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SYNTHESIS OF PROTECTED PURPUROSAMINE B AND 6-EPI-PURPUROSAMINE B

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ABSTRACT

In relation to the synthesis of antipseudomonal drugs, namely, gentamicin C_2 and 3-de-*O*-methylsporaricin A*, a protected purpurosamine B (**15**) and 6-epipurpurosamine B (**13**) were synthesized. The key intermediate, methyl 2,3,4,7-tetradeoxy-6-*O*-(methylsulfonyl)-2-phthalimido-β-L-*lyxo*-heptopyranoside (**8**), was obtained in 48% yield by Grignard addition to methyl 2,3,4-trideoxy-2-phthalimido-α-D-*erythro*-hexodialdo-1,5-pyranoside (**7**) proceeding in accordance with Cram's chelate rule, followed by methylsulfonylation. From **8**, compound **15** was readily obtained by introduction of the azide group with inversion of configuration at C-6. Compound **13** was obtained by introduction of the azide group with retention of configuration.

INTRODUCTION

Pseudomonas aeruginosa has become one of the most troublesome organisms to treat with antibiotics since the discovery of streptomycin by Waksman *et al.*[4]. Nowadays, the gentamicin C complex is widely used as an antipseudomonal drug.

Recently, sporaricin A, a novel pseudodisaccharide antibiotic, was isolated[5] and found to possess strong antibacterial activity against both Gram-positive and Gram-negative bacteria, including traditional aminoglycoside-resistant strains[6,7]. More recently, 3-de-*O*-methylsporaricin A was obtained from sporaricin B and found to be superior to sporaricin A in antimicrobial activity against *Pseudomonas aeruginosa*[2,3]

Two antipseudomonal drugs, gentamicin C_2 and 3-de-*O*-methylsporaricin A, have a similar sugar moiety; the former possesses purpurosamine B and the latter has 6-epipurpurosamine B.

*In the previous paper, we reported[1] the synthesis of the aminocyclitol part of 3-de-*O*-methylsporaricin A. In that report, we used a numbering system for sporaricins in accordance with a U.S. patent[2], and so we used the name 5-de-*O*-methylsporaricin A instead of 3-de-*O*-methylsporaricin A. Recently, Saino *et al.* have reported[3] antibacterial activity of this compound denoted as 3-de-*O*-methylsporaricin A (K-4619). Therefore, we have used the term 3-de-*O*-methylsporaricin A following this paper[3].

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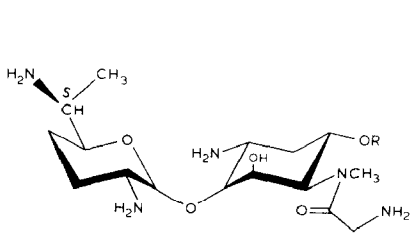
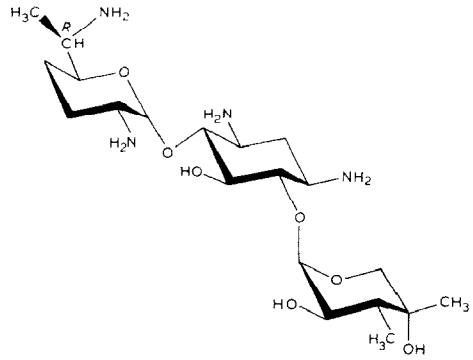


R = CH_3 Sporaricin A

R = H 3-De-*O*-methylsporaricin A



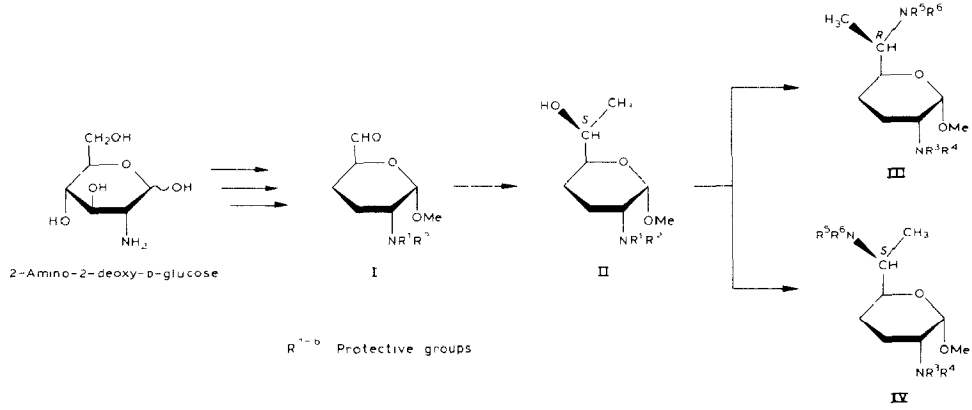
Gentamicin C_2

In relation to the synthesis of antipseudomonal drugs, we here report a novel synthesis of a protected purpurosamine B (**III**) and 6-epipurpurosamine B (**IV**).

RESULTS AND DISCUSSION

The protected purpurosamine B (**III**) and 6-epipurpurosamine B (**IV**) have been prepared by Suami *et al.*[8,9]. Their strategy was somewhat complex, and required transformation of a 6-hydroxy-7-nitroheptopyranosyl derivative into a 6-amino-7-hydroxyheptopyranosyl derivative *via* aziridine formation. Separation of diastereomeric aziridine derivatives was necessary to obtain **III**.

Our synthetic strategy (Scheme I) is simpler, involving introduction of a methyl group into the 6-aldehydo derivative **I**. We considered that Grignard reaction with **I** would afford predominantly the corresponding (6*S*) adduct (**II**), in accordance with Cram's chelate rule[10], and **II** could be readily converted into either **III** or **IV**.



2-Amino-2-deoxy-D-glucose

I

II

III

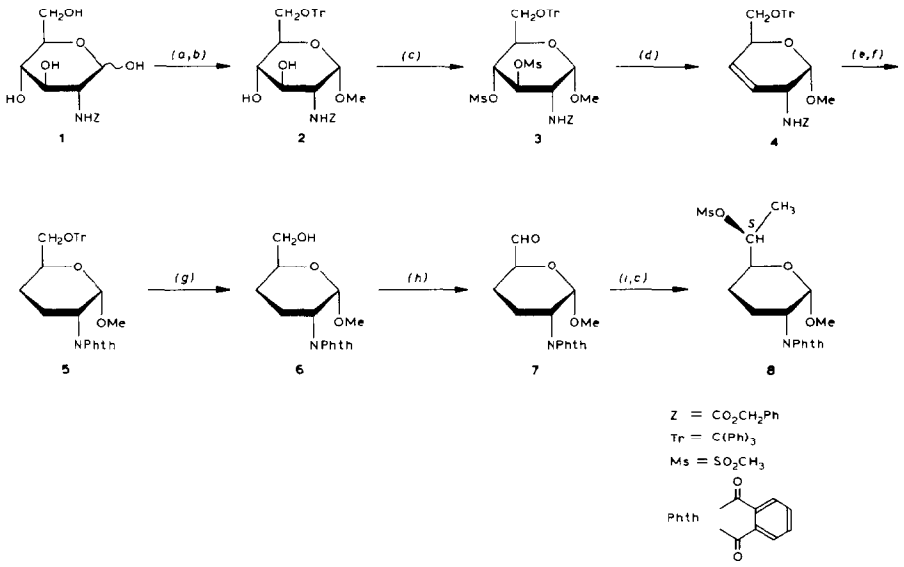
IV

R^{1-5} Protective groups

Scheme I. Strategy for total syntheses of protected purpurosamine B (**III**) and protected 6-epi-purpurosamine B (**IV**).

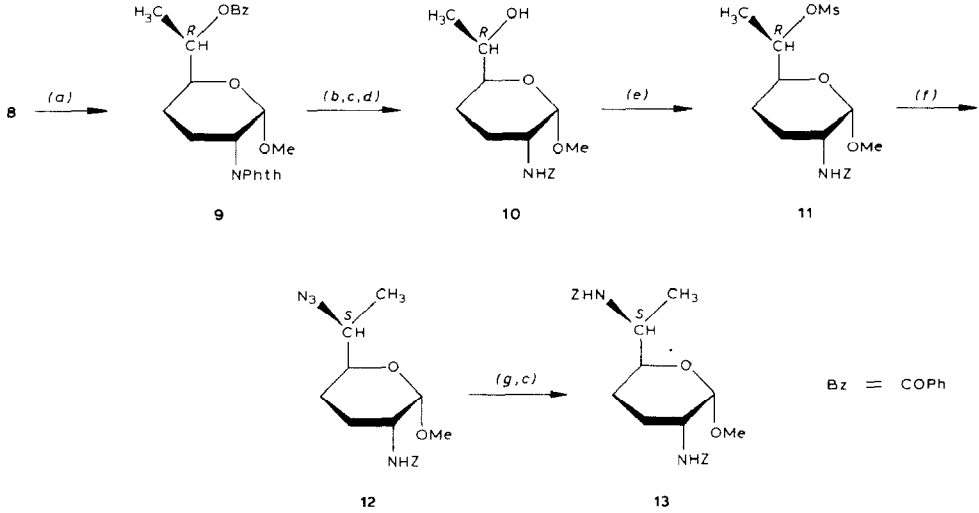
Synthesis of the key intermediate **8** is summarized in Scheme II. Treatment of 2-benzyloxycarbonylamino-2-deoxy-D-glucose[11] (**1**) with methanolic hydrogen chloride, followed by tritylation in pyridine, gave methyl 2-benzyloxycarbonylamino-2-deoxy-6-*O*-trityl-α-D-glucopyranoside (**2**) in 44% yield. Methylsulfonylation of **2** in pyridine gave the corresponding 3,4-bis(methanesulfonate) **3** in 81% yield. Treatment of **3** with an excess of zinc and sodium iodide in *N,N*-dimethylformamide[12] (DMF) afforded the corresponding 3-enose derivative **4** in 67% yield. Hydrogenation of **4** in the presence of 10% palladium-on-carbon, followed by treatment with *N*-ethoxycarbonylphthalimide and triethylamine in dichloromethane[13], gave methyl 2,3,4-trideoxy-2-phthalimido-6-*O*-trityl-α-D-glucopyranoside (**5**) in 78% yield. Removal of the trityl group in **5** with 4:1 acetic acid–water gave the corresponding 6-hydroxy derivative **6** in 81% yield. Oxidation of **6** with *N,N'*-dicyclohexylcarbodiimide–dimethyl sulfoxide–trifluoroacetic acid–pyridine gave the corresponding 6-aldehyde **7** in 78% yield. Reaction of **7** with 1.59 equivalents of methylmagnesium bromide in tetrahydrofuran for 20 min at −20 to −15° gave the corresponding adduct, which was treated (without further purification) with methanesulfonyl chloride in pyridine, followed by recrystallization from benzene to afford methyl 2,3,4,7-tetradeoxy-6-*O*-(methylsulfonyl)-2-phthalimido-β-L-*lyxo*-heptopyranoside (**8**) in 48% yield. The stereochemistry at C-6 in **8** was presumed to be (6*S*) according to Cram's chelate rule, and was confirmed by transformation of **8** into an authentic 6-epipurpurosamine B derivative (**13**) as follows.

Synthesis of the protected 6-epipurpurosamine B derivative **13** is summarized



Scheme II. Synthetic route for the key intermediate **8**. (*a*) HCl–MeOH, (*b*) TrCl–C_5H_5N, (*c*) MsCl–C_5H_5N, (*d*) Zn–NaI–DMF, (*e*) H_2–10% Pd · C–AcOH–AcOEt, (*f*) $PhthNCO_2Et$–Et_3N–CH_2Cl_2, (*g*) AcOH–H_2O (4:1), (*h*) Me_2SO–DCC–C_5H_5N–CF_3CO_2H, (*i*) MeMgBr–THF.

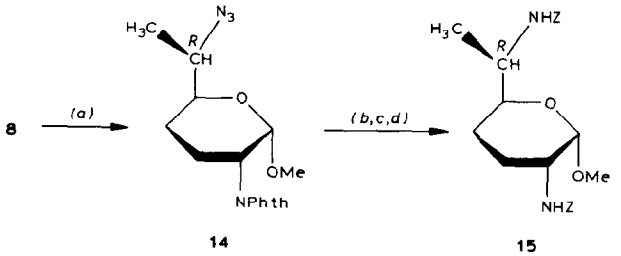
in Scheme III. Treatment of **8** with sodium benzoate in DMF gave methyl 6-*O*-benzoyl-2,3,4,7-tetradeoxy-2-phthalimido-α-D-*ribo*-heptopyranoside (**9**) in 53% yield. Exchange of the phthaloyl group at N-2 in **9** to the benzyloxycarbonyl group ($N_2H_4 \cdot H_2O$–EtOH, and then ZCl–aqueous acetone), followed by alkaline hydrolysis, gave methyl 2-benzyloxycarbonylamino-2,3,4,7-tetradeoxy-α-D-*ribo*-heptopyranoside (**10**) in 93% yield. Methylsulfonylation of **10** gave the corresponding 6-*O*-methanesulfonate **11** in 99% yield. Treatment of **11** with sodium azide in DMF afforded methyl 6-azido-2-benzyloxycarbonylamino-2,3,4,6,7-pentadeoxy-β-L-*lyxo*-heptopyranoside (**12**) in 94% yield. Hydrogenation of **12** in the presence of palladium black, followed by *N*-protection with the benzyloxycarbonyl group, gave the protected 6-epipurpurosamine B, methyl 2,6-bis(benzyloxycarbonylamino)-2,3,4,6,7-pentadeoxy-β-L-*lyxo*-heptopyranoside (**13**) in 78% yield. The sample thus prepared was identical in every respect (t.l.c., m.p., $[\alpha]_D$, i.r., ^{1}H-n.m.r., m.s.) with an authentic sample obtained from tetra-*N*-acetylsporaricin B by methanolysis[7] followed by protection with the benzyloxycarbonyl group. Thus, the protected 6-epipurpurosamine B, **13**, had been formed from **8** by introduction of the azide group with a double inversion, and the stereochemistry at C-6 in **8** was confirmed as (6*S*).



9 10 11 12 13

Scheme III. Synthetic route for protected 6-epipurpurosamine B. (*a*) BzONa–DMF, (*b*) $H_2NNH_2 \cdot H_2O$–EtOH, (*c*) ZCl, (*d*) KOH–MeOH, (*e*) MsCl–C_5H_5N, (*f*) NaN_3–DMF, (*g*) H_2–Pd–AcOH–AcOEt.

Next, the protected purpurosamine B (**15**) was synthesized by using an SN2 reaction by azide ion (Scheme IV). Treatment of **8** with sodium azide in DMF afforded methyl 6-azido-2-phthalimido-2,3,4,6,7-pentadeoxy-α-D-*ribo*-heptopyranoside (**14**) in 75% yield. Hydrogenation of **14** in the presence of palladium black, followed by treatment with hydrazine monohydrate in ethanol, and finally *N*-protection by the benzyloxycarbonyl group, gave the protected purpurosamine



Scheme IV. Synthetic route for protected purpurosamine B. (*a*) NaN_3–DMF, (*b*) H_2–Pd–AcOEt, (*c*) $H_2NNH_2 \cdot H_2O$–EtOH, (*d*) ZCl.

B, methyl 2,6-bis(benzyloxycarbonylamino)-2,3,4,6,7-pentadeoxy-α-D-*ribo*-hepto-pyranoside (**15**), in 53% yield.

Thus, Grignard reaction with the 6-*aldehydo*-hexodialdopyranose derivative (**I**) gave the key intermediate, the (6*S*) adduct (**II**), from which the protected purpurosamine B (**III**) and 6-epipurpurosamine B (**IV**) were readily synthesized.

EXPERIMENTAL

General methods. — Melting points were measured with a Yanagimoto micro melting-point apparatus and are uncorrected. Solutions were dried over magnesium sulfate and evaporated under diminished pressure below 50°. Optical rotations were measured in chloroform with a Jasco DIF-140 automatic polarimeter. I.r. spectra were recorded with a Hitachi 260-10 spectrometer. ^{1}H-N.m.r. spectra were recorded with Jeol PMX-60, MH-100, or PS-100 instruments. Chemical shifts (δ) are reported in p.p.m. from the internal standard (Me_4Si). Electron-impact (e.i.)-mass spectra were recorded with a Hitachi M-80 mass spectrometer and field-desorption (f.d.)-mass spectra were recorded with a Jeol D-100 mass spectrometer.

Methyl 2-benzyloxycarbonylamino-2-deoxy-6-O-trityl-α-D-glucopyranoside (**2**). — To methanolic hydrogen chloride, prepared from acetyl chloride (21 mL, 0.3 mol) and methanol (250 mL), was added 2-benzyloxycarbonylamino-2-deoxy-D-glucose[11] (10 g, 31.9 mmol), and the solution was boiled for 6 h under reflux. Pyridine (21 mL) was added to the mixture under ice-cooling, and the resulting solution was evaporated. The residue was dissolved in pyridine (0.2 L), and to the solution was added chlorotriphenylmethane (13.4 g, 48.1 mmol). The solution was stirred for 5.5 h at room temperature, and heated for 2 h at 100°. After evaporation, the residue was extracted with dichloromethane. The extract was washed successively with M hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and saturated aqueous sodium chloride, dried, evaporated, and chromatographed on a column of silica gel with 30:1 chloroform–ethanol as eluant to give **2** as an amorphous solid; 7.9 g, (44%); $[\alpha]_D^{24}$ +19.9° (*c* 1); ν_{max}^{Nujol} 3350 (NH) and 1720–1680 cm^{-1} (C=O); ^{1}H-n.m.r. ($CDCl_3$): δ 3.30 (s, 3 H, OCH_3), 4.67 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 5.03 (s, 2 H, CH_2Ph), and 7.14–7.53 (m, 20 H, aromatic); f.d.-m.s. *m/z* 569 ($M^+ - 1$).

Methyl 2-benzyloxycarbonylamino-2-deoxy-3,4-bis-O-(methylsulfonyl)-6-O-trityl-α-D-glucopyranoside (**3**). — A mixture of **2** (27.3 g, 47.9 mmol) and methanesulfonyl chloride (16.5 g, 144 mmol) in pyridine (0.25 L) was stirred overnight at room temperature. The solution was poured into ice–water (2.5 L) to give a precipitate. The precipitate was collected, washed with water, and dried over phosphorous pentoxide to give solid **3**; 28.1 g (81%); m.p. 162–163°, $[\alpha]_D^{24}$ +52.9° (*c* 1); ν_{max}^{Nujol} 3320 (NH), 1690 (C=O), 1540, and 1180 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.66 and 2.90 (each s, 6 H, Ms), 3.24–3.60 (m, 2 H, H-6), 3.44 (s, 3 H, OCH_3), 3.78–4.25 (m, 2 H, H-2 and H-5), 4.56–4.92 (m, 3 H, H-1, H-3, and H-4), 5.05–5.35 (m, 1 H, NH), 5.09 (s, 2 H, CH_2Ph), and 7.06–7.48 (m, 20 H, aromatic); f.d.-m.s. *m/z* 725 ($M^+ - 1$).

Anal. Calc. for $C_{36}H_{39}NO_{11}S_2$: C, 59.57; H, 5.42; N, 1.93. Found: C, 59.78; H, 5.21; N, 1.94.

Methyl 2-benzyloxycarbonylamino-2,3,4-trideoxy-6-O-trityl-α-D-erythro-hex-3-enopyranoside (**4**). — Compound **3** (5 g, 6.7 mmol) was heated with zinc powder (5.4 g, 82.6 mmol) and sodium iodide (88 g, 0.59 mol) in DMF (120 mL) for 5.5 h at 95° under nitrogen with vigorous stirring. The mixture was poured into a mixture of ice–water (0.2 L) and chloroform (0.2 L). The insoluble material was filtered off, the organic layer was separated, and the aqueous layer was extracted with chloroform (0.2 L). The combined organic solutions were washed successively with water and saturated aqueous sodium chloride, dried, and evaporated. The residue was crystallized from ethanol to give crystalline **4**; 2.41 g (67%); m.p. 135–137°, $[\alpha]_D^{24}$ −14.1° (*c* 1); ν_{max}^{Nujol} 3300 (NH), 1680 (C=O), and 1530 cm^{-1} (C=C); ^{1}H-n.m.r. ($CDCl_3$): δ 3.13–3.30 (m, 2 H, H-6), 3.40 (s, 3 H, OCH_3), 4.00–4.67 (m, 2 H, H-2 and H-5), 4.85 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.00–5.30 (broad s, 1 H, NH), 5.10 (s, 2 H, CH_2Ph), 5.58 and 5.83 (ABq, 2 H, $J_{3,4}$ 12 Hz, H-3 and H-4), and 7.10–7.60 (m, 20 H, aromatic).

Methyl 2,3,4-trideoxy-2-phthalimido-6-O-trityl-α-D-glucopyranoside (**5**). — Compound **4** (5.35 g, 10 mmol) was hydrogenated in a mixture of ethyl acetate (120 mL) and acetic acid (10 mL) in the presence of 10% palladium-on-carbon (1.6 g) for 6 h at room temperature under 1 atmosphere pressure of hydrogen. The catalyst was filtered off and washed with M hydrochloric acid. The filtrate and washings were combined and adjusted to pH 9 with 10% sodium hydroxide. The organic layer was separated, washed with saturated aqueous sodium chloride, dried, and evaporated to give methyl 2-amino-2,3,4-trideoxy-6-*O*-trityl-α-D-glucopyranoside; 3.74 g; $[\alpha]_D^{24}$ +31.2° (*c* 1); ν_{max}^{Nujol} 3360 cm^{-1} (NH_2); ^{1}H-n.m.r. ($CDCl_3$): δ 1.40–1.76 (m, 4 H, H-3 and H-4), 3.42 (s, 3 H, OCH_3), 4.54 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), and 7.08–7.52 (m, 15 H, aromatic). A mixture of the 2-amino derivative (35.4 g, 87.6 mmol) thus prepared and *N*-ethoxycarbonylphthalimide (21.3 g, 97.0 mmol) in dichloromethane (250 mL) was stirred for 2 h at room temperature, and triethylamine (12.3 mL, 88.1 mmol) was added. The mixture was stirred overnight at room temperature and boiled for 5 h under reflux. The cooled mixture was washed successively with M hydrochloric acid and saturated aqueous sodium chloride,

dried, and evaporated. The residue was crystallized from methanol to give crystalline **5**; 39.2 g (78%); m.p. 221–222°, $[\alpha]_D^{24}$ +50.1° (*c* 1); ν_{max}^{Nujol} 1765 (C=O), 1705 (C=O), 1100, and 1050 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.38–1.94 (m, 3 H, H-3 and H-4), 2.92–3.28 (m, 3 H, H-3 and H-6), 3.38 (s, 3 H, OCH_3), 3.84–4.16 (m, 1 H, H-5), 4.34 (dt, 1 H, $J_{1,2}$ 2.6 and $J_{2,3}$ 13 Hz, H-2), 4.74 (d, 1 H, $J_{1,2}$ 2.6 Hz, H-1), and 7.08–7.80 (m, 19 H, aromatic); f.d.-m.s. *m/z* 533 ($M^+ - 1$).

*Methyl 2,3,4-trideoxy-2-phthalimido-α-*D*-glucopyranoside* (**6**). — A suspension of **5** (10 g, 18.7 mmol) in 80% acetic acid (150 mL) was heated for 30 min at 100°. The mixture was cooled in an ice-bath to give a precipitate, which was filtered off. The filtrate was evaporated and the residue dissolved in chloroform. The organic solution was washed successively with saturated aqueous sodium hydrogencarbonate and saturated aqueous sodium chloride, dried, evaporated, and chromatographed on a column of silica gel with 1:1 hexane–ethyl acetate as eluant to give solid **6**; 4.39 g (81%); m.p. 144–145°, $[\alpha]_D^{24}$ +171° (*c* 1); ν_{max}^{Nujol} 3530 (OH), 1765 (C=O), and 1710 cm^{-1} (C=O); ^{1}H-n.m.r. ($CDCl_3$): δ 1.50–1.96 (m, 3 H, H-3 and H-4), 2.24–2.50 (broad s, 1 H, OH), 3.34 (s, 3 H, OCH_3), 3.20–3.42 (m, 1 H, H-3), 3.62 (broad s, 2 H, H-6), 3.82–4.08 (m, 1 H, H-5), 4.34 (dt, 1 H, $J_{1,2}$ 3 and $J_{2,3}$ 13 Hz, H-2), 4.74 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), and 7.60–7.84 (m, 4 H, Phth); f.d.-m.s. *m/z* 291 (M^+).

Anal. Calc. for $C_{15}H_{17}NO_5 \cdot 0.1\ H_2O$: C, 60.91; H, 5.86; N, 4.74. Found: C, 60.84; H, 5.90; N, 4.72.

*Methyl 2,3,4-trideoxy-2-phthalimido-α-*D*-*erythro*-hexodialdo-1,5-pyranoside* (**7**). — A mixture of **6** (12 g, 41.2 mmol), pyridine (3.3 mL, 40.8 mmol), trifluoroacetic acid (1.65 mL, 40.8 mmol), and *N,N'*-dicyclohexylcarbodiimide (25.5 g, 124 mmol) in dimethyl sulfoxide (33 mL) was stirred overnight at room temperature and heated for 30 min at 40°. To the mixture was added a methanolic solution (15 mL) of oxalic acid dihydrate (10.4 g, 82.5 mmol) at 0°. The insoluble material was filtered off and washed successively with ethyl acetate and tetrahydrofuran. The filtrate and washings were combined, washed with water, dried, evaporated, and chromatographed on a column of silica gel with 50:1 chloroform–ethanol as eluant to give a solid that was dried over phosphorus pentoxide *in vacuo* at 80° to afford solid **7**; 9.26 g (78%); m.p. 155–156°, ν_{max}^{Nujol} 1760 (C=O), 1730 (C=O), and 1700 cm^{-1} (C=O); ^{1}H-n.m.r. ($CDCl_3$): δ 3.40 (s, 3 H, OCH_3), 4.90 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 7.73–7.97 (m, 4 H, Phth), and 9.70 (s, 1 H, CHO); f.d.-m.s. *m/z* 289 (M^+).

*Methyl 2,3,4,7-tetradeoxy-6-*O*-(methylsulfonyl)-2-phthalimido-β-*L*-lyxo-heptopyranoside* (**8**). — To a solution of **7** (0.2 g, 0.69 mmol) in tetrahydrofuran (10 mL) was added dropwise 1.24M methylmagnesium bromide (0.89 mL, 1.1 mmol) under an atmosphere of argon at −20° to −15°. The mixture was stirred for 20 min at −5° to 0°. After being quenched with M hydrochloric acid, the mixture was extracted with ethyl acetate. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated. The residue was dissolved in pyridine (2 mL) and to the solution was added methanesulfonyl chloride (0.08 mL, 1 mmol) at room

temperature. After being stirred for 1 day at the same temperature, the mixture was evaporated and the residue extracted with chloroform. The extract was washed successively with M hydrochloric acid and saturated aqueous sodium chloride, dried, and evaporated. The residue was separated by preparative t.l.c. with 40:1 chloroform–methanol as developing solvent to give a solid that was recrystallized from benzene to give crystalline **8**; 128 mg (48%); m.p. 152–153°, $[\alpha]_D^{24}$ +120° (*c* 1); ν_{max}^{Nujol} 1780 (C=O), 1720 (C=O), and 1180 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.47 (d, 3 H, $J_{6,7}$ 7 Hz, H-7), 1.67–2.13 (m, 3 H, H-3 and H-4), 3.07 (s, 3 H, Ms), 3.20–3.60 (m, 1 H, H-3), 3.37 (s, 3 H, OCH_3), 3.63–4.97 (m, 4 H, H-1, H-2, H-5, and H-6), and 7.63–8.00 (m, 4 H, Phth); f.d.-m.s. *m/z* 383 (M^+).

*Methyl 6-O-benzoyl-2,3,4,7-tetradeoxy-2-phthalimido-α-*D-ribo-*heptopyranoside* (**9**). — A mixture of **8** (1 g, 2.6 mmol) and sodium benzoate (1.94 g, 13.5 mmol) in DMF (30 mL) was heated for 18 h under reflux. To the cooled mixture was added chloroform (50 mL). The resulting insoluble material was filtered off. The filtrate was evaporated and the residue extracted with chloroform. The extract was washed with water, dried, evaporated, and chromatographed on a column of silica gel with 100:1 chloroform–ethanol as eluant to give solid **9**; 559 mg (53%); m.p. 116–117°, $[\alpha]_D^{24}$ +118° (*c* 1); ν_{max}^{Nujol} 1770 (C=O), 1720 (C=O), 1705 (C=O), and 1040 cm $^{-1}$; ^{1}H-n.m.r. ($CDCl_3$): δ 1.41 (d, 3 H, $J_{6,7}$ 6 Hz, H-7), 1.71 (m, 1 H, H-3), 1.93 (m, 2 H, H-4), 3.33 (s, 3 H, OCH_3), 3.30–3.50 (m, 1 H, H-3), 3.83–4.17 (m, 1 H, H-5), 4.40 (dt, 1 H, $J_{1,2}$ 3 and $J_{2,3}$ 13 Hz, H-2), 4.78 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 5.18 (q, 1 H, $J_{5,6}$ 6 and $J_{6,7}$ 6 Hz, H-6), and 7.40–8.13 (m, 9 H, Phth and Bz); f.d.-m.s. *m/z* 409 (M^+).

*Methyl 2-benzyloxycarbonylamino-2,3,4,7-tetradeoxy-α-*D-ribo-*heptopyranoside* (**10**). — A solution of **9** (323 mg, 0.79 mmol) and hydrazine monohydrate (43 mg, 0.86 mmol) in ethanol (5 mL) was boiled for 2 h under reflux. The mixture was cooled to give a precipitate, which was filtered off. The filtrate was evaporated and the residue dissolved in a mixture of acetone (5 mL), water (3 mL), and M sodium hydroxide (2.6 mL). To the solution was added benzyl chloroformate (404 mg, 2.37 mmol) at 0°, and the mixture was stirred for 30 min at room temperature. The mixture was evaporated and the residue extracted with chloroform. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated. The residue was treated with potassium hydroxide (180 mg, 3.2 mmol) in methanol (4 mL) for 2 h at room temperature, poured into ice–water, and extracted with chloroform. The extract was dried, evaporated, and chromatographed on a column of silica gel with chloroform as eluant to give solid **10**; 226 mg (93%); m.p. 100°, $[\alpha]_D^{24}$ +76.5° (*c* 1); ν_{max}^{Nujol} 3500 (OH), 3330 (NH), 1665 (C=O), 1540, 1305, 1265, 1060, and 1010 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.15 (d, 3 H, $J_{6,7}$ 6 Hz, H-7), 1.47–2.07 (m, 4 H, H-3 and H-4), 3.37 (s, 3 H, OCH_3), 3.37–4.03 (m, 4 H, H-2, H-5, H-6, and OH), 4.63 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 4.80–5.03 (m, 1 H, NH), 5.10 (s, 2 H, CH_2Ph), and 7.30 (s, 5 H, Ph); f.d.-m.s. *m/z* 310 ($M^+ + 1$).

*Methyl 2-benzyloxycarbonylamino-2,3,4,7-tetradeoxy-6-O-(methylsulfonyl)-α-*D-ribo-*heptopyranoside* (**11**). — Methylsulfonylation of **10** (164 mg, 0.53 mmol),

as for the preparation of **3**, gave solid **11**; 203 mg (99%); m.p. 73–74°, $[\alpha]_D^{24}$ +63.8° (*c* 3.62); ν_{max}^{Nujol} 3340 (NH), 1710 (C=O), 1510, 1340, 1170, and 1040 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.40 (d, 3 H, $J_{6,7}$ 7 Hz, H-7), 1.57–2.13 (m, 4 H, H-3 and H-4), 3.00 (s, 3 H, Ms), 3.37 (s, 3 H, OCH_3), 3.57–4.00 (m, 2 H, H-2 and H-5), 4.47–5.03 (m, 3 H, H-1, H-6, and NH), 5.07 (s, 2 H, CH_2Ph), and 7.33 (s, 5 H, Ph).

*Methyl 6-azido-2-benzyloxycarbonylamino-2,3,4,6,7-pentadeoxy-β-*L*-lyxo-heptopyranoside* (**12**). — A suspension of **11** (180 mg, 0.465 mmol) and sodium azide (91 mg, 1.4 mmol) in DMF (8 mL) was heated for 1.5 h at 100°. The mixture was evaporated and the residue extracted with chloroform. The extract was washed with water, dried, evaporated, and chromatographed on a column of silica gel with 30:1 chloroform–ethanol as eluant to give solid **12**; 146 mg (94%); m.p. 90–91°, $[\alpha]_D^{24}$ +63.2° (*c* 1.88); ν_{max}^{Nujol} 3300 (NH), 2080 (N_3), 1680 (C=O), 1530, 1310, 1270, 1250, 1060, 1040, and 1000 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.20 (d, 3 H, $J_{6,7}$ 7 Hz, H-7), 1.43–2.07 (m, 4 H, H-3 and H-4), 3.20–4.00 (m, 3 H, H-2, H-5, and H-6), 3.37 (s, 3 H, OCH_3), 4.63 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 4.73–5.13 (m, 1 H, NH), 5.03 (s, 2 H, CH_2Ph), and 7.27 (s, 5 H, Ph); f.d.-m.s. *m/z* 335 (M^+ + 1).

*Methyl 2,6-bis(benzyloxycarbonylamino)-2,3,4,6,7-pentadeoxy-β-*L*-lyxo-heptopyranoside* (**13**). — Compound **12** (94 mg, 0.28 mmol) was hydrogenated in a mixture of ethyl acetate (10 mL) and acetic acid (1 mL) in the presence of palladium black (90 mg) under 3.5 atmospheres pressure of hydrogen for 5 h at room temperature. The catalyst was filtered off. The filtrate was evaporated and the residue dissolved in a mixture of tetrahydrofuran (5 mL), water (3 mL), and M sodium hydroxide (2 mL). To the mixture was added benzyl chloroformate (191 mg, 1.12 mmol) at 0°. The mixture was stirred for 1.5 h at room temperature, evaporated, and the residue extracted with chloroform. The extract was washed with saturated aqueous sodium chloride, dried, evaporated, and chromatographed on a column of silica gel with chloroform as eluant to give crystalline **13**; 93 mg (78%); m.p. 128–129° (diethyl ether–hexane), $[\alpha]_D^{24}$ +42.5° (*c* 2.5); ν_{max}^{Nujol} 3300 (NH), 1680 (C=O), 1550, and 1530 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.17 (d, 3 H, $J_{6,7}$ 6.5 Hz, H-7), 1.43–2.00 (m, 4 H, H-3 and H-4), 3.27 (s, 3 H, OCH_3), 3.40–4.07 (m, 3 H, H-2, H-5, and H-6), 4.57 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 4.77–4.93 (m, 2 H, NH), 5.03 (s, 4 H, 2 × CH_2Ph), and 7.23 (s, 10 H, 2 × Ph); f.d.-m.s. *m/z* 443 (M^+).

Anal. Calc. for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83; N, 6.33. Found: C, 64.96; H, 6.74; N, 6.29.

*Methyl 6-azido-2,3,4,6,7-pentadeoxy-2-phthalimido-α-*D*-ribo-heptopyranoside* (**14**). — Treatment of **8** (278 mg, 0.725 mmol) with sodium azide (141 mg, 2.2 mmol) as for the preparation of **12** gave solid **14**; 180 mg (75%); m.p. 119–121°, $[\alpha]_D^{24}$ +142° (*c* 1); ν_{max}^{Nujol} 2080 (N_3), 1760 (C=O), and 1700 cm^{-1} (C=O); ^{1}H-n.m.r. ($CDCl_3$): δ 1.30 (d, 3 H, $J_{6,7}$ 6 Hz, H-7), 1.57–2.20 (m, 3 H, H-3 and H-4), 3.07–3.97 (m, 3 H, H-3, H-5, and H-6), 3.30 (s, 3 H, OCH_3), 4.33 (dt, 1 H, $J_{1,2}$ 3 and $J_{2,3}$ 13 Hz, H-2), 4.73 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), and 7.50–7.87 (m, 4 H, Phth); e.i.-m.s. *m/z* 330 (M^+).

*Methyl 2,6-bis(benzyloxycarbonylamino)-2,3,4,6,7-pentadeoxy-α-*D*-ribo-hep-*

topyranoside (**15**). — Compound **14** (180 mg, 0.545 mmol) was hydrogenated in ethyl acetate (20 mL) in the presence of palladium black (90 mg) under 1 atmosphere pressure of hydrogen for 6 h at room temperature. The catalyst was filtered off and the filtrate was evaporated. The residue was boiled with hydrazine monohydrate (30 mg, 0.6 mmol) in ethanol (10 mL) for 2 h under reflux. The mixture was cooled to give a precipitate, which was filtered off. The filtrate was evaporated and the residue dissolved in a mixture of tetrahydrofuran (5.5 mL) and M sodium hydroxide (2.73 mL). To the solution was added benzyl chloroformate (372 mg, 2.18 mmol) under ice-cooling. The mixture was stirred for 2 h at room temperature and extracted with ethyl acetate. The extract was washed successively with M hydrochloric acid, M sodium hydroxide, and saturated aqueous sodium chloride, dried, evaporated, and chromatographed on a column of silica gel with 200:1 chloroform–methanol as eluant to give crystalline **15**, 128 mg (53%); m.p. 108° (diethyl ether–hexane), $[\alpha]_D^{24}$ +66.0° (*c* 3); ν_{max}^{Nujol} 3330 (NH), 1680 (C=O), 1520 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.13 (d, 3 H, $J_{6,7}$ 6.5 Hz, H-7), 1.40–2.00 (m, 4 H, H-3 and H-4), 3.27 (s, 3 H, OCH_3), 3.43–4.00 (m, 3 H, H-2, H-5, and H-6), 4.60 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 4.87–5.07 (m, 2 H, NH), 5.10 (s, 4 H, 2 × CH_2Ph), and 7.33 (s, 10 H, 2 × Ph); f.d.-m.s. *m/z* 443 (M^+).

Anal. Calc. for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.34; H, 6.83; N, 6.40.

Compound **13** *(from tetra-*N*-acetylsporaricin B).* — A suspension of methyl 2,6-bis(acetamido)-2,3,4,6,7-pentadeoxy-β-L-*lyxo*-heptopyranoside (2.44 g, 9.45 mmol), prepared from tetra-*N*-acetylsporaricin B[7], and barium hydroxide octahydrate (9.4 g, 30 mmol) in 50% aqueous methanol (100 mL) was boiled for 3 h under reflux. The mixture was adjusted to pH 6 with M sulfuric acid under ice-cooling and the insoluble material was filtered off. The filtrate was evaporated and the residue dissolved in 50% aqueous acetone (200 mL). To the solution was added dropwise a solution of benzyl chloroformate (1.7 mL, 11.9 mmol) in acetone (10 mL) at 0 to 10° with stirring, keeping the pH between 8 and 9 with M sodium hydroxide. The mixture was stirred for 1 h at the same temperature and then extracted with ethyl acetate. The extract was washed with saturated aqueous sodium chloride, dried, evaporated, and chromatographed on a column of silica gel with chloroform as eluant to give crystalline **13**; 2.58 g (96%).

REFERENCES

1 N. YASUDA, K. MATSUDA, H. TSUTSUMI, AND T. TAKAYA, *Chem. Lett.*, (1984) 1665–1668.
2 KOWA, CO. LTD , *U.S. Pat.*, (1978) 4,255,421
3 Y. SAINO, Y HATTORI, T. KOSHI, F. KOBAYASHI, T ODA, AND S. MITSUHASHI, *Antimicrob Agents Chemother.*, 26 (1984) 187–191.
4 A. SCHATZ, E. BUGIE, AND S. A. WAKSMAN, *Proc. Soc. Exp. Biol Med* , 55 (1944) 66–69
5 T. DEUSHI, A. IWASAKI, K. KAMIYA, T. KUNIEDA, T. MIZOGUCHI, M. NAKAYAMA, H. ITOH, T. MORI, AND T. ODA, *J. Antibiot.*, 32 (1979) 173–179.
6 A. IWASAKI, H. ITOH, AND T MORI, *J. Antibiot.*, 32 (1979) 180–186.
7 T. DEUSHI, M. NAKAYAMA, I. WATANABE, T. MORI, H. NAGANAWA, AND H UMEZAWA, *J Antibiot.*, 32 (1979) 187–192

8 T. SUAMI, Y. HONDA, T. KATO, M. MASU, AND K. MATSUZAWA, *Bull. Chem. Soc. Jpn.*, 53 (1980) 1372–1375.
9 Y. HONDA AND T. SUAMI, *Bull. Chem. Soc. Jpn.*, 54 (1981) 2825–2826.
10 E. L. ELIEL, in J. D. MORRISON (Ed.), *Asymmetric Synthesis*, Academic Press, New York, 1983, Vol. 2, pp. 125–155.
11 E. CHARGAFF AND M. BOVARNICK, *J. Biol. Chem.*, 118 (1937) 421–426.
12 R. S. TIPSON AND A. COHEN, *Carbohydr. Res.*, 1 (1965) 338–339.
13 G. H. L. NEFKENS, G. I. TESSER, AND R. J. F. NIVARD, *Recl. Trav. Chim. Pays-Bas*, 79 (1960) 688–698.