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Synthesis on 1,4-Diaminocyclitol Antibiotics. IV. Synthesis of 7′-Phenylfortimicin A and 7′-Phenyl-6′-epifortimicin A

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7′-Phenylfortimicin A and 7′-phenyl-6′-epifortimicin A have been synthesized by condensation of newly prepared 1-*O*-acetyl-2,6-bis(2,4-dinitrophenylamino)-2,3,4,6,7-pentadeoxy-7-phenyl-L-*lyxo*-heptopyranose and -D-*ribo*-heptopyranose, respectively, with 2,5-di-*O*-benzoyl-1,4-bis[*N*-(methoxycarbonyl)]fortamine B, followed by deprotection.

In the preceding paper,[1] the chemical synthesis of 7′-propylfortimicin A and its antibacterial assay were reported. In continuation of our study on modification of the diamino sugar moiety of antibiotic fortimicins,[1,2] replacement of the 6′-methyl group with benzyl group would be of interest because of anticipated enhancement both in its lipohilic nature and in the steric congestion. We now describe the synthesis and biological activities of 7′-phenylfortimicin A and 7′-phenyl-6′-epifortimicin A.

Results and Discussion

1-*O*-Acetyl-2,6-bis(2,4-dinitrophenylamino)-2,3,4,6,7-pentadeoxy-7-phenyl-L-*lyxo*-heptopyranose (**7**) and -D-*ribo*-heptopyranose (**8**) have been first prepared from methyl 2-acetamido-2,3,4,6-tetradeoxy-6-nitro-α-*erythro*-hexopyranoside (**1**).[1]

The nitro aldol reaction of **1** with benzaldehyde was effected in the presence of methanolic sodium methoxide in methanol for 2 h at 0 °C. The products were acetylated with acetic anhydride and boron trifluoride etherate, and then hydrogenated with sodium borohydride in dimethyl sulfoxide to give an inseparable mixture of methyl 2-acetamido-2,3,4,6,7-pentadeoxy-6-nitro-7-phenyl-β-L-*lyxo*- and -α-D-*ribo*-heptopyranoside (**2**) in 54% yield. The reaction using KF or CsF in acetonitrile instead of sodium methoxide resulted in a poor yield. However, when excess KF was used, **2** was obtained in 38% yield. Catalytic hydrogenation of **2** with Raney nickel in a mixture of ethanol and ethyl acetate, followed by *N*-acetylation with acetic anhydride, gave two compounds (**3**, 47% and **4**, 15%) after chromatography. The value of specific rotation +129° of **4** was more dextrorotatory than +28.2° of **3**. In addition, the ^{13}C NMR spectra of **3** and **4** revealed that C-7 signal of **4** shifted upfield by 1.83 ppm compared to that of **3** (Table 1). These results corresponded to those of the respective 7-propyl derivatives. The stereochemistry at C-6[3] of **3** and **4** has thus been confirmed as depicted in Scheme.

Compound **3** was *N*-deacetylated with sodium hydroxide in refluxing 95% aqueous 2-methoxyethanol and the free base was converted to the bis[*N*-(2,4-dinitrophenyl)] derivative **5** in 81% yield. Hydrolysis of **5** with acetic acid containing 2M†† hydrochloric acid, followed by acetylation, gave the acetate (**7**) in 61% yield.

Table 1. ^{13}C NMR Chemical Shifts[a] of **3** and **4**

	3	**4**
C-1	99.71	99.56
C-2	49.79	49.31
C-3	24.74	25.18
C-4	28.29	28.22
C-5	69.77	71.30
C-6	54.78	55.34
C-7	38.75	36.93
Phenyl	127.27	127.20
Phenyl	129.26	129.24
Phenyl	130.21	130.19
Phenyl	140.07	140.28
OMe	55.75	55.56
$\underline{C}OCH_3$	173.07	172.90
	172.83	172.76
$CO\underline{C}H_3$	22.38	22.45
	22.50	22.53

a) In parts per million downfield from TMS.

Condensation of **7** with 2,5-di-*O*-benzoyl-1,4-bis[*N*-(methoxycarbonyl)]fortamine B (**9**)[4] in 1,2-dichloroethane in the presence of trimethylsilyl trifluoromethanesulfonate under argon gave a single condensate (**10**) in 43% yield. The ^{1}H NMR spectrum of **10** exhibited a doublet (δ 5.38, J=3 Hz) due to H-1′, supporting the conformation of the anomeric proton to be equatorial in the α-D-glycoside. Hydrolysis of **10** in refluxing aqueous 1,4-dioxane with barium hydroxide, followed by treatment with Amberlite IRA-400 (OH^-) resin, gave 7′-phenylfortimicin B (**12**) in 70% yield. Compound **12** was converted into the tris[*N*-(benzyloxycarbonyl)] derivative (**14**) in 54% yield. Treatment of **14** with *N*-[*N*-(benzyloxycarbonyl)glycyloxy]succinimide and triethylamine afforded the tetrakis-[*N*-(benzyloxycarbonyl)] derivative of 7′-phenylfortimicin A (**16**) in 77% yield. Finally, catalytic hydrogenation of **16** in the presence of 10% palladium on

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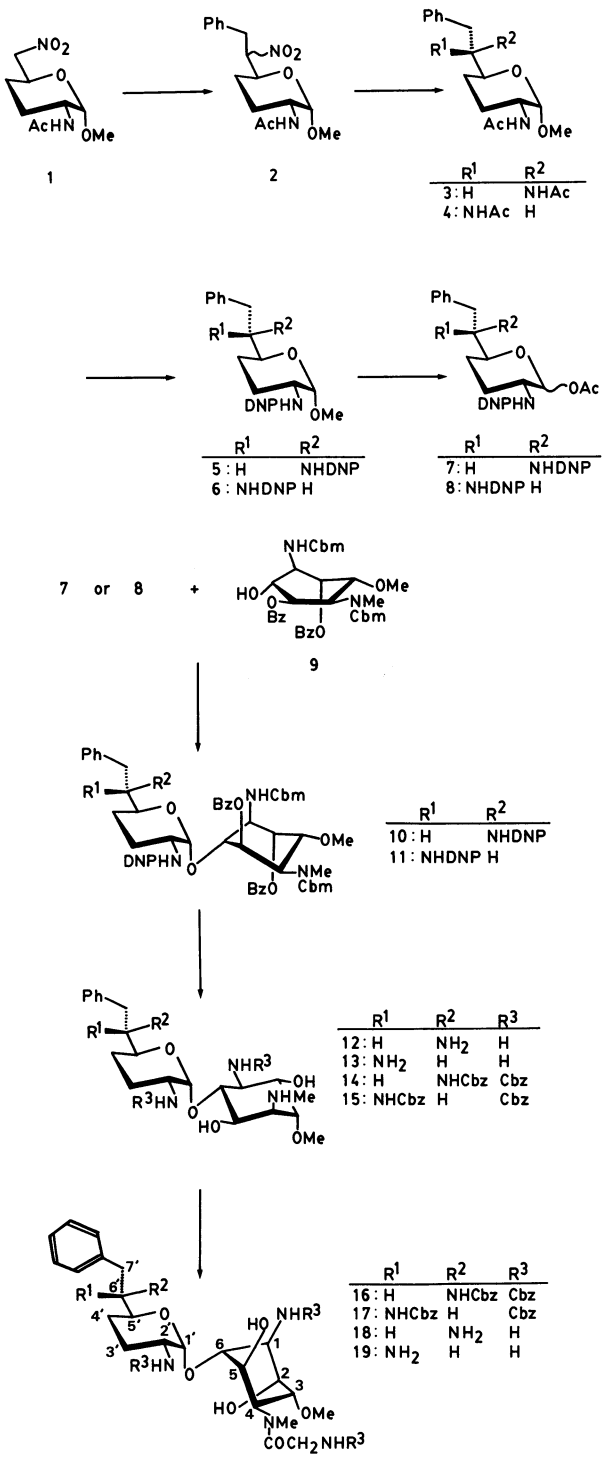
††1 M=1 mol dm^{-3}.

Table 2. Antimicrobial Activity of **18**, **19**, and Fortimicin A[a)]

Test Organisms	18	19	FM A
Streptococcus faecalis KY4280	12.5	>100	6.3
Pseudomonas aeruginosa KY4276	25	>100	6.3
Staphylococcus aureus KY4279	0.2	0.39	0.2
Escherichia coli KY4271	3.1	3.1	0.78
Bacillus subtilis KY4273	0.2	3.1	0.1
Shigella sonnei KY4281	3.1	25	1.6
Klebsiella pneumoniae KY4275	0.39	1.6	0.2

a) Minimum inhibitory concentration in μg ml^{-1}.



charcoal, followed by treatment with AG1-X2 (SO_4^{2-}) resin, gave 7′-phenylfortimicin A (**18**) as the sulfate.

7′-Phenyl-6′-epifortimicin A (**19**) has been similarly synthesized starting from **4** as described in the preparation of **18** from **3**.

The minimum inhibitory concentrations of **18** and **19** were listed together with those of fortimicin A (Table 2). 7′-Phenylfortimicin A (**18**) exhibited slightly weak activity compared to that of fortimicin A against many micro organisms. However, 7′-phenyl-6′-epifortimicin A (**19**) showed weak activity. Generally, the 6′-epi analogs[5)] of fortimicin A seem to be less active against micro organisms than those of the natural type.

Experimental[6)]

Methyl 2-Acetamido-2,3,4,6,7-pentadeoxy-6-nitro-7-phenyl-β-L-*lyxo*- and -α-D-*ribo*-heptopyranoside (2). To a solution of methyl 2-acetamido-2,3,4,6-tetradeoxy-6-nitro-α-D-*erythro*-hexopyranoside[1)] (**1**) (1.50 g) in methanol (3 ml) were added benzaldehyde (0.70 ml) and 1M sodium methoxide methanolic solution (6.7 ml) under ice cooling, and the mixture was stirred at 0 °C for 2 h. After neutralization with Amberlite IR-120 (H^+) resin, the mixture was concentrated. The residue was dissolved in acetic anhydride (10 ml) and boron trifluoride etherate (1.5 ml) was added to it under ice cooling. After stirring for 1 h, the mixture was poured into ice water (100 ml) and the mixture was extracted with dichloromethane (150 ml). The extract was successively washed with saturated aqueous $NaHCO_3$ (300 ml), brine (100 ml) and water (100 ml), and dried. After concentration, the residue was dissolved in dimethyl sulfoxide (18 ml), and a suspension of $NaBH_4$ (200 mg) in dimethyl sulfoxide (2 ml) was added to it. After stirring for 0.5 h, the mixture was acidified with Amberlite IR-120 (H^+) resin. The mixture was extracted with chloroform (100 ml) and the extract was dried. After concentration, the residue was chromatographed on silica gel with chloroform–methanol (90 : 1) to give **2** (1.13 g, 54%) and recovered **1** (0.60 g): IR (KBr) 1640 (amide), 1545, 1370 (NO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.42—2.10 (4H, m, H-3,4), 1.96 (3H, s, NAc), 3.08 (2H, m, H-7), 3.33 (3H, s, OMe), 4.15 (2H, m, H-2,5), 4.58 (1H, d, *J*=3 Hz, H-1), 4.65 (1H, m, H-6), 5.73 (1H, d, *J*=8 Hz, NH), 7.04—7.42 (5H, m, phenyl).

Found: C, 59.23; H, 6.79; N, 8.46%; *m/z*, 323.1607. Calcd for $C_{16}H_{22}N_2O_5$: C, 59.62; H, 6.88; N, 8.69%; M+1, 323.1605.

Methyl 2,6-Diacetamido-2,3,4,6,7-pentadeoxy-7-phenyl-β-L-*lyxo*- (3) and -α-D-*ribo*-heptopyranoside (4). A solution of **2** (1.10 g) in ethanol (10 ml) and ethyl acetate (10 ml) was hydrogenated in the presence of Raney nickel in an initial hydrogen pressure of 3.4 kg cm^{-2} overnight. After removal of the catalyst, the solution was concentrated. The residue was acetylated with acetic anhydride (5 ml) in methanol (10 ml). The product was purified by chromatography on silica gel with toluene–ethanol (10 : 1) to give **3** (546 mg, 47%) and **4** (170 mg, 15%): Compound **3**; mp 241—242 °C; $[\alpha]_D^{20}$ +28.2° (*c* 0.77, MeOH); ^{1}H NMR (CD_3OD) δ=1.50—1.82 (4H, m, H-3,4), 1.87, 1.94 (each 3H, s, NAc), 2.83 (1H, dd, *J*=8.5, 14 Hz, H-7a), 2.91 (1H, dd, *J*=7, 14 Hz, H-7b), 3.42 (3H, s, OMe), 3.77 (1H, ddd, *J*=2.5, 6, 8.5 Hz, H-5), 3.90 (1H, ddd, *J*=3, 4.5, 11.5 Hz, H-2), 4.18 (1H, ddd, *J*=2.5,

7, 8.5 Hz, H-6), 4.67 (1H, d, J=3 Hz, H-1), 7.24 (5H, m, phenyl).

Found: C, 64.81; H, 7.48; N, 8.21%. Calcd for $C_{18}H_{26}N_2O_4$: C, 64.65; H, 7.84; N, 8.38%.

Compound **4**; mp 266.5—267.5 °C; $[\alpha]_D^{20}$ +129° (c 1.41, MeOH); ^{1}H NMR (CD_3OD) δ=1.60—1.90 (4H, m, H-3,4), 1.79, 1.94 (each 3H, s, NAc), 2.61 (1H, dd, J=11 Hz, 14 Hz, H-7a), 3.15 (1H, dd, J=4, 14 Hz, H-7b), 3.40 (3H, s, OMe), 3.70 (1H, ddd, J=2, 6, 11 Hz, H-5), 3.93 (1H, ddd, J=3, 6, 11 Hz, H-2), 4.07 (1H, ddd, J=4, 6, 11 Hz, H-6), 4.68 (1H, d, J=3 Hz, H-1), 7.24 (5H, m, phenyl).

Found: C, 64.44; H, 7.77; N, 8.14%. Calcd for $C_{18}H_{26}N_2O_4$: C, 64.65; H, 7.84; N, 8.38%.

Methyl 2,6-Bis(2,4-dinitrophenylamino)-2,3,4,6,7-pentadeoxy-7-phenyl-β-L-*lyxo*-heptopyranoside (5). A solution of **3** (435 mg) in 95% aqueous 2-methoxyethanol (20 ml) containing sodium hydroxide (1.6 g) was refluxed for 26 h. An additional amount of sodium hydroxide (1.6 g) was added to it and the reflux was continued for further 21 h. After cooling, the mixture was neutralized with 1M hydrochloric acid and concentrated. The residue was extracted with cold ethanol and the solution was concentrated. The residue was dissolved in methanol (20 ml), and 1-fluoro-2,4-dinitrobenzene (0.50 ml) and triethylamine (2.0 ml) were added to it. After stirring for 20 h, the mixture was extracted with chloroform (30 ml), and the extract was dried and concentrated to give a residue, which was chromatographed on silica gel with toluene–2-butanone (30 : 1) to give **5** (612 mg, 81%). Recrystallization from acetone–2-propanol gave an analytical sample: mp 109—114 °C; $[\alpha]_D^{20}$ −147° (c 0.95, acetone); IR (KBr) 1620, 1590 (aromatic), 1520, 1330 (NO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.66—2.12 (4H, m, H-3,4), 3.10 (2H, d, J=7 Hz, H-7), 3.63 (3H, s, OMe), 5.00 (1H, d, J=3 Hz, H-1), 6.57, 6.95 (each 1H, d, J=10 Hz, H-6 of DNP), 8.03, 8.21 (each 1H, dd, J=3, 10 Hz, H-5 of DNP), 9.03, 9.09 (each 1H, d, J=3 Hz, H-3 of DNP).

Found: C, 53.36; H, 4.52; N, 14.45%. Calcd for $C_{26}H_{26}N_6O_{10}$: C, 53.61; H, 4.50; N, 14.43%.

1-*O*-Acetyl-2,6-bis(2,4-dinitrophenylamino)-2,3,4,6,7-pentadeoxy-7-phenyl-L-*lyxo*-heptopyranose (7). A solution of **5** (610 mg) in acetic acid (30 ml) containing 2M hydrochloric acid (5 ml) was stirred at 80 °C for 5 h. After cooling, the mixture was concentrated to the half volume and extracted with chloroform (60 ml). The extract was successively washed with saturated aqueous $NaHCO_3$ (20 ml) and water (20 ml), dried, and concentrated. The residue was acetylated with acetic anhydride (5 ml) in pyridine (10 ml). The mixture was concentrated to a residue, which was extracted with chloroform (100 ml) and the extract was successively washed with 1M hydrochloric acid (30 ml), saturated aqueous $NaHCO_3$ (30 ml) and water (30 ml), and dried. After concentration, the residue was chromatographed on silica gel with toluene–2-butanone (30 : 1) to give **7** (386 mg, 61%): mp 223 °C (decomp); $[\alpha]_D^{23}$ −172° (c 1.18, pyridine); IR (KBr) 1760 (ester), 1620, 1590 (aromatic), 1520, 1340 (NO_2) cm^{-1}; ^{1}H NMR (pyridine-d_5) δ=2.31 (3H, s, OAc), 3.20 (2H, d, J=9 Hz, H-7), 7.47 (5H, m, phenyl), 8.34 (2H, dd, J=3 Hz, 10 Hz, H-5 of DNP).

Found: C, 53.00; H, 4.33; N, 13.90%. Calcd for $C_{27}H_{26}N_6O_{11}$: C, 53.12; H, 4.29; N, 13.77%.

2,5-Di-*O*-benzoyl-2′,6′-bis[*N*-(2,4-dinitrophenyl)]-1,4-bis[*N*-(methoxycarbonyl)]-7′-phenylfortimicin B (10). To a solution of **7** (350 mg) and 2,5-di-*O*-benzoyl-1,4-bis[*N*-(methoxycarbonyl)]fortamine B (**9**)[1] (310 mg) in freshly distilled 1,2-dichloroethane in the presence of powdered molecular sieve 4A (300 mg) was added trimethylsilyl trifluoromethanesulfonate (0.12 ml), and the mixture was stirred for 5.5 h under argon. An insoluble material was filtered and washed with chloroform. The filtrate was successively washed with 5% aqueous $NaHCO_3$ (40 ml) and water (40 ml), dried, and concentrated to give a residue, which was chromatographed on silica gel with toluene–2-butanone (15 : 1) to give **10** (274 mg, 43%). Recrystallization from acetone–2-propanol gave an analytical sample: mp 147—153 °C; $[\alpha]_D^{27}$ −128° (c 1.08, acetone); ^{1}H NMR ($CDCl_3$) δ=2.84 (3H, s, NMe), 3.06 (2H, m, H-7′), 3.46 (3H, s, OMe), 3.56 (6H, s, Cbm×2), 4.12 (1H, dd, J=4, 9 Hz, H-3), 4.36 (1H, bs, H-6), 5.32 (1H, d, J=10 Hz, NH-1), 5.38 (1H, d, J=3 Hz, H-1′), 5.51 (1H, t, J=5 Hz, H-5), 5.78 (1H, bs, H-2), 6.32 and 6.84 (each 1H, d, J=9 Hz, H-6 of DNP), 7.15 (5H, s, phenyl), 7.40—7.66 (6H, m, benzoyl), 7.86 and 8.08 (3H and 1H, each d, J=8.5 Hz, benzoyl), 8.21 (2H, dd, J=3, 9 Hz, H-5 of DNP×2), 8.61 and 8.86 (each 1H, d, J=9 Hz, NH-2′,6′), 8.99 and 9.10 (each 1H, d, J=3 Hz, H-3 of DNP).

Found: C, 56.27; H, 4.84; N, 10.31%. Calcd for $C_{51}H_{53}N_8O_{19}$: C, 56.62; H, 4.94; N, 10.36%.

7′-Phenylfortimicin B (12). A stirred solution of **10** (206 mg) in dioxane (10 ml) and water (3 ml) in the presence of barium hydroxide octahydrate (3.5 g) was refluxed for 6 h. After cooling, the solid was filtered. Carbon dioxide was introduced to the filtrate and an insoluble material was filtered. After concentration, the residue was treated with Amberlite IRA-400 (OH^-) resin (10 ml) in a mixture of water (5 ml), methanol (10 ml) and acetone (10 ml). After stirring for 18 h, the resin was filtered, and the filtrate was concentrated. The residue was chromatographed on a column of Amberlite CG-50 (NH_4^+) resin (35 ml) with 0—0.15 M aq ammonia with gradient increase in concentration to give **12** (56 mg, 70%): $[\alpha]_D^{23}$ −23.8° (c 1.05, water); ^{1}H NMR (CD_3OD) δ=1.72 (4H, m, H-3′,4′), 2.39 (3H, s, NMe), 3.45 (3H, s, OMe), 7.27 (5H, s, phenyl).

Found: C, 55.79; H, 8.12; N, 12.40%. Calcd for $C_{21}H_{36}N_4O_5 \cdot 2/3H_2CO_3$: C, 55.86; H, 8.08; N, 12.03%.

1,2′,6′-Tris[*N*-(benzyloxycarbonyl)]-7′-phenylfortimicin B (14). To a solution of **12** (51 mg) in methanol (4 ml) was added *N*-(benzyloxycarbonyloxy)succinimide (92 mg) under ice cooling and the mixture was stirred for 1 h at 0 °C, and stirring was continued for 20 h at room temperature. The mixture was extracted with chloroform (60 ml) and the extract was dried. After concentration, the residue was chromatographed on silica gel with chloroform–methanol (50 : 1) to give **14** as a solid (53 mg, 54%): $[\alpha]_D^{24}$ +3.8° (c 1.98, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=1.53 (4H, m, H-3′,4′), 2.30 (3H, bs, NMe), 3.43 (3H, s, OMe), 7.18, 7.28 and 7.31 (20H in total, each s, phenyl×4).

Found: C, 65.46; H, 6.70; N, 6.65%. Calcd for $C_{45}H_{54}N_4O_{11}$: C, 65.37; H, 6.58; N, 6.78%.

1,2′,6′-Tris[*N*-(benzyloxycarbonyl)]-4-[*N*-[*N*-(benzyloxycarbonyl)glycyl]]-7′-phenylfortimicin B (16). To a solution of **14** (44 mg) in dioxane (5 ml) were added *N*-[*N*-(benzyloxycarbonyl)glycyloxy]succinimide (20 mg) and triethylamine (0.01 ml), and the mixture was stirred for 14 h at 50 °C. After addition of 5% aqueous $NaHCO_3$ (10 ml), the mixture was extracted with chloroform (30 ml) and the extract was dried. After concentration, the residue was chromatographed on silica gel with chloroform–methanol

(50 : 1) to give **16** as a solid (41 mg, 77%): $[\alpha]_D^{24}$ +24.8° (*c* 1.04, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=1.64 (4H, m, H-3′,4′), 2.80 (5H, bs, NMe and H-7′), 3.29 (3H, s, OMe), 7.22, 7.27, 7.30, and 7.34 (25H in total, each s, phenyl×5).

Found: C, 64.71; H, 6.29; N, 6.76%. Calcd for $C_{55}H_{63}N_5O_{14}$: C, 64.89; H, 6.24; N, 6.88%.

7′-Phenylfortimicin A (18). A solution of **16** (28 mg) in methanol (2 ml) was hydrogenated in the presence of 10% palladium on charcoal (30 mg) under hydrogen atmosphere for 3 h. After removal of the catalyst, the filtrate was concentrated. The residue was dissolved in water, and then the solution was passed through a column of AG1-X2 (SO_4^{2-}) resin (2 ml). The eluent was concentrated to give a solid of 7′-phenylfortimicin A (**18**, 14 mg) as the sulfate: $[\alpha]_D^{24}$ +52.5° (*c* 0.48, water); ^1H NMR (D_2O) δ=1.76, 2.10 (4H in total, each m, H-3′,4′), 3.18 (3H, s, NMe), 3.54 (3H, s, OMe), 5.37 (1H, d, *J*=3 Hz, H-1′), 7.48 (5H, m, phenyl).

MS (SIMS) Found: *m/z*, 482. Calcd for $C_{23}H_{40}N_5O_6$: M+1, 482.

Methyl 2,6-Bis(2,4-dinitrophenylamino)-2,3,4,6,7-pentadeoxy-7-phenyl-α-D-*ribo*-heptopyranoside (6). A solution of **4** (392 mg) in 95% aqueous 2-methoxyethanol (18 ml) containing sodium hydroxide (1.93 g) was refluxed for 29 h. After neutralization with 1M hydrochloric acid, the mixture was concentrated and the residue was extracted with cold ethanol. The solution was concentrated to a residue, which was treated with 1-fluoro-2,4-dinitrobenzene (0.73 ml) and triethylamine (2.0 ml) in methanol (10 ml) for 13 h. The product was purified as described for the preparation of **5** to give **6** (410 mg, 60%): mp 102—108 °C; $[\alpha]_D^{20}$ +132° (*c* 1.29, acetone); IR (KBr) 1620, 1590 (aromatic), 1515, 1335 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.95 (4H, m, H-3,4), 2.72—3.35 (2H, m, H-7), 3.53 (3H, s, OMe), 4.91 (1H, d, *J*=3 Hz, H-1), 6.06, 6.93 (each 1H, d, *J*=10 Hz, H-6 of DNP), 7.20 (5H, s, phenyl), 7.92, 8.20 (each 1H, dd, *J*=3 Hz, 10 Hz, H-5 of DNP), 8.27, 8.89 (each 1H, d, *J*=9 Hz, NH-2,6), 8.97, 9.07 (each 1H, d, *J*=3 Hz, H-3 of DNP).

Found: C, 53.70; H, 4.50; N, 14.39%. Calcd for $C_{26}H_{26}N_6O_{10}$: C, 53.61; H, 4.50; N, 14.43%.

1-*O*-Acetyl-2,6-bis(2,4-dinitrophenylamino)-2,3,4,6,7-pentadeoxy-7-phenyl-D-*ribo*-heptopyranose (8). A solution of **6** (390 mg) in acetic acid (20 ml) containing 2M hydrochloric acid (3.5 ml) was stirred at 80 °C for 6 h. The crude product was acetylated with acetic anhydride (5 ml) in pyridine (10 ml), and the product was purified as described for the preparation of **7** to give **8** (337 mg, 83%): mp 104—108 °C; $[\alpha]_D^{25}$ +52.0° (*c* 1.2, acetone); IR (KBr) 1755 (ester), 1615, 1590 (aromatic), 1515, 1330 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.19 (3H, s, OAc), 3.05 (2H, m, H-7), 4.12 (3H, m, H-2,5,6), 5.70 (1/5H, d, *J*=9 Hz, H-1), 6.34 (4/5H, d, *J*=3 Hz, H-1), 6.87, 7.08 (each 1H, d, *J*=10 Hz, H-6 of DNP), 7.21 (5H, s, phenyl), 8.06, 8.26 (each 1H, dd, *J*=3 Hz, 10 Hz, H-5 of DNP), 8.54, 8.71 (each 1H, d, *J*=9 Hz, NH-2,6), 8.98, 9.05 (each 1H, d, *J*=3 Hz, H-3 of DNP).

Found: C, 53.28; H, 4.39; N, 13.55%. Calcd for $C_{27}H_{26}N_6O_{11}$: C, 53.12; H, 4.29; N, 13.77%.

2,5-Di-*O*-benzoyl-2′,6′-bis-*N*-(2,4-dinitrophenyl)-1,4-bis-*N*-(methoxycarbonyl)-7′-phenyl-6′-epifortimicin B (11). To a solution of **10** (330 mg) and **9** (290 mg) in freshly distilled 1,2-dichloroethane (8 ml) in the presence of powdered molecular sieve 4A (300 mg) was added trimethylsilyl trifluoromethanesulfonate (0.11 ml) and the mixture was stirred for 2 h. The product was purified as described for the preparation of **10** to give **11** (206 mg, 35%). Recrystallization from acetone-2-propanol gave an analytical sample: mp 144—149 °C; $[\alpha]_D^{25}$ +60.5° (*c* 1.03, acetone); ^1H NMR ($CDCl_3$) δ=2.72 (1H, dd, *J*=10 Hz, 14 Hz, H-7′a), 2.88 (3H, s, NMe), 3.06 (1H, d, *J*=4 Hz, 14 Hz, H-7′b), 3.47 (3H, s, OMe), 3.50, 3.55 (each 3H, s, Cbm), 5.18 (1H, d, *J*=10 Hz, NH-1), 5.27 (1H, d, *J*=3 Hz, H-1′), 5.47 (1H, t, *J*=5 Hz, H-5), 5.73 (1H, bs, H-2), 6.66, 6.80 (each 1H, *J*=9 Hz, H-6 of DNP), 7.16 (5H, m, pheny), 7.38—7.66 (6H, m, benzoyl), 7.88 (3H, m, H-5 of DNP×2 and benzoyl), 8.06, 8.20 (3H in total, each d, *J*=9 Hz, benzoyl), 8.66, 8.83 (each 1H, d, *J*=9 Hz, NH-2′,6′), 8.98 (1H, d, *J*=3 Hz, H-3 of DNP), 9.06 (1H, bs, H-3 of DNP).

Found: C, 56.23; H, 4.84; N, 10.07%. Calcd for $C_{51}H_{53}N_8O_{19}$: C, 56.62; H, 4.94; N, 10.36%.

7′-Phenyl-6′-epifortimicin B (13). A stirred solution of **11** (172 mg) in dioxane (10 ml) and water (3 ml) in the presence of barium hydroxide octahydrate (3.0 g) was refluxed for 21 h. The solid was filtered and carbon dioxide was introduced to the filtrate, and then an insoluble material was filtered. After concentration, the residue was treated with Amberlite IRA-400 (OH^-) resin (10 ml) in a mixture of water (5 ml), methanol (10 ml), and acetone (10 ml) for 43 h. The product was purified as described for the preparation of **12** to give **13** (47 mg, 70%): $[\alpha]_D^{26}$ +42.8° (*c* 0.57, H_2O); ^1H NMR (CD_3OD) δ=1.69 (4H, m, H-3′,4′), 2.42 (3H, s, NMe), 3.45 (3H, s, OMe), 4.98 (1H, d, *J*=3 Hz, H-1′), 7.32 (5H, s, phenyl).

Found: C, 57.12; H, 8.33; N, 12.66%. Calcd for $C_{21}H_{36}N_4O_5 \cdot 1/3H_2CO_3$: C, 57.56; H, 8.30; N, 12.58%.

1,2′,6′-Tris[*N*-(benzyloxycarbonyl)]-7′-phenyl-6′-epifortimicin B (15). To a solution of **13** (37 mg) in methanol (3 ml) was added *N*-(benzyloxycarbonyloxy)succinimide (65 mg) under ice cooling and the mixture was stirred for 1 h at 0 °C, and stirring was continued for 6 h at room temperature. The product was purified as described for the preparation of **14** to give **15** as a solid (39 mg, 56%): $[\alpha]_D^{26}$ +32.3° (*c* 0.36, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=1.58 (4H, m, H-3′,4′), 2.34 (3H, bs, NMe), 3.42 (3H, s, OMe), 7.18, 7.28, and 7.33 (20H in total, each s, phenyl×4).

Found: C, 64.94; H, 6.56; N, 6.29%. Calcd for $C_{45}H_{54}N_4O_{11} \cdot 1/2H_2O$: C, 64.66; H, 6.63; N, 6.70%.

1,2′,6′-Tris[*N*-(benzyloxycarbonyl)]-4-[*N*-[*N*-(benzyloxycarbonyl)glycyl]]-7′-phenyl-6′-epifortimicin B (17). To a solution of **15** (29 mg) in dioxane (3 ml) were added *N*-[*N*-(benzyloxycarbonyl)glycyloxy]succinimide (15 mg) and triethylamine (0.01 ml), and the mixture was stirred for 21 h at 50 °C. The product was purified as described for the preparation of **16** to give **17** as a solid (29 mg, 79%): $[\alpha]_D^{26}$ +60.0° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=1.65 (4H, m, H-3′,4′), 2.70 (3H, bs, NMe), 3.30 (3H, bs, OMe), 7.21, 7.29, 7.35 (25H in total, each s, phenyl×5).

Found: C, 64.49; H, 6.29; N, 6.72%. Calcd for $C_{55}H_{63}N_5O_{14}$: C, 64.89; H, 6.24; N, 6.88%.

7′-Phenyl-6′-epifortimicin A (19). A solution of **17** (26 mg) in methanol (2 ml) was hydrogenated in the presence of 10% palladium on charcoal (30 mg) under hydrogen atmosphere for 3 h. The product was purified as described for the preparation of **18** to give a solid of 7′-phenyl-6′-epifortimicin A (**19**, 11 mg) as the sulfate: $[\alpha]_D^{26}$ +104° (*c* 0.55, water); ^1H NMR (D_2O) δ=1.70, 1.92 (each 2H, m, H-3′,4′), 3.12 (3H, s, NMe), 3.50 (3H, s, OMe), 7.44 (5H, m, phenyl).

MS (SIMS) Found: *m/z*, 482. Calcd for $C_{23}H_{40}N_5O_6$: M+1, 482.

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3) In a manner as described in the preceding paper,[1] the structure of **4** could be assigned on the basis of both ^{13}C NMR (the upfield shift of C-7 of **4** compared to that of **3** due to antiperiplanar arrangement of C-7/C-6/C-5/O-5) and the ^{1}H NMR ($J_{5,6}$=6 Hz) data.

4) Judging from the ^{1}H NMR data, the conformation of **9** is assumed to adopt the skew-boat form[1] and that of the fortamine moiety of **10** or **11** the chair form. However, the conformations of the fortamine moieties of **12**—**19** would not be deduced by analogy with these results.

5) J. Tadanier, R. Hallas, J. R. Martin, and R. S. Stanaszek, *Tetrahedron*, **37**, 1309 (1981).

6) The general procedures used in the present work have been described in the preceding paper.[1]