodium hydride (60% dispersion in mineral oil, 16 mg) and benzyl bromide (45 μl), and the mixture was stirred for 2 h under ice cooling. The mixture was chilled to −15 °C again, and sodium hydride (7 mg) and benzyl bromide (12 μl) were added. The mixture was stirred for 12 h at 5 °C. Coevaporation with ethanol gave a pale yellow syrup, which was chromatographed (chloroform–methanol (v/v) 30:1) to afford 109 mg (56%) of **6b** as a colorless syrup: R_f=0.44 on TLC (ethyl acetate); ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.32, 1.46 (3H×2, s×2, CMe_2), 1.91 (3H, s, NHAc), 2.13 (3H, s, SMe), 2.85 (1H, d, *J*=4 Hz, OH), 5.76 (1H, d, *J*=4 Hz, H-1), 5.84 (1H, d, *J*=10 Hz, NH), 7.15—7.54 (10H, m, Ph×2). Although contaminated with 6,7-di-*O*-benzyl compound (<1/10, judged from NMR spectrum), the product was used in the next step without further purification. Both isomers had a similar mobility in a column chromatography.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-β-L-*erythro*-L-talooctofuranose-(1,4) (12b). A mixture of **6b** (146 mg), sodium hydroxide (270 mg) and 95% aqueous 2-methoxyethanol (3 ml) was heated for 75 min under reflux. The mixture was partitioned between water and ethyl acetate. The organic layer was washed twice with water, dried and concentrated to dryness. The pale brown syrupy residue was dissolved in THF (3 ml), and to the solution were added triethylamine (68 μl) and 2,4-dinitrofluorobenzene (98 mg). The mixture was stirred for 18 h at room temperature, and partitioned between water and ethyl acetate. The organic layer was washed twice with water, dried and concentrated to dryness. The syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 6:1) to give 141 mg (79%) of **12b** as yellow amorphous solids: R_f=0.47 on TLC (toluene–ethyl acetate (v/v) 2:1); $[\alpha]_D^{22}$ +33.7° (*c* 1.21, $CHCl_3$); IR (KBr) 1520 cm^{-1} (NO_2); ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.33, 1.52 (3H×2, s×2, CMe_2), 1.99 (3H, s, SMe), 2.76 (1H, d, *J*=4 Hz, OH), 5.88 (1H, d, *J*=4 Hz, H-1), 7.06 (1H, d, *J*=10 Hz, H-6′), 7.19—7.42 (10H, m, Ph×2), 7.99 (1H, dd, *J*=10, 3 Hz, H-5′), 9.03 (1H, d, *J*=3 Hz, H-3′).

Found: C, 58.06; H, 5.95; N, 5.88; S, 4.67%. Calcd for $C_{33}H_{39}N_3O_{11}S$: C, 57.80; H, 5.73; N, 6.13; S, 4.67%.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-7-*O*-methylsulfonyl-3-*O*-methylthiomethyl-β-L-*erythro*-L-talooctofuranose-(1,4) (13b). To a solution of **12b** (150 mg) in dry pyridine (3 ml) was added methanesulfonyl chloride (70 μl) under ice cooling, and the mixture was stirred for 2 h. After 1 h at room temperature additionally, the mixture was partitioned between 3% aqueous sodium hydrogencarbonate and ethyl acetate. The organic layer was washed with water, dried and concentrated to dryness. The syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 8:1) to give 146 mg (88%) of **13b** as yellow amorphous solids: R_f=0.62 on TLC (toluene–ethyl acetate (v/v) 2:1); $[\alpha]_D^{22}$ +11.6° (*c* 1.35, $CHCl_3$); IR (KBr) 3320 (NH), 1525, 1515 (NO_2) cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.33, 1.52 (3H×2, s×2, CMe_2), 1.92 (3H, s, SMe), 2.96 (3H, s, SO_2Me), 5.85 (1H, d, *J*=4 Hz, H-1), 6.89 (1H, d, *J*=10 Hz, H-6′), 7.24—7.43 (10H, m, Ph×2), 7.86 (1H, dd, *J*=3, 10 Hz, H-5′), 8.72 (1H, d, *J*=10 Hz, NH), 8.99 (1H, d, *J*=3 Hz, H-3′).

Found: C, 53.32; H, 5.47; N, 5.21; S, 8.25%. Calcd for $C_{34}H_{41}N_3O_{13}S_2$: C, 53.46; H, 5.41; N, 5.50; S, 8.39%.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-7-*O*-methylsulfonyl-β-L-*erythro*-L-talooctofuranose-(1,4) (14b). To a mixture of **13b** (146 mg), sodium hydrogencarbonate (81 mg) and 90% aqueous acetone (2.4 ml) was added iodomethane (0.25 ml) three times at intervals of 2 h under reflux, and then furthermore the mixture was refluxed for 2 h. The reaction mixture was diluted with ethyl acetate, dried and concentrated to dryness. The syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 8:1) to afford 86 mg (64%) of **14b** as yellow amorphous solids: R_f=0.30 on TLC (toluene–ethyl acetate (v/v) 3:1); $[\alpha]_D^{20}$ −68.9° (*c* 2.11, $CHCl_3$); IR (KBr) 1525, 1520 cm^{-1} (NO_2); ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.35, 1.52 (3H×2, s×2, CMe_2), 2.34 (1H, d, *J*=12 Hz, OH), 2.98 (3H, s, SO_2Me), 5.87 (1H, d, *J*=4 Hz, H-1), 6.91 (1H, d, *J*=10 Hz, H-6′), 7.24—7.44 (10H, m, Ph×2), 7.92 (1H, dd, *J*=3, 10 Hz, H-5′), 8.62 (1H, d, *J*=10 Hz, NH), 9.02 (1H, d, *J*=3 Hz,

H-3′).

Found: C, 54.61; H, 5.51; N, 5.71; S, 4.52%. Calcd for $C_{32}H_{37}N_3O_{13}S$: C, 54.62; H, 5.30; N, 5.97; S, 4.56%.

3,7-Anhydro-6,8-di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-α-D-*threo*-L-talooctofuranose-(1,4) (15). To a solution of **14b** (31.8 mg) in anhydrous DMF (0.3 ml) was added sodium hydride (8 mg) under ice cooling, and the mixture was stirred for 3 h at room temperature. The mixture was partitioned between water and ethyl acetate. The organic layer was washed with water repeatedly, dried and concentrated to dryness. The syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 5:1) to give 16.2 mg (59%) of **15** as yellow amorphous solids: R_f=0.51 on TLC (toluene–ethyl acetate (v/v) 2:1); $[\alpha]_D^{21}$ −39.7° (*c* 0.79, $CHCl_3$); IR (KBr) 3450 (NH), 1525, 1520 (NO_2) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.33, 1.57 (3H×2, s×2, CMe_2), 3.29 (1H, dd, *J*=3, 9 Hz, H-3), 3.68—3.97 (4H, H-5, 7, 8), 4.09 (1H, d, *J*=2 Hz, H-6), 4.23 (1H, dd, *J*=9, 9 Hz, H-4), 4.44—4.60 (2H, CH_2Ph), 4.65—4.78 (3H, H-2, CH_2Ph), 5.79 (1H, d, *J*=4 Hz, H-1), 7.02 (1H, d, *J*=10 Hz, H-6′), 7.18—7.39 (10H, m, Ph×2), 8.16 (1H, dd, *J*=3, 10 Hz, H-5′), 9.03 (1H, d, *J*=10 Hz, NH), 9.05 (1H, d, *J*=3 Hz, H-3′).

Found: C, 61,03; H, 5.55; N, 6.70%. Calcd for $C_{31}H_{33}N_3O_{10}$: C, 61.28; H, 5.47; N, 6.92%.

5-Acetamido-6,8-di-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-β-L-*erythro*-D-allooctofuranose-(1,4) (6a). To a solution of **5a** (509 mg) in anhydrous THF (5 ml) were added sodium hydride (108 mg) and benzyl bromide (0.14 ml) under ice cooling, and the mixture was stirred for 12 h at 5 °C. The reaction mixture was partitioned between water and ethyl acetate. The organic layer was dried and concentrated to dryness. The syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 3:2) to afford 294 mg (48.6%) of **6a** as crystals: R_f=0.50 on TLC (ethyl acetate); mp 130—132 °C; $[\alpha]_D^{20}$ +9.32° (*c* 1.03, $CHCl_3$); IR (KBr) 1630 cm^{-1} (NHCO); ^1H NMR (90 MHz, $CDCl_3$) δ=1.34, 1.54 (3H×2, s×2, CMe_2), 1.97 (3H, s, NHAc), 2.17 (3H, s, SMe), 5.79 (1H, d, *J*=4 Hz, H-1), 7.29, 7.35 (5H×2, s×2, Ph×2).

Found: C, 62.29; H, 7.01; N, 2.33; S, 5.57%. Calcd for $C_{29}H_{39}NO_8S$: C, 62.29; H, 7.00; N, 2.49; S, 5.71%.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-β-L-*erythro*-D-allooctofuranose-(1,4) (12a). A solution of **6a** (0.47 g) and sodium hydroxide (0.4 g) in 95% aqueous 2-methoxyethanol (5 ml) was heated for 6 h under reflux. The mixture was partitioned between water and ethyl acetate. The organic layer was washed twice with water, dried and concentrated to dryness. The residue was dissolved in THF (5 ml), and to the solution were added triethylamine (0.18 ml) and 2,4-dinitrofluorobenzene (190 mg). After 12 h at room temperature the mixture was partitioned between water and ethyl acetate. The organic layer was washed with water, dried and concentrated to dryness. The residue was chromatographed (toluene–ethyl acetate (v/v) 3:1) to give 433 mg (75%) of **12a** as yellow amorphous solids: R_f=0.37 on TLC (toluene–ethyl acetate (v/v) 4:1); $[\alpha]_D^{25}$ −103 °C (*c* 2.91, $CHCl_3$); IR (KBr) 1520 cm^{-1} (NO_2); ^1H NMR (90 MHz, $CDCl_3$) δ=1.32, 1.46 (3H×2, s×2, CMe_2), 1.86 (3H, s, SMe), 2.48 (1H, d, *J*=5 Hz), 5.78 (1H, d, *J*=4 Hz, H-1), 7.35 (10H, bs, Ph×2), 8.20 (1H, dd, *J*=3, 10 Hz, H-5′), 9.02 (1H, d, *J*=8 Hz, NH), 9.11 (1H, d, *J*=3 Hz, H-3′).

Found: M, 685. Calcd for $C_{33}H_{39}N_3O_{11}S$: *m/z*, 685.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-7-*O*-methylsulfonyl-3-*O*-methylthiomethyl-β-L-*erythro*-D-allooctofuranose-(1,4) (13a). To a solution of **12a** (128 mg) in dry pyridine (3 ml) was added methanesulfonyl chloride (43 μl) under ice cooling, and the mixture was allowed to stand overnight in a refrigerator. The reaction mixture was partitioned between saturated aqueous sodium hydrogencarbonate and ethyl acetate. The organic layer was washed with water repeatedly, dried and concentrated to dryness. The residue was chromatographed (toluene–ethyl acetate (v/v) 10:1) to afford 132 mg (93%) of **13a** as yellow amorphous solids: R_f=0.44 on TLC (toluene–ethyl acetate (v/v) 4:1); $[\alpha]_D^{26}$ −47.1° (*c* 1.05, $CHCl_3$); IR (KBr) 3330 (NH), 1525, 1515 (NO_2) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.33, 1.48 (3H×2, s×2, CMe_2), 1.95 (3H, s, SMe), 2.89 (3H, s, SO_2Me), 5.78 (1H, d, *J*=4 Hz, H-1), 7.08 (1H, d, *J*=8 Hz, H-6′), 7.32, 7.37 (5H×2, s×2, Ph×2), 8.18 (1H, dd, *J*=3, 8 Hz, H-5′), 9.12 (1H, d, *J*=3 Hz, H-3′).

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-7-*O*-methylsulfonyl-β-L-*erythro*-D-allooctofuranose-(1,4) (14a). To a mixture of **13a** (107 mg), sodium hydrogencarbonate (59 mg) and 90% aqueous acetone (2 ml) was added iodomethane (0.18 ml) three times at intervals of 1 h under reflux, and furthermore the mixture refluxed for 2 h. The reaction mixture was diluted with ethyl acetate, dried and concentrated to dryness. The syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 3:1) to give 52 mg (53%) of **14a** as yellow amorphous solids: R_f=0.15 on TLC (toluene–ethyl acetate (v/v) 4:1); $[\alpha]_D^{26}$ −43.2° (*c* 1.08, $CHCl_3$); IR (KBr) 3460 (OH), 3330 (NH), 1525, 1515 (NO_2); ^1H NMR (90 MHz, $CDCl_3$) δ=1.34, 1.47 (3H×2, s×2, CMe_2), 2.34 (1H, bs, OH), 2.91 (3H, s, SO_2Me), 5.78 (1H, d, *J*=4 Hz, H-1), 7.09 (1H, d, *J*=10 Hz, H-6′), 7.34, 7.38 (5H×2, s×2, Ph×2), 8.16 (1H, dd, *J*=3, 10 Hz, H-5′), 9.11 (1H, d, *J*=3 Hz).

A Reaction of 14a with NaH. To a solution of **14a** (23.8 mg) in anhydrous DMF (0.5 ml) was added sodium hydride (5.7 mg) under ice cooling, and the mixture was stirred for 3.5 h at room temperature. The mixture was partitioned between water and ethyl acetate. The organic layer was washed twice with water, dried and concentrated to dryness. The residue was chromatographed (toluene–ethyl acetate (v/v) 8:1) to afford 5.2 mg (25%) of an olefinic compound **16** as yellow amorphous solids: R_f=0.37 on TLC (toluene–ethyl acetate (v/v) 4:1); $[\alpha]_D^{26}$ +20.0° (*c* 0.52, $CHCl_3$); IR (KBr) 3480 (OH), 3350 (NH), 1515, 1505 (NO_2) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.30, 1.52 (3H×2, s×2, CMe_2), 3.08 (1H, d, *J*=6 Hz, OH), 5.57 (1H, d, *J*=5 Hz, H-1), 6.64 (1H, d, *J*=14 Hz, H-8), 7.00 (1H, d *J*=10 Hz, H-6′), 7.25, 7.28 (5H×2, s×2, Ph×2), 8.09 (1H, dd, *J*=3, 10 Hz, H-5′), 8.95 (1H, d, *J*=7 Hz, NH), 9.03 (1H, d, *J*=3 Hz, H-3′).

Found: M, 607. Calcd for $C_{31}H_{33}N_3O_{10}$: *m/z*, 607.

5-Acetamido-6,8-di-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-7-*O*-methylsulfonyl-3-*O*-methylthiomethyl-β-L-*erythro*-D-allooctofuranose-(1,4) (7a). To a solution of **6a** (1.14 g) in dry pyridine (11 ml) was added methanesulfonyl chloride (0.47 ml) under ice cooling, and the mixture was stirred for 2 h at room temperature. The reaction mixture was coevaporated with toluene, and the residue was partitioned between water and ethyl acetate. The organic layer was

washed with water repeatedly, dried and concentrated to dryness. The residue was chromatographed (toluene–ethyl acetate (v/v) 3:1) to give 1.01 g of **7a** as a colorless syrup: R_f=0.50 on TLC (toluene–ethyl acetate (v/v) 1:1); $[\alpha]_D^{19}$ +11.7° (*c* 1.23, $CHCl_3$); IR ($CHCl_3$) 3390 (NH), 1670 (NHCO), 1350, 1170 (SO_2Me) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.33, 1.54 (3H×2, s×2, CMe_2), 1.91 (3H, s, NHAc), 2.19 (3H, s, SMe), 3.01 (3H, s, SO_2Me), 5.73 (1H, d, *J*=4 Hz, H-1), 7.30, 7.33 (5H×2, s×2, Ph×2).

5-Acetamido-6,8-di-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-α-D-*threo*-D-allooctofuranose-(1,4) (17). To a solution of **7a** (905 mg) in anhydrous DMF (9 ml) was added sodium hydride (227 mg) under ice cooling, and the mixture was stirred for 40 min at room temperature. The reaction mixture was partitioned between water and ethyl acetate. The organic layer was washed with water repeatedly, dried and concentrated to dryness. The syrupy residue was dissolved in a small amount of toluene, and a silica-gel column was charged with the solution. After 3 h elution (toluene–ethyl acetate (v/v) 1:2) afforded 733 mg (92.3%) of **17** as a colorless syrup: R_f=0.66 on TLC (ethyl acetate); $[\alpha]_D^{21.5}$ +24.2 (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 1670 cm^{-1} (NHCO); ^1H NMR (90 MHz, $CDCl_3$) δ=1.33, 1.53 (3H×2, s×2, CMe_2), 1.92 (3H, s, NHAc), 2.19 (3H, s, SMe), 2.52 (1H, d, *J*=3 Hz, OH), 5.75 (1H, d, *J*=4 Hz, H-1), 7.35 (10H, s, Ph×2).

Found: C, 62.06; H, 6.97; N, 2.47; S, 5.87%. Calcd for $C_{29}H_{39}NO_8S$: C, 62.01; H, 7.00; N, 2.49; S, 5.71%.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-α-D-*threo*-D-allooctofuranose-(1,4) (18). A mixture of **17** (565 mg), sodium hydroxide (452 mg) and 95% aqueous 2-methoxyethanol (5.7 ml) was heated for 1.5 h under reflux. The reaction mixture was partitioned between water and chloroform. The organic layer was washed twice with water, dried and concentrated to dryness. The pale brown syrup was dissolved in THF (5.6 ml) and to the solution were added triethylamine (0.21 ml) and 2,4-dinitrofluorobenzene (225 mg). After 12 h at room temperature the reaction mixture was partitioned between water and ethyl acetate. The organic layer was washed twice with water, dried and concentrated to dryness. The deep yellow syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 3:1) to give 548 mg (79.3%) of **18** as a yellow syrup: R_f=0.18 on TLC (toluene–ethyl acetate (v/v) 5:1); $[\alpha]_D^{20}$ +18.6° (*c* 1.07, $CHCl_3$); IR ($CHCl_3$) 1520, 1330 cm^{-1} (NO_2); ^1H NMR (90 Hz, $CDCl_3$) δ=1.32, 1.50 (3H×2, s×2, CMe_2), 2.00 (3H, s, SMe), 2.48 (1H, d, *J*=3 Hz, OH), 5.72 (1H, d, *J*=4 Hz, H-1), 6.91 (1H, d, *J*=10 Hz, H-6′), 7.32 (10H, s, Ph×2), 8.02 (1H, dd, *J*=3, 10 Hz, H-5′), 9.05 (1H, d, *J*=3 Hz, H-3′).

Found: C, 58.07; H, 5.89; N, 5.90; S, 4.43%. Calcd for $C_{33}H_{39}N_3O_{11}S$: C, 57.80; H, 5.73; N, 6.13; S, 4.68%.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-7-*O*-methylsulfonyl-3-*O*-methylthiomethyl-α-D-*threo*-D-allooctofuranose-(1,4) (19). To a solution of **18** (554 mg) in dry pyridine (5.5 ml) was added methanesulfonyl chloride (0.19 ml) under ice cooling, and the mixture was stirred overnight at room temperature. The mixture was coevaporated with toluene, and the residue was partitioned between water and ethyl acetate. The organic layer was washed with water repeatedly, dried and concentrated to dryness. The syrupy residue was chromatographed (toluene–ethyl acetate (v/v) 10:1) to give 537 mg (86.9%) of **19** as yellow amorphous solids: R_f=0.43 on TLC (toluene–ethyl acetate (v/v) 5:1); $[\alpha]_D^{21.5}$ +23.8° (*c* 0.88, $CHCl_3$); IR (KBr) 1520 (NO_2), 1170 (SO_2Me) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.33, 1.50 (3H×2, s×2, CMe_2), 2.02 (3H, s, SMe), 2.93 (3H, s, SO_2Me), 5.78 (1H, d, *J*=4 Hz, H-1), 6.87 (1H, d, *J*=10 Hz, H-6′), 7.40 (10H, s, Ph×2), 8.09 (1H, dd, *J*=3, 10 Hz, H-5′), 9.09 (1H, d, *J*=3 Hz, H-3′).

Found: C, 53.26; H, 5.40; N, 5.43; S, 8.28%. Calcd for $C_{34}H_{41}N_3O_{13}S_2$: C, 53.46; H, 5.41; N, 5.51; S, 8.39%.

6,8-Di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-7-*O*-methylsulfonyl-α-D-*threo*-D-allooctofuranose-(1,4) (20). To a mixture of **19** (485 mg), sodium hydrogencarbonate (267 mg) and 90% aqueous acetone (5 ml) was added iodomethane (0.8 ml) nine times at intervals of 1 h under reflux. Furthermore, the mixture was refluxed for 6 h. The reaction mixture was poured into water and the mixture was extracted with ethyl acetate. The organic layer was washed with water, dried and concentrated to dryness. The residue was chromatographed (toluene–ethyl acetate (v/v) 5:1) to yield 338 mg (86.7%) of **20** as yellow amorphous solids: R_f=0.68 on TLC (toluene–ethyl acetate (v/v) 3:1); $[\alpha]_D^{22}$ +21.2° (0.965, $CHCl_3$); IR ($CHCl_3$) 1520, 1340 (NO_2), 1300, 1170 (SO_2Me) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.31, 1.48 (3H×2, s×2, CMe_2), 2.92 (3H, s, SO_2Me), 5.73 (1H, d, *J*=4 Hz, H-1), 6.80 (1H, d, *J*=10 Hz, H-6′), 7.40 (10H, s, Ph×2), 8.02 (1H, dd, *J*=3, 10 Hz, H-5′), 9.05 (1H, d, *J*=3 Hz, H-3′).

Found: C, 54.33; H, 5.35; N, 5.70; S, 4.33%. Calcd for $C_{32}H_{37}N_3O_{13}S$: C, 54.61; H, 5.30; N, 5.97; S, 4.56%.

3,7-Anhydro-6,8-di-*O*-benzyl-5-deoxy-5-(2,4-dinitrophenylamino)-1,2-*O*-isopropylidene-β-L-*erythro*-D-allooctofuranose-(1,4) (21). To a solution of **20** (154 mg) in anhydrous DMSO (1.5 ml) was added sodium hydride (35 mg) under ice cooling, and the mixture was stirred for 2 h at room temperature. The mixture was partitioned between water and chloroform. The organic layer was washed with water repeatedly, dried and concentrated to dryness. The residue was chromatographed (toluene–ethyl acetate (v/v) 10:1) to afford 92 mg (66%) of **21** as yellow amorphous solids: R_f=0.49 on TLC (toluene–ethyl acetate (v/v) 5:1); $[\alpha]_D^{23}$ +182° (*c* 0.585, $CHCl_3$); IR (KBr) 1520, 1330 cm^{-1} (NO_2); ^1H NMR (400 MHz, $CDCl_3$) δ=1.38, 1.66 (3H×2, s×2, CMe_2), 3.61—3.70 (2H, m, H-8), 3.80 (1H, dd, *J*=10.5, 4.0 Hz, H-3), 3.92 (1H, m, H-6), 4.26 (1H, m, H-5), 4.31 (1H, d, *J*=12.5 Hz, CH_2Ph), 4.42 (1H, m, H-7), 4.54 (1H, dd, *J*=4.5, 10.5 Hz, H-4), 4.55 (1H, d, *J*=12.5 Hz, CH_2Ph), 4.71 (1H, dd, *J*=3.5, 4.0 Hz, H-2), 4.77 (1H, d, *J*=12.5 Hz, CH_2Ph), 5.79 (1H, d, *J*=3.5 Hz, H-1), 6.24 (1H, d, *J*=9.5 Hz, H-6′), 7.02—7.42 (10H, m, Ph×2), 7.86 (1H, dd, *J*=3.0, 9.5 Hz, H-5′), 8.68 (1H, d, *J*=6.0 Hz, NH), 8.96 (1H, d, *J*=3.0 Hz, H-3′). The assignment was established by a spectrum of two dimensions.

Found: C, 61.51; H, 5.42; N, 6.82%. Calcd for $C_{31}H_{33}N_3O_{10}$: C, 61.28; H, 5.47; N, 6.92%.

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