Synthesis of (+)-Furanomycin: Use of Radical Cyclization

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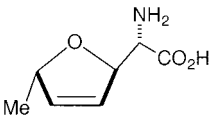
The bacterial metabolite furanomycin (**1**)[1,2] is an antibiotic substance that is a competitive antagonist of L-isoleucine.[1,3] It also inhibits the growth of T-even coliphage.[1] The gross structure was established by deg-



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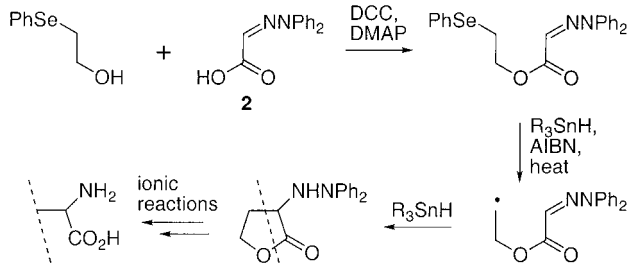
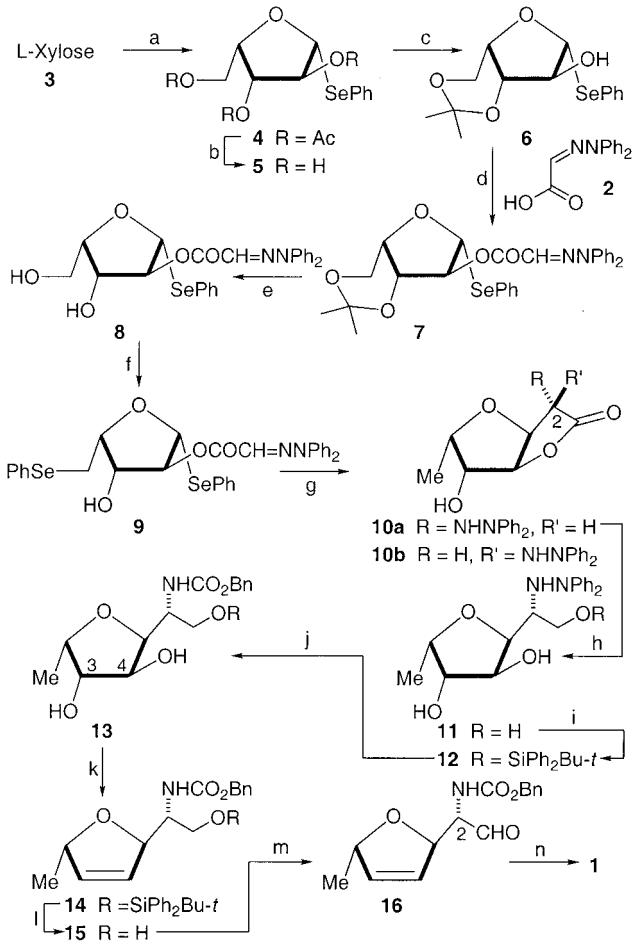
radative and spectroscopic studies,[1] but the stereochemical assignment was made on the basis of total synthesis,[4ab,5] and later corroborated by X-ray analysis of the derived *N*-acetate.[6] We report a synthesis based on radical cyclization along the lines summarized in Scheme 1,[7] using a starting material from the chiral pool.

L-Xylose (**3**) was converted into its methyl glycosides (MeOH, HCl), acetylated (Ac_2O, pyridine), subjected to acetolysis (AcOH, Ac_2O, H_2SO_4), and treated with PhSeH/$BF_3{\cdot}Et_2O$, to afford triacetate **4** (Scheme 2). These steps are best done without isolation of the intermediates, in which case the overall yield is 77%. Mild basic hydrolysis (K_2CO_3, MeOH; 99%) then liberated the three hydroxyl groups (**4** → **5**), and those at C(3) and C(5) were protected as a ketal (**5** → **6**; TsOH, acetone; 89% or 94% after correction for recovered **5**). DCC-mediated coupling with (2,2-diphenylhydrazono)acetic acid (**2**, see Scheme 1) then gave the hydrazono ester **7** in excellent yield (95%). Although the ester underwent radical cyclization (83%), it was better to delay this process, so that another radical reaction—deoxygenation at C(5)—could be accomplished at the same time as the required ring closure (see later, **9** → **10a**,**b**). To this end, selenide ester **7** was deprotected (**7** → **8**; CSA, MeOH; 96%) in order to liberate the two hydroxyls. The primary hydroxyl was selectively replaced by a PhSe group (**8** → **9**; PhSeCN, Bu_3P; 75%; 89% after

Scheme 1



Scheme 2[a]



[a] (a) MeOH, HCl, 5−10 °C; Ac_2O, pyridine; AcOH, Ac_2O, H_2SO_4; PhSeH, $BF_3{\cdot}OEt_2$, CH_2Cl_2; 77% overall from **3**. (b) K_2CO_3, MeOH; 99%. (c) TsOH, acetone; 89% or 94% after correction for recovered **5**. (d) DCC, DMAP, CH_2Cl_2; 95%. (e) CSA, MeOH; 96%. (f) PhSeCN, Bu_3P, THF; 75% or 89% after correction for recovered **8**. (g) Ph_3SnH, AIBN, PhMe; 42% for **10a**, 37% for **10b**. (h) $LiAlH_4$, THF, 0 °C. (i) *t*-$BuPh_2SiCl$, imidazole; 74% overall from **10a**. (j) CSA, 10% Pd−C, H_2 (50 psi); BnOCOCl, $NaHCO_3$; 80% from **12**. (k) Ph_3P, CHI_3, imidazole, PhMe; 64%. (l) Bu_4NF, THF; 96%. (m) Dess−Martin oxidation. (n) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene; PhSMe, CF_3CO_2H; 71% from **15**.

correction for recovered **8**), and then treatment with Ph_3SnH under conditions previously established[7] (slow addition of Ph_3SnH and AIBN, PhMe at reflux) served not only to induce radical cyclization but also to generate a methyl group at C(5). That experiment afforded a 42:37 isomer mixture of chromatographically separable hy-

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drazino lactones epimeric at C(2) (**9** → **10a**,**b**). These were readily distinguished by NOE measurements. Conversion of the hydrazino unit of the major isomer (**10a**) into an amino unit and removal of the two hydroxyls were initially problematical, but eventually the following route was developed. Reduction ($LiAlH_4$) gave a triol (**10a** → **11**), and the primary hydroxyl was selectively protected as its *tert*-butyldiphenylsilyl ether (**11** → **12**; *t*-$BuPh_2SiCl$, imidazole; 74% from **10**). Hydrogenolysis in an acidic medium (CSA, 4:1 EtOAc−MeOH, H_2, Pd−C) followed by acylation (BnOCOCl, $NaHCO_3$) then afforded benzyl carbamate **13** (80% from **12**). At that point the two remaining hydroxyls were removed by treatment with Ph_3P and CHI_3,[8] so as to generate a C(3)−C(4) double bond (**13** → **14**). This step was accompanied by extensive bis-dehydration (to the corresponding furan), but under optimum conditions, gave **14** in 64% yield. Desilylation with Bu_4NF took the route as far as alcohol **15**, which has been reported recently in another synthesis[4d] of furanomycin. The remaining steps required are oxidation of the hydroxyl and deprotection of the amino group. In our hands the hydroxyl was best oxidized by the Dess−Martin reagent (ca. 100%), since use of the Swern procedure led to significant amounts (in one experiment ca. 30%) of epimerization at C(2).[9,10] Further oxidation of the crude aldehyde **16**, using buffered $NaClO_2$,[11] generated the required acid, and treatment with CF_3CO_2H in the presence of PhSMe[12] served to deprotect the amino group and liberate furanomycin (**1**) of 98% purity (71% from **15**). A single crystallization on a small scale gave pure, crystalline **1** (52% from **15**).[13]

Experimental Section

General Procedures. Unless stated to the contrary, the general procedures used previously[14] were followed. Optical rotations were measured at room temperature. The symbols s′, d′, t′, and q′ used for ^{13}C NMR signals indicate zero, one, two, or three attached hydrogens, respectively.

Phenyl 2,3,5-Tri-*O*-acetyl-1-seleno-β-L-xylofuranoside (4). Methanolic hydrogen chloride [1.06 M, prepared by addition of AcCl (235 μL) to stirred and cooled (0 °C) dry MeOH (3.15 mL)] was added to a stirred mixture of anhydrous L-xylose (0.500 g, 3.330 mmol) and dry MeOH (10 mL). Stirring at 5−10 °C was continued overnight. Pyridine (2 mL) was then added to neutralize the acid, and the mixture was evaporated at room temperature, the pyridine being removed under high vacuum. The residue was dissolved in pyridine (4 mL), and Ac_2O (1.5 mL) was added with ice-bath cooling. The cold bath was left in place, and the solution was stirred for 24 h. Evaporation of the solvents under high vacuum gave a syrupy product which was dissolved in a mixture of AcOH (5 mL) and Ac_2O (1.25 mL). Concentrated H_2SO_4 (0.25 mL) was added at 0 °C. The solution was left overnight at room temperature and then poured onto crushed ice (7.5 g). The mixture was stirred for 1.5 h and extracted with $CHCl_3$ (3 × 25 mL). The combined extracts were washed with water (5 mL) and saturated aqueous $NaHCO_3$ (4 × 5 mL), dried (Na_2SO_4), and evaporated. The residue was kept under high vacuum for 4 h and then dissolved in dry CH_2Cl_2 (35 mL). PhSeH (600 μL, 5.649 mmol) was added, and the mixture was stirred and cooled (0 °C). $BF_3{\cdot}Et_2O$ (387 μL, 3.1446 mmol) was added dropwise over 0.5 h. Stirring was continued for 36 h at 0 °C, and then saturated aqueous $NaHCO_3$ (2 mL) was added. The organic phase was washed with water (2 × 5 mL) and brine (5 mL), dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (1.6 × 28 cm), using first 10% EtOAc−hexane (200 mL) and then 20% EtOAc−hexane, gave **4** (1.0671 g, 77%) as a colorless oil: $[\alpha]_D$ = 107.2 (*c* 1.18, $CHCl_3$); FTIR (CH_2Cl_2 cast) 1748 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 2.06 (s, 3 H), 2.07 (s, 3 H), 2.10 (s, 3 H), 4.26 (dd, *J* = 11.7, 6.9 Hz, 1 H), 4.34 (dd, *J* = 11.7, 5.1 Hz, 1 H), 4.50 (dt, *J* = 6.8, 4.9 Hz, 1 H), 5.33 (dd, *J* = 4.6, 1.5 Hz, 1 H), 5.41 (t, *J* = 1.7 Hz, 1 H), 5.55 (d, *J* = 1.8 Hz, 1 H), 7.29−7.34 (m, 3 H), 7.62−7.66 (m, 2 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 20.79 (q′), 20.87 (q′), 20.90 (q′), 62.26 (t′), 75.16 (d′), 79.74 (d′), 81.88 (d′), 86.28 (d′), 128.29 (d′), 129.47 (d′), 129.98 (s′), 134.69 (d′), 169.52 (s′), 169.68 (s′), 170.63 (s′); exact mass (electrospray) *m*/*z* calcd for $C_{17}H_{20}NaO_7Se$ (M + Na) 439.0272, found 439.0279.

Phenyl 1-Seleno-β-L-xylofuranoside (5). K_2CO_3 (345.9 mg, 2.503 mmol) was added to a stirred solution of **4** (1.0386 g, 2.503 mmol) in 1:1 THF−MeOH (20 mL), and the mixture was stirred vigorously for 20 min, filtered through a pad (2 mm × 1 cm) of flash chromatography silica gel, and evaporated. Flash chromatography of the residue over silica gel (1.6 × 28 cm), using 2% MeOH−EtOAc, gave **5** (0.7156 g, 99%) as a pale yellow oil: $[\alpha]_D$ = 189.2 (*c* 1.0, MeOH); FTIR (CH_2Cl_2 cast) 3407 cm^{-1}; ^1H NMR (CD_2Cl_2), 400 MHz) δ 2.31−2.35 (m, 2 H), 3.74 (d, *J* = 5.5 Hz, 1 H), 3.88−3.94 (m, 1 H), 3.97−4.02 (m, 1 H), 4.24−4.30 (m, 2 H), 4.39−4.41 (m, 1 H), 5.56 (d, *J* = 2.4 Hz, 1 H), 7.29−7.35 (m, 3 H), 7.60−7.66 (m, 2 H); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 61.97 (t′), 77.12 (d′), 84.32 (d′), 84.80 (d′), 90.59 (d′), 128.16 (d′), 130.01 (d′), 132.93 (s′), 134.34 (d′); exact mass *m*/*z* calcd for $C_{11}H_{14}NaO_4Se$ 312.9955, found 312.9944.

Phenyl 3,5-*O*-Isopropylidene-1-seleno-β-L-xylofuranoside (6). *p*-$MeC_6H_4SO_3H{\cdot}H_2O$ (6.0 mg, 0.03 mmol) was added to a stirred solution of **5** (506.2 mg, 1.752 mmol) in dry acetone (10 mL). Stirring was continued for 1.5 h, $NaHCO_3$ (20 mg) was added, stirring was continued for 0.5 h, and the mixture was filtered through a pad (2 mm × 1 cm) of flash chromatography silica gel. Evaporation of the filtrate and flash chromatography of the residue over silica gel (1.6 × 27 cm), using 30% EtOAc−hexane, gave **6** [510.9 mg, 89% or 94% after correction for recovered starting material (28 mg)] as a white powder: mp 130−131 °C; $[\alpha]_D$ = 178.6 (*c* 1.1, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3419 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.43 (s, 6 H), 2.26 (d, *J* = 4.1 Hz, 1 H), 4.00−4.11 (m, 3 H), 4.23 (dd, *J* = 3.0, 1.0 Hz, 1 H), 4.60 (d, *J* = 4.0 Hz, 1 H), 5.54 (s, 1 H), 7.23−7.32 (m, 3 H), 7.59−7.65 (m, 2 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 19.66 (q′), 28.42 (q′), 60.56 (t′), 74.54 (d′), 75.23 (d′), 83.11 (d′), 91.59 (d′), 97.97 (s′), 127.35 (d′), 129.41 (d′), 132.83 (s′), 133.20 (d′); exact mass (electrospray) *m*/*z* calcd for $C_{14}H_{18}NaO_4Se$ (M + Na) 353.0268, found 353.0269.

Phenyl 2-*O*-[(Diphenylhydrazono)acetyl]-3,5-*O*-isopropylidene-1-seleno-β-L-xylofuranoside (7). (2,2-Diphenylhydrazono)acetic acid (**2**[7]) (225.8 mg, 0.941 mmol) was added to a stirred mixture of **6** (258.0 mg, 0.784 mmol), DCC (213.5 mg, 1.035 mmol), and DMAP (11.5 mg, 0.094 mmol) in dry CH_2Cl_2 (15 mL). Stirring was continued for 12 h, and the mixture was then filtered. The insoluble material was washed with dry CH_2Cl_2, and the combined filtrates were evaporated. Flash chromatography of the residue over silica gel (1.6 × 26 cm), using 10% EtOAc−hexane, gave **7** (409.2 mg, 95%) as a white powder: mp 158−160 °C; $[\alpha]_D$ = 160.9 (*c* 1.17, $CHCl_3$); FTIR (CH_2Cl_2 cast) 1733, 1706 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.45 (s, 3 H),

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(13) The epimerization observed in oxidizing alcohol **15** under Swern conditions suggested that it might be possible to elaborate **10b** to the corresponding aldehyde and *then* effect epimerization; in this way, both products from the radical cyclization step would be convertible into furanomycin. In the event, however, the aldehyde from **10b** [i.e. the C(2) epimer of **16**] could not be epimerized under the conditions we examined: DBU (0.1 equiv) in CH_2Cl_2 at −78 °C; DBU (0.25 equiv) in CH_2Cl_2 at room temperature; Et_3N (excess) in CH_2Cl_2 at room temperature.

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1.47 (s, 3 H), 4.02−4.14 (m, 3 H), 4.38−4.42 (m, 1 H), 5.57 (s, 1 H), 5.65 (s, 1 H), 6.43 (s, 1 H), 7.13−7.49 (m, 13 H), 7.62−7.68 (m, 2 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 19.70 (q′), 28.39 (q′), 60.41 (t′), 72.66 (d′), 75.58 (d′), 84.30 (d′), 89.10 (d′), 98.18 (s′), 123.09 (d′), 127.51 (d′), 129.36 (d′), 130.35 (d′), 132.68 (s′), 133.64 (d′), 163.19 (s′); exact mass (electrospray) *m*/*z* calcd for $C_{28}H_{28}N_2NaO_5Se$ (M + Na) 575.1061, found 575.1067.

Phenyl 2-*O*-[(Diphenylhydrazono)acetyl]-1-seleno-*β*-L-xylofuranoside (8). Camphorsulfonic acid (158.9 mg, 0.684 mmol) was added to a stirred solution of **7** (377.0 mg, 0.684 mmol) in MeOH (225 mL). Stirring was continued for 3.5 h, $NaHCO_3$ (57.5 mg, 0.684 mmol) was added, and stirring was continued for 0.5 h. The mixture was then evaporated. Flash chromatography of the residue over silica gel (1.6 × 28 cm), using 50% EtOAc−hexane, gave **8** (336.0 mg, 96%) as a pale yellow foam: $[\alpha]_D$ = 132.7 (*c* 1.12, $CHCl_3$), FTIR (CH_2Cl_2 cast) 3427, 1706 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 2.60 (br s, 1 H), 3.92−4.06 (m, 2 H), 4.15−4.22 (m, 1 H), 4.28 (dd, *J* = 8.1, 4.3 Hz, 1 H), 4.43−4.46 (m, 1 H), 5.42 (d, *J* = 1.6 Hz, 1 H), 5.71 (d, *J* = 2.0 Hz, 1 H), 6.45 (s, 1 H), 7.15−7.51 (m, 13 H), 7.62−7.70 (m, 2 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 61.4 (t′), 76.48 (d′), 82.74 (d′), 85.08 (d′), 86.15 (d′), 123.05 (d′), 128.12 (d′), 129.55 (d′), 130.38 (d′), 130.59 (s′), 134.21 (d′), 164.04 (s′); exact mass (electrospray) *m*/*z* calcd for $C_{25}H_{24}N_2NaO_5Se$ (M + Na) 535.0748, found 535.0746.

Phenyl 5-Deoxy-2-*O*-[(Diphenylhydrazono)acetyl]-5-phenylseleno-1-seleno-*β*-L-xylofuranoside (9). Freshly prepared PhSeCN[15] (107.8 mg, 0.592 mmol) in THF (2 mL) was added over 6 h by syringe pump to a stirred solution of **8** (275.0 mg, 0.538 mmol) and Bu_3P (161 μL, 0.6458 mmol) in THF (2 mL). Stirring was continued for 1.5 h, and the mixture was then evaporated. Flash chromatography of the residue over silica gel (1.6 × 26 cm), using first 10% EtOAc−hexane (100 mL) and then 30% EtOAc−hexane, gave **9** [349.8 mg, 75% or 89% after correction for recovered starting material (44 mg)] as a pale yellow oil: $[\alpha]_D$ = 135.1 (*c* 1.04, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3419, 1705 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 2.84 (d, *J* = 6.1 Hz, 1 H), 3.23−3.35 (m, 2 H), 4.36−4.45 (m, 2 H), 5.43−5.44 (m, 1 H), 5.64 (d, *J* = 1.8 Hz, 1 H), 6.44 (s, 1 H), 7.14−7.50 (m, 16 H), 7.53−7.69 (m, 4 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 26.15 (t′), 75.08 (d′), 83.79 (d′), 84.97 (d′), 85.32 (d′), 123.01 (d′), 127.45 (d′), 128.21 (d′), 129.53 (d′), 130.42 (d′), 132.95 (d′), 134.61 (d′), 163.99 (s′); exact mass (electrospray) *m*/*z* calcd for $C_{31}H_{28}N_2NaO_4Se_2$ (M + Na) 675.0277, found 675.0264.

3,6-Anhydro-2,7-dideoxy-2-(2,2-diphenylhydrazino)-L-*glycero*-D-*ido*-heptono-1,4-lactone (10a) and 3,6-Anhydro-2,7-dideoxy-2-(2,2-diphenylhydrazino)-L-*glycero*-D-*gulo*-heptono-1,4-lactone (10b). This experiment was carried out in a 200 mL round-bottomed flask equipped with a Teflon-coated stirring bar and a reflux condenser sealed with a rubber septum. The flask was charged with **9** (858.0 mg, 1.320 mmol), and the system was flushed with argon for 5−10 min. Dry PhMe (80 mL) was injected, and the flask was placed in an oil bath preheated to 110 °C. Solutions of Ph_3SnH (2.5483 g, 7.260 mmol) in PhMe (10 mL) and of AIBN (130.0 mg, 0.792 mmol) in PhMe (10 mL) were injected simultaneously by syringe pump over 10 h. Refluxing was continued for 2 h after the addition. The mixture was cooled, and the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 × 29 cm), using first 20% EtOAc−hexane (300 mL) and then 30% EtOAc−hexane, gave two fractions which all contained a small amount of triphenyltin residues (^{1}H NMR). Each fraction was further purified by flash chromatography over silica gel (1.6 × 28 cm), using 30% EtOAc−hexane, to give **10a** (187.4 mg, 42%) and **10b** (166.1 mg, 37%), both as colorless oils.

Compound **10a**: $[\alpha]_D$ = −23.1 (*c* 1.19, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3452, 1779 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 1.23 (d, *J* = 6.4 Hz, 3 H), 1.95 (d, *J* = 6.1 Hz, 1 H), 3.76 (t, *J* = 1.0 Hz, 1 H), 4.02 (qd, *J* = 6.3, 2.8 Hz, 1 H), 4.22 (dd, *J* = 5.8, 2.8 Hz, 1 H), 4.31 (d, *J* = 2.0 Hz, 1 H), 4.86 (d, *J* = 4.9 Hz, 1 H), 5.08 (d, *J* = 4.9 Hz, 1 H), 7.05−7.18 (m, 6 H), 7.30−7.38 (m, 4 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 13.16 (q′), 62.96 (d′), 75.33 (d′), 77.21 (d′), 80.26 (d′), 88.25 (d′), 121.13 (d′), 123.70 (d′), 129.75 (d′), 147.43 (s′), 174.79 (s′); exact mass *m*/*z* calcd for $C_{19}H_{20}N_2O_4$ 340.1423, found 340.1422.

Compound **10b**: $[\alpha]_D$ = −48.7 (*c* 0.94, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3455, 1781 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.28 (d, *J* = 6.4 Hz, 3 H), 2.02 (d, *J* = 4.3 Hz, 1 H), 3.75 (d, *J* = 5.7 Hz, 1 H), 4.08−4.15 (m, 1 H), 4.20−4.24 (m, 1 H), 4.60 (dd, *J* = 5.7, 4.0 Hz, 1 H), 4.77 (d, *J* = 4.0 Hz, 1 H), 4.89 (s, 1 H), 7.00−7.05 (m, 2 H), 7.25−7.34 (m, 8 H); ^{13}C NMR.(CD_2Cl_2, 100.6 MHz) δ 13.35 (q′), 60.14 (d′), 75.64 (d′), 76.43 (d′), 77.80 (d′), 85.79 (d′), 120.93 (d′), 123.09 (d′), 129.47 (d′), 147.46 (s′), 174.95 (s′); exact mass *m*/*z* calcd for $C_{19}H_{20}N_2O_4$ 340.1423, found 340.1422.

2,5-Anhydro-1,6-dideoxy-7-*O*-[(1,1-dimethylethyl)diphenylsilyl]-6-(2,2-diphenylhydrazino)-D-*glycero*-L-*ido*-heptitol (12). A solution of **10a** (186.0 mg, 0.547 mmol) in THF (1 mL, plus 2 × 1 mL as a rinse) was added to a stirred and cooled (0 °C) suspension of $LiAlH_4$ (68.5 mg, 1.81 mmol) in THF (2 mL). Stirring was continued for 0.5 h at 0 °C and then for 1.5 h after removal of the ice bath. MeOH (0.3 mL) was added carefully to quench the reaction, followed by saturated aqueous $NaHCO_3$ (0.3 mL). The mixture was stirred for 15 min, diluted with THF (5 mL), and filtered through a pad (2 mm × 1 cm) of Celite, using THF (40 mL). Evaporation of the filtrate gave the expected triol **11**, which was used directly in the next step.

t-$BuPh_2SiCl$ (151 μL, 0.5813 mmol) was added dropwise to a stirred solution of the triol (all the material from the above experiment) and imidazole (69.6 mg, 1.02 mmol) in THF (4 mL). Stirring was continued for 6 h, and the solvent was evaporated. Flash chromatography of the residue over silica gel (1.6 × 28 cm), using 30% EtOAc−hexane, gave **12** (236.0 mg, 74%) as a colorless oil: $[\alpha]_D$ = −42.1 (*c* 1.19, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3439 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 1.01 (s, 9 H), 1.25 (d, *J* = 6.5 Hz, 3 H), 1.71 (d, *J* = 5.0 Hz, 1 H), 3.51 (td, *J* = 9.0, 2.4 Hz, 1 H), 3.58−3.65 (m, 1 H), 3.79 (d, *J* = 2.1 Hz, 1 H), 3.94 (dd, *J* = 10.1, 2.5 Hz, 1 H), 4.00−4.05 (m, 2 H), 4.27−4.38 (m, 2 H), 4.78 (s, 1 H), 6.91−7.00 (m, 6 H), 7.17−7.63 (m, 14 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 13.89 (q′), 19.17 (s′), 26.95 (q′), 59.44 (d′), 64.24 (t′), 76.65 (d′), 78.54 (d′), 78.67 (d′), 82.88 (d′), 120.63 (d′), 122.56 (d′), 128.28 (d′), 129.27 (d′), 130.41 (d′), 130.47 (d′), 132.42 (s′), 132.52 (s′), 135.85 (d′), 135.96 (d′), 148.26 (s′); exact mass (electrospray) *m*/*z* calcd for $C_{35}H_{43}N_2O_4Si$ (M + H) 583.2992, found 583.2994.

2,5-Anhydro-7-*O*-[(1,1-dimethylethyl)diphenylsilyl]-6-[[(phenylmethoxy)carbonyl]amino]-1,6-dideoxy-D-*glycero*-L-*iodo*-heptitol (13). Camphorsulfonic acid (199.0 mg, 0.858 mmol) and then 10% Pd−C (90.0 mg) were added to a solution of **12** (227.0 mg, 0.390 mmol) in a mixture of EtOAc (5.6 mL) and MeOH (1.4 mL). The mixture was shaken under H_2 (50 psi) for 2 h (Parr shaker) and then filtered through a pad of Celite. The pad was washed with EtOAc (3 × 12 mL), and the combined filtrates were evaporated. THF (7.5 mL), water (2.5 mL), and $NaHCO_3$ (170.3 mg, 2.027 mmol) were added to the resulting yellow foam. The mixture was stirred and cooled (0 °C), and BnOCOCl (84 μL, 0.5846 mmol) was added dropwise. Stirring was continued for 0.5 h at 0 °C, and then for 0.5 h after removing the cold bath. The mixture was extracted with CH_2Cl_2 (50 mL), and the organic extract was washed with brine (10 mL), dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (1.6 × 28 cm), using 40% EtOAc−hexane, gave **13** (171.5 mg, 80%) as a colorless oil: $[\alpha]_D$ = −4.8 (*c* 1.04, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3434, 1700 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.06 (s, 9 H), 1.19 (d, *J* = 6.5 Hz, 3 H), 2.05 (s, 1 H), 3.34 (s, 1 H), 3.62−3.69 (m, 1 H), 3.78 (dd, *J* = 10.2, 4.4 Hz, 1 H), 3.95−4.02 (m, 1 H), 4.03−4.12 (m, 1 H), 4.15−4.22 (m, 2 H), 4.27 (qd, *J* = 6.5, 3.5 Hz, 1 H), 5.06 (s, 2 H), 5.20 (br d, *J* = 6.3 Hz, 1 H), 7.28−7.48 (m, 11 H), 7.63−7.72 (m, 4 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 14.14 (q′), 19.40 (s′), 26.95 (q′), 52.69 (d′), 64.93 (t′), 67.11 (t′), 76.56 (d′), 78.67 (d′), 78.99 (d′), 79.26 (d′),128.21 (d′), 128.37 (d′), 128.81 (d′), 130.30 (d′), 133.09 (s′), 135.96 (d′), 137.08 (s′), 156.87 (s′); exact mass (electrospray) *m*/*z* calcd for $C_{31}H_{40}NO_6Si$ (M + H) 550.2625, found 550.2641.

2,5-Anhydro-1,3,4,6-tetradeoxy-7-*O*-[(1,1-dimethylethyl)diphenylsilyl]-6-[[(phenylmethoxy)carbonyl]amino]-D-*xylo*-hept-3-enitol (14). Ph_3P (324.9 mg, 1.239 mmol), CHI_3 (243.8 mg, 0.619 mmol), and imidazole (42.2 mg, 0.619 mmol) were added to a stirred solution of diol **13** (170.0 mg, 0.310 mmol) in dry PhMe (5 mL). The mixture was refluxed for 22 h, cooled to room temperature, and extracted with PhMe (50 mL). The

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organic extract was washed with saturated aqueous $NaHCO_3$ (10 mL), saturated aqueous $Na_2S_2O_3$ (5 mL), and brine (10 mL), dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (1.6 × 28 cm), using 10% EtOAc−hexane, gave **14** (102.2 mg, 64%) and phenylmethyl (*R*)-[[2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-(5-methylfuran-2-yl)]ethyl]carbamate (33 mg, 21%).

Compound **14**: mp 111−112 °C; $[\alpha]_D = 80.6$ (*c* 1.08, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3321, 1715, 1693 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.05 (s, 9 H), 1.21 (d, $J = 6.4$ Hz, 3 H), 3.71 (d, $J = 6.4$ Hz, 2 H), 3.85−3.95 (m, 1 H), 4.80−4.95 (m, 2 H), 5.03 (s, 2 H), 5.13−5.18 (m, 1 H), 5.72 (br d, $J = 5.3$ Hz, 1 H), 5.83−5.89 (m, 1 H), 7.26−7.46 (m, 11 H), 7.64−7.72 (m, 4 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 19.46 (s′), 21.98 (q′), 26.95 (q′), 55.81 (d′), 64.10 (t′), 66.75 (t′), 83.05 (d′), 84.26 (d′), 127.17 (d′), 128.07 (d′), 128.14 (d′), 128.27 (d′), 128.77 (d′), 130.06 (d′), 130.10 (d′), 133.53 (d′), 133.81 (s′), 135.99 (d′), 137.40 (s′), 156.62 (s′); exact mass (electrospray) *m*/*z* calcd for $C_{31}H_{38}NO_4Si$ (M + H) 516.2570, found 516.2582.

Phenylmethyl (*R*)-[[2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-(5-methylfuran-2-yl)]ethyl]carbamate: $[\alpha]_D = 15.3$ (*c* 1.05, $CHCl_3$); FTIR (CH_2Cl_2 cast) 3445, 3332, 1725 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.01 (s, 9 H), 2.25 (s, 3 H), 3.91 (d, $J = 4.7$ Hz, 2 H), 4.83−4.93 (m, 1 H), 5.10 (d, $J = 1.2$ Hz, 2 H), 5.35−5.45 (m, 1 H), 5.91−5.97 (m, 1 H), 6.13 (d, $J = 3.0$ Hz, 1 H), 7.28−7.75 (m, 15 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 13.61 (q′), 19.46 (s′), 26.88 (q′), 51.51 (d′), 65.51 (t′), 67.07 (t′), 106.45 (d′), 107.92 (d′), 128.09 (d′), 128.33 (d′), 128.38 (d′), 128.83 (d′), 129.98 (d′), 130.11 (d′), 133.50 (s′), 133.63 (s′), 135.14 (d′), 135.92 (d′), 137.22 (s′), 151.33 (s′), 151.93 (s′), 156.02 (s′); exact mass *m*/*z* calcd for $C_{31}H_{35}NO_4Si$ 513.2335, found 513.2335.

2,5-Anhydro-1,3,4,6-tetradeoxy-6-[[(phenylmethoxy)carbonyl]amino]-D-*xylo*-hept-3-enitol (15). Bu_4NF (1.0 M solution in THF, 335 μL, 0.3347 mmol) was added dropwise to a stirred solution of **14** (114.9 mg, 0.223 mmol) in THF (3.6 mL). Stirring was continued for 0.5 h, and the mixture was then evaporated. Flash chromatography of the residue over silica gel (1.6 × 28 cm), using first 40% EtOAc−hexane (100 mL) and then 60% EtOAc−hexane, gave **15** (59.4 mg, 96%) as a white solid: mp 69.5−71.5 °C; $[\alpha]_D = 196$ (*c* 1.0, $CHCl_3$) [lit.[4d] $[\alpha]^{28}_D = 195.8$ (*c* 0.99, $CHCl_3$)]; FTIR (CH_2Cl_2 cast) 3425, 3327, 1702 cm^{-1}; ^1H NMR (CD_2Cl_2, 360 MHz) δ 1.21 (d, $J = 6.3$ Hz, 3 H), 2.60−2.68 (br, 1 H), 3.64−3.88 (m, 3 H), 4.93−5.01 (m, 1 H), 5.03−5.10 (m, 3 H), 5.23 (br d, $J = 6.6$ Hz, 1 H), 5.73 (d, $J = 6.0$ Hz, 1 H), 5.86 (ddd, $J = 6.2, 2.1, 1.5$ Hz, 1 H), 7.28−7.39 (m, 5 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 21.93 (q′), 55.14 (d′), 64.99 (t′), 66.88 (t′), 83.47 (d′), 87.16 (d′), 126.94 (d′), 128.16 (d′), 128.31 (d′), 128.77 (d′), 133.43 (d′), 137.28 (s′), 157.02 (s′); exact mass *m*/*z* calcd for $C_{15}H_{19}NO_4$ 277.1314, found 277.1308.

2-Amino-3,6-anhydro-2,4,5,7-tetradeoxy-L-x*y*lo-hept-4-enonic acid (furanomycin) (1). A solution of **15** (44.0 mg, 0.159 mmol) in CH_2Cl_2 (1 mL, plus 2 × 0.5 mL as a rinse) was added dropwise to a stirred solution of Dess−Martin reagent (87.6 mg, 0.207 mmol) in CH_2Cl_2 (0.8 mL). Stirring was continued for 0.5 h, and Et_2O (5 mL) was added, followed by saturated aqueous $NaHCO_3$ (1.7 mL) containing $Na_2S_2O_3$ (409 mg). The mixture was stirred for 5 min, and Et_2O (10 mL) was added. The organic phase was washed with saturated aqueous $NaHCO_3$ (2 mL) and brine (2 mL), dried (Na_2SO_4), and evaporated. The residue (aldehyde **16**) was dissolved in *t*-BuOH (3.2 mL) and 2-methyl-2-butene (1.6 mL), and a solution of $NaClO_2$ (53.9 mg, 80%, 0.476 mmol) and NaH_2PO_4 (65.7 mg, 0.476 mmol) in water (657 μL) were added over 5 min. The pale yellow reaction mixture was stirred at room temperature for 10 h. Volatile components were evaporated under water pump vacuum, and the residue was dissolved in water (5 mL) and extracted with hexane (2 × 2 mL). The aqueous layer was acidified to pH 3 with 3% HCl and extracted with Et_2O (3 × 15 mL). The combined organic extracts were washed with brine (5 mL), dried (Na_2SO_4), and evaporated.

TFA (5 mL) followed by PhSMe[12] (136 μL, 1.155 mmol) was added to the resulting pale yellow oil (crude furanomycin benzyl ester), and stirring was continued for 12 h at room temperature. The solvents were then evaporated under oil-pump vacuum. The resulting residue was dissolved in water (10 mL) and passed through an ion-exchange column (AG 50W-X8, 1.4 × 9 cm), the column being washed slowly with water (100 mL) and then eluted with NH_4OH (0.5 N). Ninhydrin positive fractions were collected and evaporated to give **1** (17.8 mg, 71%) as a white powder of at least 98% purity (^1H NMR, 300 MHz). Recrystallization from an acetone−water mixture gave crystalline material (13 mg, 52%) (we suspect that a better yield could be obtained if the crystallization is practiced and done on a larger scale; we tried the crystallization once): mp 221−223 °C (dec) [lit.[4b] mp 222.5−224.5 (dec)]; $[\alpha]^{25}_D = 142.6$ (*c* 0.53, H_2O) [lit.[4b] $[\alpha]_D = 140$ (*c* 1, H_2O)]; the ^1H NMR spectrum (360 MHz, D_2O was identical to that reported previously.[4b]

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Supporting Information Available: Copies of NMR spectra for compounds not analyzed. This material is available free of charge via the Internet at http://pubs.acs.org.

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